The Role of Primary Care Pharmacists in the Detection of Atrial Fibrillation

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DECLARATION

I certify that this work has not been accepted in substance for any degree, and is not concurrently being submitted for any degree other than that of Doctor of Philosophy being studied at the Universities of Greenwich and Kent. I also declare that this work is the result of my own investigations except where otherwise identified by references and that I have not plagiarised the work of others.

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ABSTRACT

Atrial fibrillation (AF) affects up to 10% of ≥ 65-year-olds and contributes to one in four ischaemic strokes, costing the UK economy > £1 billion each year. Clinical pharmacists' (CPs) integration into general practitioner (GP) surgeries and care homes offers an opportunity to facilitate AF screening. This thesis aimed to explore the role of primary care CPs in AF screening excluding the community pharmacy environment.

The 'Pharmacists Detecting Atrial Fibrillation' (PDAF) study recruited 604 participants aged ≥ 65 years in GP surgeries over two influenza vaccination seasons. CP-led AF screening, using pulse palpation and single-lead electrocardiogram ($_{SL}$ECG) devices, identified 'new' AF in 1.3% of individuals who qualified for oral anticoagulant (OAC) therapy. This intervention had a 72% probability of being cost-effective, particularly with $_{SL}$ECG devices rather than pulse palpation which produced 5.2% more false positive AF diagnoses. Patients, CPs and practice staff praised the convenience of screening and emphasised the role of CPs in reassuring patients. Their vision of AF screening involved a personalised cardiovascular disease (CVD) service targeting at-risk groups. The PDAF study therefore extended into care homes. A further 53 participants were recruited, and 9.6% were found to have undiagnosed AF qualifying for OAC therapy. Screening using $_{SL}$ECG devices in this setting was 89% cost-effective but suffered from under-recruitment, low follow-up rates and poor diagnostic accuracy.

Another initiative used $_{SL}$ECG devices to deliver AF screening within a South Asian community setting. Pharmacy undergraduates of matching heritage screened 572 participants over nine days under CP supervision. Out of ≥ 65s, 1.5% had a newly detected AF and could be considered for OAC therapy. The intervention had a 95% probability of being cost-effective and was viewed as a valuable cause for local community, although its future implementation could be compromised by ineffective referrals to GP surgeries.

Semi-structured interviews with 10 GPs showed that clinicians were overall in favour of structured AF screening programmes targeting ≥ 65s or those at-risk of AF/stroke. Sustainable, widespread AF screening in GP surgeries could be achieved by obtaining further clinical evidence and additional support from the Government and utilising local champions. Pharmacist-led AF screening was viewed as an option, yet nurses or healthcare assistants were preferred due to their intrinsic clinical skillset.

This enquiry demonstrates that CPs can facilitate effective, cost-effective and well-accepted AF screening in GP surgeries, care homes and community settings. Future research should explore the feasibility of integrating such pharmacist-led AF screening programmes within CVD care packages and should investigate their impact on clinical endpoints.

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ABBREVIATIONS

$AUD	Australian dollars
$CA	Canadian dollars
$_{12}$ECG	12-lead electrocardiogram
$_{6L}$ECG	Six-lead electrocardiogram
ABC	Atrial fibrillation, blood pressure and cholesterol
AEB	Atrial ectopic beat
AF	Atrial fibrillation
AFC	Agenda for change
AFFIRM	Atrial Fibrillation Follow-up Investigation of Rhythm Management
AF-SMART	Atrial Fibrillation Screen, Management And guideline Recommended Therapy
AHRE	Atrial high rate episode
AHSN	Academic Health Science Network
AIDS	Acquired immune deficiency syndrome
ARIC	Atherosclerosis Risk in Communities
AV	Atrioventricular
AVB	Atrioventricular block
BAFTA	Birmingham Atrial Fibrillation Treatment of the Aged
BAME	Black, Asian and Minority Ethnic
BBB	Bundle branch block
BHF	British Heart Foundation
BMA	British Medical Association
BMI	Body mass index
BP	Blood pressure
bpm	Beats per minute
BSc	Bachelor of Science
CCG	Clinical commissioning group
CE	Conformitè Europëenne
CEBM	Centre for Evidence-based Medicine
CHA_2DS_2-VASc	Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, previous Stroke/TIA/thromboembolism, Vascular disease, Age 65-74 years, Sex category
CIED	Cardiac implantable electronic device
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease

COREQ	Consolidated Criteria for Reporting Qualitative
COVID-19	Corona virus disease 2019
CP	Clinical pharmacist
CPGP	Clinical Pharmacists in General Practice
CRF	Case report form
CRYSTAL AF	Cryptogenic Stroke and Underlying Atrial Fibrillation
CVD	Cardiovascular disease
DOAC	Direct-acting oral anticoagulant
DVT	Deep vein thrombosis
EARLY	Early diagnosis of Atrial fibrillation: a Randomized triaL in primarY care
ECG	Electrocardiogram
EHCH	Enhanced Health in Care Homes
EMBRACE	Event Monitor Belt for Recording Atrial fibrillation after a Cerebral ischaemic Event
EQUATOR	Enhancing the QUAlity and Transparency Of health Research
ERP	Effective refractory period
ESC	European Society of Cardiology
FDA	Food and Drug Administration
FDR	False discovery rate
FN	False negative
FP	False positive
FPR	False positive rate
FTE	Full-time equivalent
GMC	General Medical Council
GMS	General Medical Services
GP	General practitioner
GPS	General practice staff
GPwER	General practitioner with an extended role
GRASP-AF	Guidance on Risk Assessment and Stroke Prevention in the Atrial Fibrillation
HAS-BLED	Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile International Normalised Ratio, Elderly, Drugs/Alcohol concomitantly
HbA1c	Glycated haemoglobin
HCA	Healthcare assistant

HCP	Healthcare professional
HELP-AF	Home-based Education and Learning Program for Atrial Fibrillation
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
HR	Heart rate
HRA	Health Research Authority
HTN	Hypertension
IBM	International Business Machines
ICD	Implantable cardiac defibrillator
ICER	Incremental cost-effectiveness ratio
ICM	Insertable cardiac monitor
IHD	Ischaemic heart disease
INB	Incremental net benefit
INR	International Normalised Ratio
ISRCTN	International Standard Randomised Controlled Trial Number
IT	Information technology
JBI	Joanna Briggs Institute
KMD	Kardia Mobile® device
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
LVSD	Left ventricular systolic dysfunction
mBPM	Modified blood pressure monitor
MDT	Multidisciplinary team
MI	Myocardial infarction
MOCH	Medicines Optimisation in Care Homes
MOT	Ministry of Transport
MPharm	Master of Pharmacy
MRC	Medical Research Council
MSOP	Medway School of Pharmacy
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NOAC	Non-vitamin K antagonist oral anticoagulants
NPV	Negative predictive value
NT-proBNP	N-terminal prohormone of brain natriuretic peptide
OAC	Oral anticoagulant

ORBIT-AF	Outcomes Registry for Better Informed Treatment of Atrial Fibrillation
PAD	Peripheral arterial disease
PAF	Paroxysmal atrial fibrillation
PCC	Population, Concept, Context
PCN	Primary Care Network
PDAF	Pharmacists Detecting Atrial Fibrillation
PE	Pulmonary embolism
PI	Principal investigator
PIAAF	Program for the Identification of 'Actionable' Atrial Fibrillation
PICO	Population, Intervention, Control, Outcomes
PIL	Participant information leaflet
PIPS	Patient Involvement in Pharmacy Studies
Pitx2	Pituitary homeobox 2
PPG	Photoplethysmography
PPO	Professional patient organisation
PPV	Positive predictive value
PSA	Probabilistic sensitivity analysis
PSNC	Pharmaceutical Services Negotiating Committee
PT	Patient
QALY	Quality-adjusted life year
QOF	Quality and Outcomes Framework
QOL	Quality of life
RACE	RAte Control versus Electrical cardioversion for persistent atrial fibrillation
RCT	Randomised controlled trial
REC	Research ethics committee
REHEARSE-AF	Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation
SA	Sinoatrial node
SAFE	Screening for Atrial Fibrillation in the Elderly
SAFER	Screening for Atrial Fibrillation with ECG to Reduce stroke
SAFETY	The evaluation of the Screening for Atrial Fibrillation Using Economical and accurate Technology
SEARCH-AF	The Screening Education And Recognition in Community pHarmacies of Atrial Fibrillation

SEE	Systemic embolic event
$_{SL}$ECG	Single-lead electrocardiogram
SNP	Single nucleotide polymorphism
SPSS	Statistical Package for Social Sciences
SR	Sinus rhythm
STARD	Standards for Reporting of Diagnostic Accuracy Studies
SVT	Supraventricular tachycardia
T2DM	Type 2 diabetes mellitus
TDF	Theoretical Domains Framework
TIA	Transient ischaemic attack
TN	True negative
TP	True positive
UK	United Kingdom
UK NSC	United Kingdom National Screening Committee
UN	Unclassified
UPIN	Unique participant identification number
UR	Unreadable
US	United States
VEB	Ventricular ectopic beat
VKA	Vitamin K antagonist
VTE	Venous thromboembolism
WTP	Willingness to pay

PUBLICATIONS RELATED TO THIS THESIS

Veale E.L., Stewart A.J., Mathie A., Lall S.K., Rees-Roberts M., Savickas V.*, et al.* (2018) Pharmacists detecting atrial fibrillation (PDAF) in primary care during the influenza vaccination season: a multisite, cross-sectional screening protocol. *BMJ Open* **8**(3), e021121

Savickas V., Stewart A.J., Mathie A., Bhamra S.K., Corlett S.A. & Veale E.L. (2018) P4470 Atrial fibrillation screening in general practice by clinical pharmacists using pulse palpation and single-lead ECG during the influenza vaccination season: a multi-site feasibility study. *European Heart Journal* **39**(suppl_1), ehy563.P4470-ehy563.P4470

Savickas V., Stewart A.J., Short V.J., Mathie A., Bhamra S.K., Corlett S.A.*, et al.* (2019) P6145 Atrial fibrillation screening in care homes by clinical pharmacists using pulse palpation and single-lead ECG: a feasibility study. *European Heart Journal* **40**(Supplement_1)

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Savickas V., Stewart A.J., Rees-Roberts M., Short V., Bhamra S.K., Corlett S.A.*, et al.* (2020) Opportunistic screening for atrial fibrillation by clinical pharmacists in UK general practice during the influenza vaccination season: A cross-sectional feasibility study. *PLoS Medicine* **17**(7), e1003197.

PRESENTATIONS RELATED TO THIS THESIS

Oral presentations:

National survey of UK general practice pharmacy services (5-minute presentation, 12th European Public Health Conference 2019, November 2019, Marseille)

Pharmacists detecting atrial fibrillation in general practice surgeries: the PDAF study; my experience and outcomes (South East London Local Practice Forum Meeting, October 2019, Kingston-upon-Thames)

Funny heart beats and thirty life-saving seconds (10-minute presentation, U3A and University of Kent Research Showcase Event, May 2019, Canterbury)

Funny heart beats and thirty life-saving seconds (30-minute presentations, Pint of Science Festival, April-May 2019, Rochester and Tonbridge)

Atrial fibrillation screening in general practice by clinical pharmacists: quantitative findings and economic analysis (20-minute presentation, April 2019, Medway Maritime Hospital, Gillingham)

Atrial fibrillation screening in care homes by clinical pharmacists (3-minute thesis competition entries, February-March 2019, Gillingham and London)

Atrial fibrillation screening in general practice by clinical pharmacists: quantitative findings (20-minute presentation, West Kent Local Practice Forum Meeting, November 2018, Maidstone)

Atrial Fibrillation screening in general practice by clinical pharmacists (3-minute thesis competition entry, June 2018, Gillingham)

Poster presentations:

Atrial fibrillation screening in care homes by clinical pharmacists using pulse palpation and single-lead ECG: a feasibility study (European Society of Cardiology Congress/World Cardiology Congress 2019, August-September 2019, Paris)

Atrial fibrillation screening in general practice by clinical pharmacists using pulse palpation and single-lead ECG during the influenza vaccination season: a multi-site feasibility study (European Society of Cardiology Congress 2018, August-September 2018, Munich).

Chapter 1: Introduction and Literature Review

1.1 Atrial fibrillation (AF) – a public health priority

1.1.1 Cardiac conduction and AF

The vital role of human heart in normal physiological processes and homeostasis was recognised as early as ancient Greece. Aristotle (384-322 BC) envisaged the heart as the central component of human physiology whereas Galen (200-130 BC) recognised its intrinsic ability to pulsate despite believing that arteries themselves were responsible for the circulation of blood (Meletis & Konstantopoulos 2010; Aird 2011). It was not until 1628 that this paradigm was challenged by Dr William Harvey who defined the mechanical function of the heart as a pump within the contemporary image of systemic and pulmonary circulation (Meletis & Konstantopoulos 2010; Aird 2011). In an average person, this tireless organ ejects approximately 14,000 litres of blood each day, facilitating an effective distribution of oxygen and nutrients throughout the human body, and helping remove the excess of carbon dioxide and other waste products (Betts *et al.* 2017).

The incredible mechanical efficiency of the heart is largely the result of orderly contraction (systole) and relaxation (diastole) of its chambers (atria and ventricles) during the cardiac cycle, which is regulated tightly by electrical activity. In a healthy heart, electrical impulses (action potentials) originate in specialised cells of the sinoatrial (SA) node, which is located in the right atrium and maintains the normal heart rhythm, also called the sinus rhythm (SR) (Betts *et al.* 2017) (**Figure 1.1A**). During the ventricular diastole, action potentials are generated as a result of depolarisation, or a change in cardiac (myocardial) cell membrane potential, which becomes less negative due to the gradual reduction in the outward potassium (K^+) current and the influx of sodium (Na^+) and calcium (Ca^{2+}) ions (Sporton & Antoniou 2012). These electrical signals then propagate across the atria, triggering their contraction through the process known as excitation-contraction coupling and producing a distinct P wave on an electrocardiogram (ECG) trace. The spread of signals is slowed down once they reach the atrioventricular (AV) node, the electrical gatekeeper between the atria and the ventricles, allowing for efficient atrial emptying to occur before ventricular contraction. This rather slow electrical journey across the AV node is denoted by the isoelectric PR interval of the ECG (Sporton & Antoniou 2012). A rapid signal propagation down the His-Purkinje system then follows, represented by a narrow QRS complex on the ECG, activating the ventricles and leading to the ventricular systole, which ejects the blood

into the arterial system (Sporton & Antoniou 2012; Betts *et al.* 2017). As the influx of Ca^{2+} decreases and the efflux of K^{+} increases, the membrane potential becomes more negative, producing a wave of repolarisation across the heart – first the atria and then the ventricles (Sporton & Antoniou 2012). The repolarisation of the atria occurs during the QRS complex and is not visible on the ECG whereas the repolarisation of the larger ventricles is observed as a T wave, which is accompanied by the ventricular diastole (Sporton & Antoniou 2012; Betts *et al.* 2017). The rate of electrical signals produced by the SA node and hence the heart rate (HR) is determined by the autonomic nervous system, with sympathetic and parasympathetic (vagal) inputs increasing and decreasing the HR accordingly. Under normal circumstances, the balance between sympathetic and parasympathetic drives maintains the resting HR between 60 and 100 bpm in an average adult, increasing up to approximately 220 bpm upon exercise (Betts *et al.* 2017).

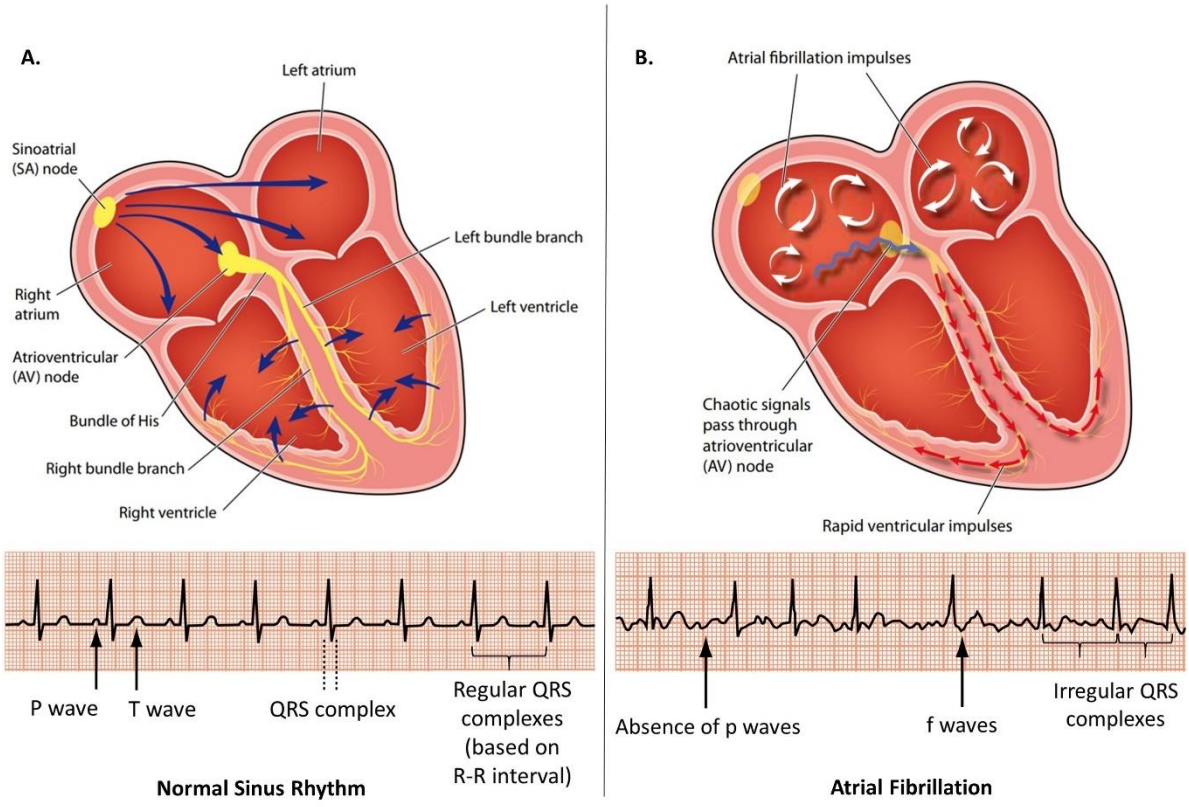


Figure 1.1 Normal cardiac electrical conduction system and atrial fibrillation (AF)

A. Normal cardiac electrical conduction, with impulses originating in the sinoatrial node, spreading across the myocardium and producing a normal sinus rhythm on an electrocardiogram (ECG). B. Impaired cardiac electrical conduction in the presence of AF, which produces distinct features on an ECG. Adapted from: Cottrell (2012a); Cottrell (2012b).

Considering its complexity, the normal cardiac conduction system may be impaired anywhere from the SA node to bundle branches of the ventricles. This may occur due to numerous factors: from electrolyte or hormonal disturbances (e.g. hypokalaemia or hyperthyroidism) to ischaemic or structural heart disease, emotional stress, age-related tissue fibrosis and medicines, such as digoxin (Bunce & Ray 2017; NIH 2020b; NIH 2020a). Some of the resulting abnormalities, such as the first-degree atrioventricular block (AVB), which causes a delay in electrical signal conduction through the AV node, are largely benign, and do not require any further intervention (Brignole *et al.* 2013; Bunce & Ray 2017). Other abnormalities, for instance the left bundle branch block (BBB), which delays the activation of the left ventricle, may be associated with clinical conditions, such as heart failure and may warrant a further treatment with cardiac resynchronisation therapy using a cardiac implantable electronic device (CIED), i.e. a pacemaker or an implantable cardiac defibrillator (ICD) (Ponikowski *et al.* 2016; Bunce & Ray 2017).

Cardiac conduction abnormalities may also produce alterations of the heart rhythm, referred to as arrhythmias, which are typically subdivided into bradycardias (resting HR < 60 bpm) and tachycardias (resting HR > 100 bpm) (Bunce & Ray 2017). Depending on the anatomical part of the heart, arrhythmias may also be classified as *'supraventricular'* (i.e. arising from the atria or AV node) and *'ventricular'* (i.e. arising from the ventricles) (Bunce & Ray 2017). A number of arrhythmias sustain the normal heart rhythm, producing either sinus bradycardia or tachycardia, which may for example occur as a consequence of the SA node malfunction in sick sinus syndromes (Bunce & Ray 2017). In other cases, the SR of the heart may be distorted by abnormal automaticity (where cells other than those in the SA node, termed *'ectopic'* or abnormal foci produce extra action potentials also referred to as *'focal activity'*), by triggered activity (where oscillations in the myocyte cell membrane potential trigger an *'afterdepolarisation'* thus increasing the likelihood of focal activity) or by re-entry (where a premature action potential propagates around the non-conducting obstacle (e.g. a scarred myocardium) as a circular or a spiral wave (rotor), re-exciting the site of its origin or the nearby cells) (Antzelevitch & Burashnikov 2011; Sporton & Antoniou 2012; Bunce & Ray 2017; Cosío 2017; Staerk *et al.* 2017).

In 1749, the French physician Dr Jean-Baptiste de Senac was perhaps the first to document a case of arrhythmia in humans (McMichael 1982). It took another 150 years for his physical observations to be confirmed by Sir Thomas Lewis who for the first time used a newly invented ECG to reveal AF, an *'extremely common'* and *'entirely disorderly'* heart rhythm (Lewis 1909). The international medical and academic consensus defines AF as:

'A supraventricular tachyarrhythmia characterised by uncoordinated atrial activation with consequent deterioration of mechanical function' (Fuster *et al.* 2006).

AF is associated with a continuous, rapid activation of the atria (≈ 300-600 impulses/minute), which is sustained by multiple rapidly depolarising ectopic foci (Fuster *et al.* 2006; Bunce & Ray 2017) (**Figure 1.1B**). This disorganised atrial activation is denoted by the absence of distinct or consistent p waves on an ECG trace. The p waves are replaced by chaotic oscillations or fibrillatory (f) waves – hence, the term *'atrial fibrillation'*. The slow electrical conduction across the AV node means that only some of the atrial signals are passed onto the ventricles, resulting in an "irregularly irregular" ventricular rate, typically between 120 and 180 bpm. The latter is observed on an ECG as rapid and irregular QRS complexes (or R-R intervals) (Fuster *et al.* 2006; Bunce & Ray 2017). Less commonly, AF may present with a normal or slow (< 60 bpm) ventricular rate (termed *'slow AF'*), owing to the AV node disease, a BBB, hypothermia or increased vagal tone (Reid *et al.* 1973; McCullough & Arora 2004; Carpenter *et al.* 2015).

Due to the impairment of cardiac mechanical function, individuals with AF may experience a wide range of symptoms, including dyspnoea, dizziness, lethargy/fatigue, syncope, chest pain/tightness and palpitations, although up to 40% of all cases may be asymptomatic (termed *'silent AF'*) (Freeman *et al.* 2015; Kirchhof *et al.* 2016; Bunce & Ray 2017). Others may experience an alternating pattern of symptomatic and asymptomatic AF episodes (Nieuwlaat *et al.* 2005; Hindricks *et al.* 2005). Based on the presentation and duration, the European Society of Cardiology (ESC), distinguishes between five different patterns of AF:

- *First diagnosed AF* – AF that has not been diagnosed before, irrespective of its duration or symptoms.
- *Paroxysmal AF (PAF)* – AF that is self-terminating, most commonly within 48 hours, however it may include any AF that self-converts or is cardioverted into normal SR within seven days. Newly diagnosed AF that lasts < 48 hours is also sometimes referred to as the *'recent-onset AF'*.
- *Persistent AF* – AF that lasts longer than 7 days.

- *Long-standing persistent AF* – AF that lasts for ≥ 1 year but is treated using a rhythm control strategy.
- *Permanent AF* – AF that has been accepted by the patient and clinician, and is not treated using a rhythm control strategy (Kirchhof *et al.* 2016).

Permanent AF occurs in approximately 40-50% of cases, with PAF and persistent/long-standing persistent AF accounting for the remaining 20-30% each (Zoni-Berisso *et al.* 2014).

By convention, a 30-second ECG trace showing AF is diagnostic, and a 12-lead ECG ($_{12L}$ECG) is typically recommended to establish the diagnosis as well as to screen the patient for any concomitant cardiovascular comorbidities (NICE 2014a; Kirchhof *et al.* 2016). A continuous 24-hour multiple-lead ambulatory ECG (Holter) monitoring may help confirm a suspected PAF (particularly if extended to 7 days) (Andrade *et al.* 2015), and is recommended by the National Institute for Health and Care Excellence (NICE) (2014a) if the condition remains undetected following a standard $_{12L}$ECG. This may for instance include patients experiencing asymptomatic PAF who are admitted to hospital with a cryptogenic stroke (stroke without an identifiable cause) (Andrade *et al.* 2015; Kirchhof *et al.* 2016). Where symptomatic episodes of PAF are more than 24 hours apart, multiple-lead external event recorder ECG of up to 30 days may be utilised instead of the Holter monitor to detect arrhythmia, and is triggered by patients upon symptoms (NICE 2014a; Andrade *et al.* 2015).

1.1.2 Epidemiology and pathophysiology

As postulated by Lewis (1909), AF is indeed the most common sustained cardiac rhythm disturbance in the world (Fuster *et al.* 2006), and has over the years emerged as a growing global epidemic (Lip *et al.* 2007; Chugh *et al.* 2014a; CDC 2012). In 2017, AF affected an estimated 37.6 million people or 0.5% of the population worldwide – a nearly 70% increase from 22.2 million in 1997 (Lippi *et al.* 2020) (**Figure 1.2**). The burden of AF varies between the developing and developed regions of the world, with greater AF incidence, prevalence, related mortality and disability amongst individuals from high-income Western European, North American and Australasian regions compared to those of low- or middle-income areas of Sub-Saharan Africa and South Asia (Chugh *et al.* 2014a; Chugh *et al.* 2014b). It is estimated that approximately 1.5 million people in England live with AF, an equivalent of 2.5% of the total population (Public Health England 2019a).

The likelihood of developing AF doubles with each advancing decade of age (Benjamin *et al.* 1994). Whilst the condition occurs in only 0.1-0.5% of those under 55 years of age (Go *et al.* 2001; Wolf *et al.* 1991), the prevalence of AF begins to rise exponentially from the age of 65 (Feinberg *et al.* 1995) to the high of 27.8% of selected Western populations at the age of ≥ 85 years (Stefansdottir *et al.* 2011). In England, AF affects 5-10% of the ≥ 65 year-olds (Sudlow *et al.* 1998b; Majeed *et al.* 2001; Public Health England 2017a). Men are subject to approximately 1.5 greater odds of developing AF compared to women (Benjamin *et al.* 1994; Chugh *et al.* 2014a), which may be attributed to their overall larger left atria – an independent predictor of AF (Vaziri *et al.* 1994; Ko *et al.* 2016).

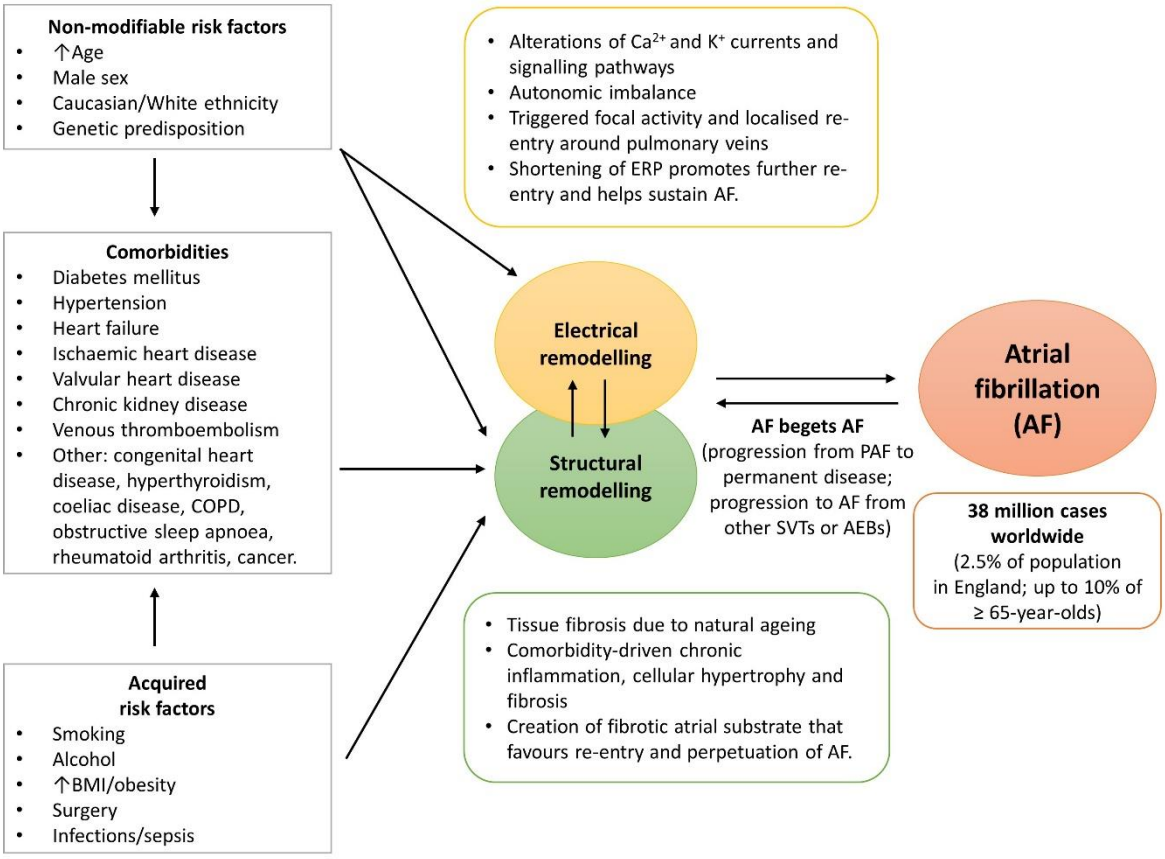


Figure 1.2 Epidemiology and pathophysiology of atrial fibrillation (AF)

Adapted from: Benjamin et al. (1994); Halligan et al. (2004); Marcus et al. (2010); Schotten et al. (2011); Chong et al. (2011); Ball et al. (2013); Chugh et al. (2014a); Kirchhof et al. (2016); Staerk et al. (2017); Public Health England (2017a). Abbreviations: AEBs – atrial ectopic beats; AF – atrial fibrillation; BMI – body mass index; COPD – chronic obstructive pulmonary disease; ERP – effective refractory period; SVTs – supraventricular tachycardias.

Owing to the longer life expectancy of women (Office for National Statistics 2018b), the average lifetime risk of developing AF is similar for individuals of both sexes, and is approximately one in four from the age of 40 years (Lloyd-Jones *et al.* 2004; Heeringa *et al.* 2006). This lifetime risk of AF however rises to one in three, in the presence of one or more risk factors, such as adverse lifestyle, obesity (body mass index (BMI) ≥ 30 kg/m^2) or cardiovascular disease (CVD) (Staerk *et al.* 2018). As such, lone or idiopathic AF is uncommon and occurs in only 3-10% of all cases, mostly amongst individuals < 60 years old (Weijs *et al.* 2012; Oldgren *et al.* 2014). Long-term alcohol consumption and smoking increases the individual's risk of AF by up to 1.3 and 2-fold, respectively (Djoussé *et al.* 2004; Chamberlain *et al.* 2011). Each additional kg/m^2 of the BMI produces a 4-5% increase in the risk of AF culminating in a 1.5-fold risk amongst obese individuals (Wang *et al.* 2004; Tedrow *et al.* 2010). Diabetes is independent predictor of AF, increasing the risk of this condition by a further 40-60% (Benjamin *et al.* 1994; Huxley *et al.* 2012). Hypertension, which is prevalent in up to 80% of all AF cases, is by far the most common risk factor (Kannel *et al.* 1998; Oldgren *et al.* 2014), giving rise to an additional 1.5-fold odds of developing the condition (Benjamin *et al.* 1994).

The presence of heart failure increases the odds of AF by 4.5- and 5.9-fold in men and women, respectively (Benjamin *et al.* 1994), affecting about a third of AF patients worldwide (Oldgren *et al.* 2014; Santhanakrishnan *et al.* 2016). The prevalence of AF is also greater in individuals with ischaemic heart disease (IHD) (Krahn *et al.* 1995; Michniewicz *et al.* 2018), although this effect appears to be only significant in men who experience a 1.4-fold risk of AF following a myocardial infarction (MI) (Benjamin *et al.* 1994), perhaps due to a generally higher prevalence of IHD in men than women (NHS Digital 2017a). Women seem to be more susceptible to valvular heart disease-induced AF (also termed *'valvular AF'*), the odds of which are 3.4 in women but only 1.8 in men (Benjamin *et al.* 1994). The risk of AF may be exacerbated by up to another 2.9-fold in the presence of chronic kidney disease (CKD) (Watanabe *et al.* 2009; Baber *et al.* 2011). Venous thromboembolism (VTE), particularly pulmonary embolism (PE), may trigger AF due to increased right atrial pressure or shared risk factors (e.g. high BMI) (Holst *et al.* 2010; Staerk *et al.* 2017), exposing patients to a 63% greater likelihood of developing AF (Hald *et al.* 2014). Emerging evidence had also proposed a link between the development of AF and acute pericarditis or congenital heart disease albeit these associations could be influenced by related confounders, such as myocardial ischaemia and surgical interventions (Chhabra *et al.* 2015; Mayosi 2015; Moe *et al.* 2017).

AF is the most common peri-operative arrhythmia occurring in 10-65% of individuals after cardiac surgery (Maisel *et al.* 2001), yet it may also occur in up to a quarter of those undergoing other major surgery (e.g. orthopaedic), thus giving rise to the term *'post-operative AF'* (Bhave *et al.* 2012; Joshi *et al.* 2015). The association between AF and non-CVD comorbidities is somewhat less established. Several observational studies had reported a potential predisposition to AF amongst individuals with chronic obstructive pulmonary disease (COPD) (Grymonprez *et al.* 2019), obstructive sleep apnoea (Gami *et al.* 2004), hyperthyroidism (Auer *et al.* 2001), coeliac disease (Emilsson *et al.* 2011), rheumatoid arthritis (Lindhardsen *et al.* 2012), multiple cancers (Jakobsen *et al.* 2019) and acute infections/sepsis (Walkey *et al.* 2014). A recent single-site study also suggested that critically-ill patients with corona virus disease 2019 (COVID-19) may display a near five-fold increase in the risk of developing AF compared to those with a mild illness (Bhatla *et al.* 2020).

Since the prevalence of most CVD and non-CVD comorbidities outlined above increases with age (Jaul & Barron 2017), the ever-growing burden of AF in ageing Western populations comes as no surprise (Chugh *et al.* 2014a). It is estimated that by 2050 one in four people in the UK will be aged ≥ 65 years (a rise from one in five in 2018) (Office for National Statistics 2019), and that at least 17% of the population in England will have ≥ 4 long-term illnesses (Kingston *et al.* 2018). It is therefore anticipated that by 2060 the prevalence of AF in England may be up to 1.8 million cases or more than double of 700,000 in 2010 (Lane *et al.* 2017). One may argue that the generally longer life expectancy leading to age-related comorbidities (World Health Organization 2016; Jaul & Barron 2017), and improved AF detection in developed countries, such as UK or United States (US) (Mairesse *et al.* 2017; Freedman *et al.* 2017), may account for their higher prevalence of AF compared to the developing countries in Africa or Asia (Chugh *et al.* 2014a; Chugh *et al.* 2014b). Nevertheless, it is also possible that these variations in AF prevalence are influenced by racial or ethnic factors, and that individuals of White European descent, who form the vast majority of developed Western populations (Office for National Statistics 2018c; United States Census Bureau 2019), have an elevated risk of AF compared to individuals from other ethnic backgrounds (Amponsah *et al.* 2013). The **A**therosclerosis **R**isk in **C**ommunities (ARIC) study in US discovered that individuals of Black African-American ethnicity experienced a 41% lower age-adjusted risk of AF compared to their White American counterparts despite the higher prevalence of conventional CVD-AF risk factors, such as smoking, hypertension or diabetes (Alonso *et al.* 2009). This tendency was confirmed by the subsequent meta-analysis and genome investigation (Marcus *et al.* 2010). Similar results were also produced by UK-based studies which suggested that individuals

of either Black African-Caribbean or South Asian origins may display a lower prevalence of AF than the White British, irrespective of their overall higher CVD risk (Gunarathne *et al.* 2008; Mathur *et al.* 2013; Conway & Lip 2003). This trend may not apply to other ethnic minority groups, for instance the Canadian East Asian population, who experience both the lower prevalence of AF and a lower or similar burden of AF risk factors compared to White Canadians (Khan *et al.* 2013). On the other side of the risk spectrum, indigenous (Aboriginal) Australians may be more likely than non-indigenous people to experience AF accompanied by CVD comorbidities before the age of 60 (Wong *et al.* 2014; Gwynn *et al.* 2020).

Ethnic variations in the risk of AF hint that hereditary or genetic factors may play a significant role in the development of this disease. Approximately 5% of all AF cases and 15% of lone AFs may be hereditary (*'familial AF'*), with a typical onset before the age of 50 years (Darbar *et al.* 2003). First-degree relatives of those with a recorded history of AF, particularly the lone type, may therefore display up to six-fold increased odds of AF compared to the general population (Gundlund *et al.* 2016; Marcus *et al.* 2008). Familial AF-focused studies suggested that this condition may be associated with a selection of rare monogenic mutations (*'monogenic AF'*), both those affecting ion channel coding genes (e.g. K^+ channels) and non-ion channel coding ones (e.g. atrial natriuretic peptide) (Mahida *et al.* 2011; Kirchhof *et al.* 2016). Nevertheless, as shown by genome wide association studies, for most individuals the susceptibility to AF is mediated by the complex interaction of multiple genes in as many 100 genetic loci (*'polygenic AF'*), which relate to cardiac development and structural integrity as well as the electrophysiological conduction and contractile pathways (Nielsen *et al.* 2018; Roselli *et al.* 2020; Kirchhof *et al.* 2016). Single nucleotide polymorphisms (SNPs) located near the pituitary homeobox 2 (Pitx2) gene on chromosome 4q25 may be of a particular significance and have been associated with up to five-fold greater risk of AF compared to non-carriers regardless of their ethnicity (Gudbjartsson *et al.* 2007; Lubitz *et al.* 2014). This effect in the carriers of certain Pitx2-related SNPs may be mediated by unusually large pulmonary veins (Kiliszek *et al.* 2011) – the historical site for the genesis of AF (Haïssaguerre *et al.* 1998).

The onset of non-valvular AF is typically attributed to a focal ectopic source of action potentials within the *'myocyte sleeves'* of pulmonary veins (Schotten *et al.* 2011; Staerk *et al.* 2017). The cells of this tissue appear to possess distinct electrical properties which may give rise to focal ectopic activity and re-entry circuits (Hocini *et al.* 2002; Perez-Lugones *et al.* 2003), likely due to alterations in Ca^{2+} signalling (El-Armouche *et al.* 2006; Patterson *et al.* 2007), as well as the functional barrier provided by slow conduction in the rest of the

pulmonary vein tissue (Arora *et al.* 2003). During the first few days of AF development, a fall in inward Ca^{2+} currents (Van Wagoner David *et al.* 1999) and several changes in K^+ currents shorten the refractory period – the time during which myocytes are unable to fire new action potentials (Workman *et al.* 2001). The result of this electrical remodelling is an increase in the likelihood of multiple re-entrant currents (rotors or independent wavelets) which propagate across the atrial tissue and sustain the progression of AF (Nattel 2002; Staerk *et al.* 2017). An imbalance between the sympathetic and vagal stimulations may also contribute to the initiation and maintenance of AF by increasing the intracellular Ca^{2+} levels and by altering the refractory period (Chen & Tan 2007; Chen *et al.* 2014).

Changes in cardiac electrical activity that may precipitate AF are likely a composite of ageing, genetics and acquired risk factors discussed above (Schotten *et al.* 2011; Staerk *et al.* 2017). Rare mutations in genes encoding K^+ channels may lead to a shortening of the refractory period amongst patients who develop familial AF (Chen *et al.* 2003). Considering the ample comorbidities which accompany AF however, structural remodelling of the atria due to external stressors, such as hypertension, IHD, heart failure or diabetes, is a more common culprit (Schotten *et al.* 2011; Staerk *et al.* 2017). This slow process is mediated by the cascade involving chronic inflammation, fibrosis and myocyte hypertrophy (Frustaci *et al.* 1997; Verheule *et al.* 2004; Nguyen *et al.* 2009; Venteclef *et al.* 2015), some of which may occur as part of the natural course of cardiac ageing, but is more often consistent with cardiac or non-cardiac comorbidities (Chimenti *et al.* 2010; Sun & Hu 2010; Schotten *et al.* 2011). The ultimate result of the ongoing structural remodelling is the generation of a non-uniform atrial substrate characterised by isolated fibrotic areas and impaired electrical connections between the myocytes which may slow the electrical conduction and/or decrease the refractory period thus favouring re-entry and the development of AF (Spach & Boineau 1997; Allessie *et al.* 2010; Guichard *et al.* 2020).

The presence of AF itself promotes a further electrical and structural remodelling of the myocardium, continuing the vicious cycle and giving rise to the phrase *'AF begets AF'* (Wijffels Maurits *et al.* 1995). It is therefore not surprising that up to 25% of patients experiencing the episodes of PAF and up to 30% of those with persistent AF overtime over time progress to a permanent disease (Kerr *et al.* 2005; Nieuwlaat *et al.* 2008). The risk of this progression increases with age, left atrial size and comorbidities, such as heart failure (Kerr *et al.* 2005; Nieuwlaat *et al.* 2008), perhaps explaining why PAF is more frequently discovered in younger and overall healthier individuals than those with persistent or permanent AF (Nieuwlaat *et al.* 2005; Nabauer *et al.* 2009). The deterioration to AF may also occur in patients with other supraventricular tachycardias (e.g. atrial flutter) (Hurwitz *et*

al. 1990; Halligan *et al.* 2004; Kirchhof *et al.* 2016) and even atrial ectopic beats (AEBs), which unless frequent, are generally benign and prevalent in up to 5% of the general population (Chong *et al.* 2011; Ofoma *et al.* 2012; Nguyen & Thomas 2010).

1.1.3 Complications and consequences

Owing to the pronounced electrical and structural remodelling, AF itself is an independent predictor of all-cause mortality, increasing the risk of death by up to 1.5-fold in males and up to two-fold in females (Benjamin E. *et al.* 1998; Stewart *et al.* 2002; Chugh *et al.* 2014a) (**Figure 1.3**). This level of AF-induced mortality may be increased up to 2.6-fold in the presence of one or more cardiovascular comorbidities (Stewart *et al.* 2002; Andersson *et al.* 2013). The shared pathophysiological pathways of AF and its comorbidities also reveal the possibility of a close bidirectional relationship whereby the comorbidities are able to trigger the development of AF and vice versa (Ball *et al.* 2013; Staerk *et al.* 2017). Changes in Ca^{2+} signalling, fibrosis, tachycardia and irregular ventricular filling observed amongst patients with AF reduce the cardiac contractile function and cardiac output (amount of blood expelled from the heart in one minute), predisposing them to the development of heart failure (Anter *et al.* 2009; Denham *et al.* 2018). As such, AF may be found in up to 60% of individuals with newly diagnosed heart failure, and a quarter of patients with AF exhibit a left ventricular systolic dysfunction (left ventricular ejection fraction (LVEF) < 50%; inability to expel the blood effectively) (Kannel *et al.* 1998; Oldgren *et al.* 2014; Ponikowski *et al.* 2016). Despite the shared risk profile (Anter *et al.* 2009), AF is an independent predictor of HF diagnosis, displaying a 2.3-fold risk of heart failure with preserved ejection fraction (LVEF ≥ 50%) and a 1.3-fold risk of heart failure with reduced ejection fraction (LVEF < 40%) (Santhanakrishnan *et al.* 2016; Ponikowski *et al.* 2016).

Apart from ventricular dysfunction, AF also produces atrial contractile dysfunction, which manifests as impaired atrial emptying, particularly from the left atrial appendage (Goldman *et al.* 1999; Schotten *et al.* 2002). Blood stasis in this “pouch” of the left atrium creates a pro-thrombotic environment that is activated further by ongoing inflammation and myocardial damage, in turn leading to endothelial dysfunction, thrombin generation and ultimately platelet aggregation (Asakura *et al.* 1992; Lim *et al.* 2013; Kamel *et al.* 2016). The common consequence of this hypercoagulable state is ischaemic stroke: either cardioembolic, which is caused directly by AF-triggered embolus from the left atrial appendage migrating to block one of the cerebral arteries (77% of strokes in patients with AF), or thrombotic, which is precipitated by AF-related atherosclerotic cardiovascular comorbidities or risk factors (Lodder *et al.* 1990; Arboix & Alió 2010; Chen-Scarabelli *et al.* 2015; Kamel *et al.* 2016). A contemporary meta-analysis showed that AF may be present

in up to 24% of individuals who experience an ischaemic stroke (Sposato *et al.* 2015), increasing their risk by up to five-fold, independently of age or comorbidities (Wolf *et al.* 1991). Some of the events reported as ischaemic strokes in the Framingham Heart Study (Lin *et al.* 1996; Wolf *et al.* 1991) may have also included transient ischaemic attacks (TIAs; cerebral ischaemic events lasting < 24 hours), up to 10% of which may be associated with AF (Scheef & Al-Khaled 2016).

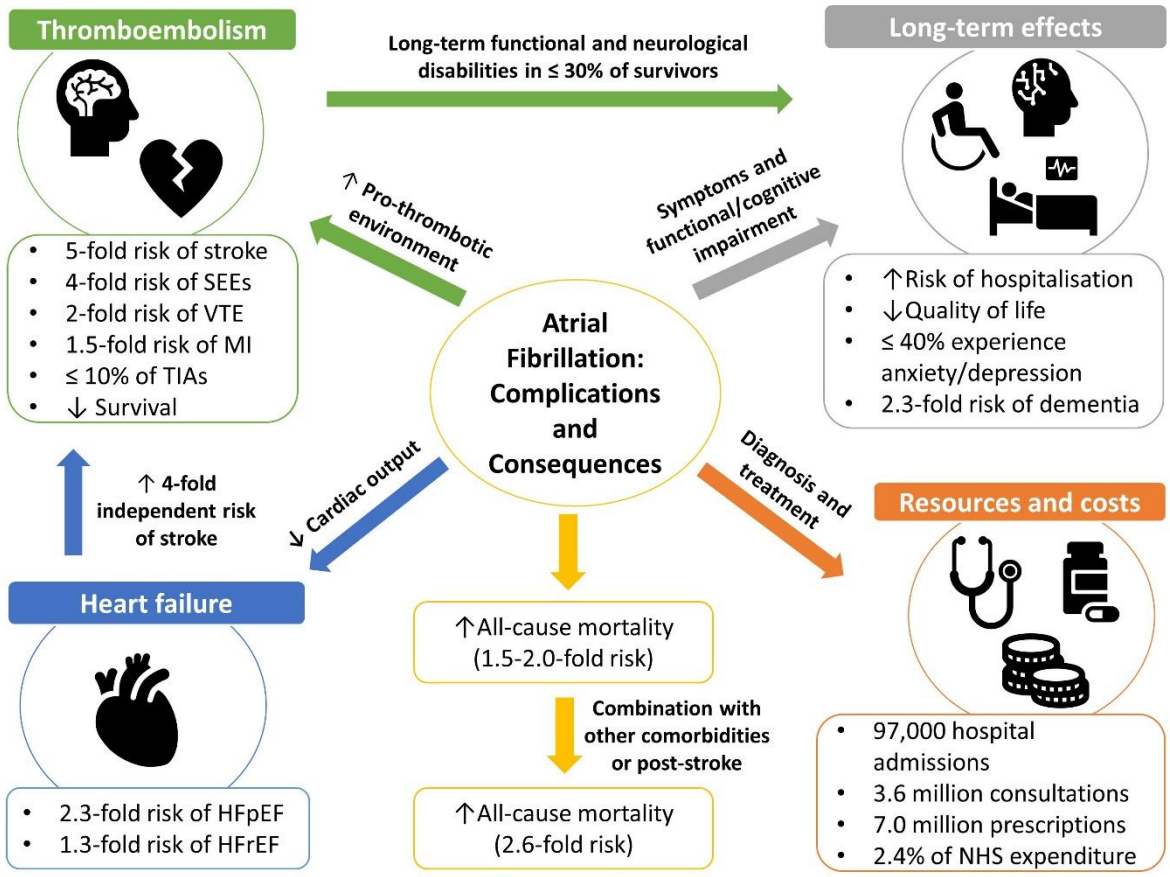


Figure 1.3 Complications and consequences of atrial fibrillation

Adapted from: Lin et al. (1996); Wolf et al. (1991); Ott et al. (1997); Benjamin E. et al. (1998); Frost et al. (2001); Stewart et al. (2002); Stewart et al. (2004); Thrall et al. (2006); Thrall et al. (2007); Thompson et al. (2014); Wang et al. (2015); Freeman et al. (2015); Santhanakrishnan et al. (2016); Scheef & Al-Khaled (2016); Kirchhof et al. (2016); Staerk et al. (2017); Ruddox et al. (2017); Polikandrioti et al. (2018). Abbreviations: HFpEF – heart failure with preserved ejection fraction; HFrEF – heart failure with reduced ejection fraction; MI – myocardial infarction; SEE - systemic embolic events; TIAs – transient ischaemic attacks; VTE – venous thromboembolism.

Recent registry data suggest that ischaemic strokes that occur in the presence of AF may account for approximately 10% of all deaths amongst AF patients (Bassand *et al.* 2016). As

much as 65% of deaths may be attributed to the aforementioned chronic heart failure, IHD, respiratory failure, malignancies and acute infections (Bassand *et al.* 2016). Despite comprising a relatively small proportion of deaths, AF strokes tend to be more severe and are associated with up to 1.8-fold increase in early mortality rate compared to non-AF strokes (Lin *et al.* 1996; Jørgensen *et al.* 1996; Sandercock *et al.* 1992). Individuals with AF strokes also display a higher likelihood of stroke recurrence and a poorer long-term survival than those with non-AF events (Lin *et al.* 1996; Marini *et al.* 2005). The severity of AF strokes has a substantial impact on individual's recovery, resulting in up to 10-day longer hospital stays, a lower discharge rate to their own homes and a 1.5-fold greater likelihood of significant neurological and functional disabilities, which may be sustained in up to three quarters of patients long-term (Lin *et al.* 1996; Jørgensen *et al.* 1996; Lamassa *et al.* 2001).

Besides cerebral embolism, AF-related thrombogenesis may produce up to a four-fold risk of extracranial systemic embolic events (SEEs), particularly in the arteries of lower extremities and the abdomen (Frost *et al.* 2001; Bekwelem *et al.* 2015). These events however carry a lower risk of all-cause death and may produce less post-event disability compared to AF strokes (Lin *et al.* 1996; Frost *et al.* 2001; Bekwelem *et al.* 2015). The bidirectional association between AF and VTE generates a further two-fold risk of deep vein thrombosis (DVT) or PE, particularly within the first six months of the AF diagnosis (Enga *et al.* 2015; Wang *et al.* 2015). AF also displays a bidirectional relationship with IHD, inflicting an up to 1.5-fold independent risk of MI, which may peak at 2.5-fold amongst Black African Americans (Soliman *et al.* 2014; Ruddox *et al.* 2017).

Several other population groups, most of which are at risk of developing AF, also experience an increased risk of AF-related thrombogenesis (Ball *et al.* 2013; Staerk *et al.* 2017). This applies to women, older individuals, and those with a history of heart failure, hypertension, previous stroke/TIA/SEE, PE or vascular disease (IHD, peripheral arterial disease (PAD) or an aortic plaque) (Olesen *et al.* 2011; Ko *et al.* 2016). Evidence supporting the link between some of these factors and the risk of AF-related thrombogenesis led to the development of numerous risk stratification schemes, most notable of which is the widely adopted **C**ongestive heart failure, **H**ypertension, **A**ge ≥ 75 years, **D**iabetes, previous **S**troke/TIA/thromboembolism, **V**ascular disease, **A**ge 65-74 years, **S**ex **c**ategory (CHA_2DS_2-VASc) score that has been validated in a variety of European and Asian cohorts (Lip *et al.* 2010; Olesen *et al.* 2011; Friberg *et al.* 2012; Okumura *et al.* 2014). Based on this score, the annual risk of strokes/TIAs/SEEs in an individual with AF may range from 0.3% (score of 0) to 17.4% (score of 9), and may allow the stratification of patients into 'low risk' (score of 0), 'intermediate risk' (score of 1) or 'high risk' (score > 1) (Olesen *et al.* 2011;

Friberg *et al.* 2012) categories, which may in turn guide the initiation of stroke prevention measures (NICE 2014a; Kirchhof *et al.* 2016).

Even short episodes of AF (≥ 5 minutes) may induce thrombogenesis (Lim *et al.* 2013; Boriani *et al.* 2013), perhaps explaining why patients with PAF still experience ischaemic strokes/SEEs, albeit possibly at a lower rate than those with persistent or permanent disease who usually display higher CHA_2DS_2-VASc scores (Chiang *et al.* 2012; Banerjee *et al.* 2013; Steinberg *et al.* 2015; Vanassche *et al.* 2015; Link *et al.* 2017). This trend also applies to all-cause mortality which seems to be lower amongst individuals with PAF compared to patients with persistent or permanent AF (Banerjee *et al.* 2013; Steinberg *et al.* 2015; Link *et al.* 2017), likely due to the generally younger age and a lower burden of comorbidities (Zoni-Berisso *et al.* 2014). An ongoing debate surrounds the risk of ischaemic stroke/SEE and mortality in patients with silent AF (Dalen & Alpert 2017). A pooled analysis by Boriani *et al.* (2013) failed to show a significant difference in the yearly incidence of stroke between those experiencing asymptomatic AF and those without AF. The **RA**te **C**ontrol versus **E**lectrical cardioversion for persistent AF (RACE) study suggested that individuals with asymptomatic AF faced only half of morbidity and mortality encountered by those with the symptomatic disease, although the risk of thromboembolic complications did not differ substantially between the two groups (Rienstra *et al.* 2014). Similarly, data from the **A**trial **F**ibrillation **F**ollow-up **I**nvestigation of **R**hythm **M**anagement (AFFIRM) study showed that asymptomatic AF may carry a comparable risk of ischaemic stroke and all-cause mortality as the symptomatic disease (Flaker *et al.* 2005) whereas the Belgrade AF Study proposed that individuals with asymptomatic AF may in fact have a greater long-term risk of AF progression and ischaemic stroke than the symptomatic population (Potpara *et al.* 2013). A subsequent UK Clinical Practice Research Datalink-based cohort study (Martinez *et al.* 2014) demonstrated that patients with incidentally-detected (asymptomatic) AF may have a significantly greater risk of stroke, MI and all-cause mortality compared to controls without AF.

Asymptomatic AF may be associated with silent cortical strokes which precede the major symptomatic event (Hara *et al.* 1995). Neurological damage sustained as a result of these covert infarctions may accompany cerebral hypoperfusion (insufficient supply of blood/oxygen to the brain) seen in patients with AF (Lavy *et al.* 1980; Gardarsdottir *et al.* 2018), giving the grounds for the well-established link between AF and a cognitive decline. A number of population-based studies and meta-analyses showed that AF was an independent predictor of both cognitive impairment (≤ 1.7-fold risk) and dementia (≤ 2.3-fold risk), irrespective of the individual's history of stroke (Ott *et al.* 1997; Kwok *et al.* 2011;

Dublin *et al.* 2011; Santangeli *et al.* 2012; Kalantarian *et al.* 2013; de Bruijn *et al.* 2015). A meta-analysis by Kwok *et al.* (2011) also showed that the presence of AF could be associated with increased progression from mild cognitive impairment to dementia.

AF-related symptoms and physical or cognitive deterioration that occurs in a course of its complications may have a significant effect on individual's activities of daily living and their quality of life (QOL). According to data from the **O**utcomes **R**egistry for **B**etter **I**nformed **T**reatment of **A**trial **F**ibrillation (ORBIT-AF), more than 16% of AF patients experience severe or disabling symptoms (Freeman *et al.* 2015). Individuals with PAF may experience a greater burden of symptoms, such as palpitations, compared to those with persistent or permanent disease (Lévy *et al.* 1999; Nieuwlaat *et al.* 2005; Freeman *et al.* 2015). Patients with AF display a level of physical/social functioning, mental and general health that is either lower or comparable to that observed in patients with IHD or heart failure, resulting in a significantly lower QOL than reported by the general population (Dorian *et al.* 2000; Thrall *et al.* 2006). Up to 40% of patients with AF may experience the symptoms of anxiety or depression, both of which affect the individual's QOL, and may amplify AF-related symptoms (Thrall *et al.* 2007; Thompson *et al.* 2014; Polikandrioti *et al.* 2018). The QOL experienced by AF patients appears to be unaffected by the pattern of the disease, although those with permanent AF may exhibit a greater psychosocial function (Peinado *et al.* 2010) whereas women, those with newly diagnosed AF and patients with comorbidities, such as COPD or symptomatic heart failure, may report an overall lower QOL (Randolph *et al.* 2016). The increasing patient and population burden of AF may be expressed as disability-adjusted life years (the number of years lost due to ill health), which have risen worldwide by nearly 20% from 54.3/100,000 people in 1990 to 64.5 in 2010 (Chugh *et al.* 2014a).

Aside from implications for individual patients, AF-associated morbidity and mortality has a pronounced impact on healthcare resources and economy, which may be expected to rise further in the ageing population alongside the ever-increasing prevalence of AF (Wolowacz *et al.* 2011; Kim *et al.* 2011; Chugh *et al.* 2014a). In 2000, the costs of AF care and complications accounted for approximately £459 million or 0.9-2.4% of the NHS expenditure (Stewart *et al.* 2004) – an equivalent of £1.4-3.7 billion when applied to the £152.9 billion NHS expenditure in 2019 (Harker 2020). The principal contributor to this bill, accounting for £303.5 million (66% of all AF costs), were an estimated 97,000 hospital admissions (0.9% of all NHS admissions in 2000) and follow-up outpatient care, particularly relating to patients with AF-associated stroke or heart failure (NHS Digital 2001; Stewart *et al.* 2004). In turn, primary or community-based care of AF patients included an estimated 3.6 million of general practice consultations (> 1.6% of all consultations) and 7.0 million prescriptions for

medicines (1.3% of all prescriptions), totalling £155.7 million or 34% of all direct AF costs (Stewart *et al.* 2004; Hippisley-Cox & Vinogradova 2009; The NHS Information Centre 2011). A further cost of £111 million was incurred by the care of AF patients residing in UK nursing homes (Stewart *et al.* 2004) where AF prevalence might be as high as 14% or six times above the population average (Gordon *et al.* 2014; Public Health England 2019a).

1.1.4 Treatment and stroke prevention

The considerable public health burden posed by AF and related complications calls for an early diagnosis and effective treatment. Most critically ill patients who present with recent-onset acute AF and haemodynamic instability (unstable blood pressure (BP) causing inadequate blood flow) or life-threatening symptoms require urgent rhythm control using emergency electrical cardioversion (direct-current cardioversion; DCCV) in order to re-set the electrical circuitry of the heart and SR, thus relieving the symptoms (Rienstra *et al.* 2012; NICE 2014a; Kirchhof *et al.* 2016). Limited evidence also suggests that cardioversion may to an extent help reverse AF-mediated cardiomyopathy and improve the left ventricular systolic function (Peters & Kienzle 1988; Van Gelder *et al.* 1993). Patients with recent-onset AF who do not display a life-threatening haemodynamic instability may either be offered electrical or pharmacological (anti-arrhythmic-agent based) cardioversion depending on clinical circumstances and resources available (NICE 2014a; Kirchhof *et al.* 2016). Electrical cardioversion is a quicker and more effective means of restoring SR in up to 93% of patients with recent-onset AF compared to 74% achievement following acute pharmacological cardioversion, although AF re-occurs in at least 30% of cases following either of the two strategies (Cristoni *et al.* 2011; Bellone *et al.* 2012; Gitt *et al.* 2013; Crijns *et al.* 2014). A number of anti-arrhythmic medicines are available to facilitate pharmacological cardioversion, typically blocking the Na^+, K^+ or Ca^{2+} currents of the myocardium (e.g. flecainide or amiodarone) and/or affecting the autonomic tone (beta-blockers, e.g. sotalol). Adequate rate control (i.e. slowing the resting HR to 60-100 bpm without restoring SR) is possibly as important as rhythm control and may help to further minimise the symptoms as well as reduce the development of tachycardia-mediated cardiomyopathy (Grogan *et al.* 1992; Lazzari & Gonzalez 1997; Camm *et al.* 2007; Kotecha *et al.* 2017). In the UK, rate control alone is indicated for patients without haemodynamic instability/severe symptoms who present with acute AF of > 48 hours duration or where the duration of the arrhythmia is uncertain (NICE 2014a). Beta-blockers (e.g. metoprolol), rate-limiting calcium channel blockers (e.g. diltiazem) or digoxin are generally used for rate control in preference to other anti-arrhythmic medicines due to their more favourable adverse effect profiles (NICE 2014a; Kirchhof *et al.* 2016).

Following the acute period, patients are considered for either long-term rate or rhythm control (NICE 2014a; Kirchhof *et al.* 2016). Neither of the two strategies had to date shown an appreciable effect on long-term clinical endpoints, such as survival (Van Gelder *et al.* 2006; Friberg *et al.* 2009; Kirchhof *et al.* 2016), however either of them may improve the QOL, possibly owing to the lower symptom burden (Grönefeld *et al.* 2003; Hagens *et al.* 2004a). The rate control strategy is associated with a lower rate of hospitalisations and is overall more cost-effective than rhythm control due to the lesser need for hospital-based care (e.g. DCCV) (Hagens *et al.* 2004b; Marshall *et al.* 2004; Chatterjee *et al.* 2013). Current NICE guidelines recommend long-term rate control as the first-line option for most patients with AF unless they have a recent-onset condition, their AF is induced by a reversible cause or heart failure or they are experiencing atrial flutter and are eligible for ablation (scarring or destroying the tissue causing the arrhythmia) (NICE 2014a). Rhythm control may also have a role in individuals with persistent or long-standing persistent AF who remain symptomatic after an optimised rate control therapy or whose rate cannot be successfully controlled (NICE 2014a; Kirchhof *et al.* 2016). In the UK, elective DCCV is preferred to long-term pharmacological rhythm control, but may in some instances be accompanied by anti-arrhythmic therapy, which may facilitate the success of cardioversion and may help reduce the recurrence of AF (Singh *et al.* 2009; Kirchhof *et al.* 2012; NICE 2014a). Where anti-arrhythmic therapy fails to maintain SR or is unsuitable, patients with PAF or (long-standing) persistent AF may be offered left atrial catheter ablation, usually by isolating the pulmonary veins responsible for the generation of the arrhythmia (NICE 2014a; Kirchhof *et al.* 2016). In such patients, catheter ablation with or without anti-arrhythmic therapy is associated with a significantly lower rate of AF recurrence compared to anti-arrhythmic therapy alone and produces a similar rate of complications (Calkins *et al.* 2009; Wilber *et al.* 2010; Mont *et al.* 2014). The last resort for rhythm control includes more invasive surgical procedures (i.e. a surgical ablation) with or without other rhythm control interventions, which approximately doubles the chances of freedom from AF yet at an increased risk of peri-operative infections or the need for pacemaker insertion (Huffman *et al.* 2016; Kirchhof *et al.* 2016; McClure *et al.* 2018).

Where the patient is selected for long-term rate control strategy, this may be achieved using a monotherapy or a combination treatment from the selection of beta-blockers, rate-limiting calcium channel blockers and digoxin. In cases where adequate long-term rate control or rhythm control interventions described above fail to control patient's symptoms, they may be offered a *'pace and ablate strategy'* which involves an implantation of a permanent pacemaker and an ablation of the AV node, electrically isolating ventricles from the fibrillating atria (NICE 2014a; Kirchhof *et al.* 2016). This low-risk procedure is typically

undertaken for individuals with permanent AF and may help alleviate their symptoms, whereas patients with a left ventricular systolic dysfunction may experience a small improvement of the LVEF (Lim *et al.* 2007; Chatterjee *et al.* 2012). Long-term outcomes, such as the reduction in AF frequency, duration, symptoms and recurrence, may also be improved by the optimal management of AF risk factors and comorbidities, such as obesity, hypertension, diabetes and dyslipidaemia (Pathak *et al.* 2014; Kirchhof *et al.* 2016).

Apart from the inherently pro-thrombotic state of AF itself, the risk of ischaemic stroke/TIA/SEEs is increased by several of the interventions offered to individuals with AF, particularly DCCV and catheter ablation (Haeusler *et al.* 2012; Airaksinen *et al.* 2013). It is therefore of a paramount importance to offer all at-risk individuals with AF an appropriate and timely stroke prevention, commonly using an oral anticoagulant (OAC) therapy, which reduces the formation of thrombi and hence the risk of thromboembolic events (NICE 2014a; Kirchhof *et al.* 2016). The CHA_2DS_2-VASc score guides the initial decision to initiate OAC therapy, which should generally be offered to any patients with AF regardless of its pattern or symptoms, if the score is ≥ 2 (NICE 2014a; Kirchhof *et al.* 2016). Anticoagulation may also be beneficial and should be considered for men with a score of ≥ 1 (female sex alone is not considered to carry a sufficiently high risk of stroke in the absence of other factors) (Mikkelsen *et al.* 2012; NICE 2014a; Kirchhof *et al.* 2016). Prior to initiating the treatment, clinicians should have an informed consultation with the patient, weighing up the risks of OAC-related bleeding against the benefits of stroke prevention (NICE 2014a; Kirchhof *et al.* 2016). Several bleeding risk stratification schemes are available to facilitate this consultation, with the validated **H**ypertension, **A**bnormal Renal/Liver Function, **S**troke, **B**leeding History or Predisposition, **L**abile International Normalised Ratio (INR), **E**lderly, **D**rugs/Alcohol concomitantly (HAS-BLED) score perhaps the most widely used (Pisters *et al.* 2010; Lip *et al.* 2011; Friberg *et al.* 2012). Based on this score, the annual risk of OAC-related major bleeding (either fatal or clinically overt haemorrhage) may vary from 0.9% (score of 0) to 9.1% (score of ≥ 5) (Pisters *et al.* 2010). A number of risk factors included in this score, such as age or hypertension, however overlap with risk factors for stroke (Pisters *et al.* 2010; Lip *et al.* 2010). As such, a high bleeding-risk score itself should not generally result in withholding the OAC therapy, and clinicians should instead focus on the management of modifiable risk factors for bleeding, for instance an excessive alcohol consumption (NICE 2014a; Kirchhof *et al.* 2016).

As shown by evidence from multiple early RCTs evaluating the effectiveness and safety of warfarin, a vitamin K antagonist (VKA) (Petersen *et al.* 1989; Connolly *et al.* 1991; Mcbride 1991; Ezekowitz *et al.* 1992; EAFT Study Group 1993), for the majority of AF patients, the

benefits of long-term stroke/TIA/SEE prevention using OAC therapy outweigh the risks of bleeding (NICE 2014a). A practice-changing meta-analysis of 29 RCTs relating to patients with AF showed that warfarin produced a 64% reduction in the risk of stroke compared to placebo and a 39% risk reduction compared to antiplatelet therapy (mostly, aspirin), which had been historically used for stroke prevention in AF. This level of risk reduction in stroke was observed without a significant increase in the risk of major extracranial bleeding and whilst delivering a 25% reduction in overall mortality (Hart *et al.* 2007). The efficacy of OAC therapy seems to be unaffected by the pattern of AF, despite the generally lower risk of ischaemic stroke/SEE in those with PAF (Steinberg *et al.* 2015; Link *et al.* 2017). Similarly, according to the cohort study by Martinez *et al.* (2014), the benefits of stroke and mortality reduction seen with warfarin in the general AF population are also likely to be transferable to the subgroup of patients with incidentally detected asymptomatic AF.

Despite being highly effective, warfarin therapy suffers from numerous drawbacks, especially the slow onset of action, multiple food/drug interactions, unpredictable pharmacokinetics and the narrow therapeutic index, thus necessitating a regular monitoring of INR (a measurement of blood clotting) to ensure it is within a desired range (usually between two and three) (Routledge & Shetty 2012; Mekaj *et al.* 2015). This means that patients taking warfarin need to adhere to certain dietary restrictions whereas the dose of warfarin may change substantially (Routledge & Shetty 2012), overall affecting patient convenience and producing a degree of non-adherence in up to 90% of individuals (Kimmel *et al.* 2007; Banerjee *et al.* 2020). The issues surrounding the use of warfarin therapy urged research and medical communities to seek alternative pharmacological options, giving rise to a heterogenous group of OACs termed *'direct-acting OACs'* (DOACs) or *'non-vitamin K antagonist OACs'* (NOACs) (Franchini *et al.* 2016). In contrast to warfarin which inhibits a vitamin K-dependent production of selected clotting factors without affecting those already in circulation, DOACs bind directly to either thrombin (activated factor II) or activated factor X, thus producing a rapid onset of action (Mekaj *et al.* 2015). A quicker offset of action makes DOACs more convenient for use in patients undergoing emergency surgery (Mekaj *et al.* 2015) whereas a smaller likelihood and/or magnitude of interactions with foods and drugs helps avoid the dietary restrictions and fluctuations in anticoagulant action seen with warfarin (Routledge & Shetty 2012; Mekaj *et al.* 2015; Oxfordshire CCG 2019).

Four DOACs are commercially available in the UK, and all have been approved for use in AF stroke prevention by NICE, provided the patient has one or more risk factors: dabigatran (factor IIa inhibitor), rivaroxaban, apixaban and edoxaban (factor Xa inhibitors) (NICE 2014a; Oxfordshire CCG 2019). The evidence from landmark phase three RCTs in patients

with AF suggested that all DOACs were at least comparable to warfarin in reducing the risk of stroke/SEE and all-cause or cardiovascular mortality, with a lower risk of major bleeding and/or haemorrhagic stroke, but at an expense of an increased incidence of gastrointestinal haemorrhage (Connolly *et al.* 2009; Granger *et al.* 2011; Patel *et al.* 2011; Giugliano *et al.* 2013). A meta-analysis of these RCTs demonstrated that the use of DOACs may in fact be associated with a 19% reduction in the risk of stroke/SEE and a 10% lower all-cause mortality compared to warfarin (Ruff *et al.* 2014). These encouraging data urged the ESC to recommend DOACs as the first-line stroke prevention for eligible patients with newly diagnosed AF, unless they had a valvular AF or contraindications for DOAC therapy in which case warfarin would be a preferred choice (Kirchhof *et al.* 2016). The OAC therapy should be initiated as soon as possible after the AF diagnosis and continued long-term. Where the patient undergoes cardioversion or ablation, OAC should be continued for at least four and eight weeks after the respective procedure (or life-long if the patient remains at a high risk of stroke) (Kirchhof *et al.* 2016).

Left atrial appendage occlusion or exclusion, either performed surgically or using a percutaneous device, is an alternative option of non-pharmacological stroke prevention in AF patients who either cannot tolerate OACs or where such a therapy is contra-indicated (e.g. those with a previous life-threatening bleed) (NICE 2014a; Kirchhof *et al.* 2016). This approach, particularly using the new percutaneous devices, may help reduce the risk of stroke/SEE and all-cause mortality to a similar extent as observed with warfarin and possibly DOACs (Holmes *et al.* 2015; Briceno D. *et al.* 2015; Osmancik *et al.* 2020). Its routine use is compromised by the lack of adequately-powered RCT evidence and adverse events or complications, such as device embolisation and ischaemic stroke itself (Reddy *et al.* 2013; Aryana *et al.* 2015; Santoro *et al.* 2016).

1.2 Screening for asymptomatic AF in primary care

1.2.1 Definitions and rationale for AF screening

The World Health Organisation (WHO) defines disease screening as:

'The presumptive identification of unrecognised disease in an apparently healthy, asymptomatic population by means of tests, examinations or other procedures that can be applied rapidly and easily to the target population.' (WHO 2020)

In order to assist clinicians and decision-makers involved in the design and implementation of widespread health screening programmes, back in 1968 the WHO proposed a set of 10

principles for early disease detection, commonly referred to as the *'Wilson and Jungner's screening criteria'*, which should be considered for the programme to be viable and effective (Wilson & Jungner 1968) (**Table 1.1**). Multiple effective and cost-effective health screening programmes built around these principles have been successfully implemented in the UK over the last few decades. These range from screening for cervical, breast and bowel cancers (Bains *et al.* 2019; Public Health England 2019b; Public Health England 2016; Morton *et al.* 2017; NHS England 2019a), to abdominal aortic aneurysm and diabetic retinopathy screening in selected population groups (Glover *et al.* 2014; Davis *et al.* 2013; Public Health England 2017b; James *et al.* 2000).

Screening for asymptomatic AF appears to meet most of the Wilson and Jungner's criteria (Wilson & Jungner 1968). As outlined above, it is a global public health problem of an increasing prevalence that is associated with devastating consequences for patients, healthcare institutions and the economy, both in the UK and elsewhere (Ball *et al.* 2013; Staerk *et al.* 2017; Public Health England 2019a; Lippi *et al.* 2020). The pathophysiology and natural history of AF have been widely studied and understood – from modifiable and non-modifiable factors which may predispose an individual to AF development and progression, to underlying structural and electrical remodelling processes (Nattel 2002; Schotten *et al.* 2011; Staerk *et al.* 2017). It has also been largely recognised that over time AF tends to progress from short, infrequent and more commonly symptomatic episodes of PAF to the less symptomatic yet more established permanent disease, which may carry a greater risk of negative health consequences, such as ischaemic stroke, and all-cause mortality (Kerr *et al.* 2005; Banerjee *et al.* 2013; Kirchhof *et al.* 2016; Link *et al.* 2017).

The relatively extensive evidence supporting various AF treatment strategies has led to the development of agreed national and international treatment policies or pathways to manage patients with different AF patterns, symptoms and comorbidities (NICE 2014a; Kirchhof *et al.* 2016; January *et al.* 2019). Effective rhythm or rate control in AF may alleviate the person's symptoms and potentially slow down the progression of their illness, overall improving the QOL (Camm *et al.* 2007; Rienstra *et al.* 2012; Grönefeld *et al.* 2003; Hagens *et al.* 2004a). In turn, the timely initiation of stroke prevention, particularly using an appropriate OAC therapy in eligible patients, may produce a substantial reduction in the long-term risk of stroke/SEE and mortality, with a relatively negligible increase in the risk of bleeding (Hart *et al.* 2007; Ruff *et al.* 2014). Importantly, these effects are maintained regardless of the AF pattern (Steinberg *et al.* 2015; Link *et al.* 2017), and also possibly in patients with asymptomatic AF (Martinez *et al.* 2014), a silent cause of almost a quarter of all ischaemic strokes and TIAs (Sposato *et al.* 2015).

Table 1.1 Wilson and Jungner's Screening Criteria and their applicability to AF screening

Adapted from: Wilson & Jungner (1968); NICE (2014a); Kirchhof et al. (2016); Taggar et al. (2016b); Public Health England (2017a); Welton et al. (2017); NHS England and BMA (2019a); NHS England and BMA (2019b); Lowres et al. (2019); Duarte et al. (2019). Abbreviations: 12LECG – 12-lead electrocardiogram; AF – atrial fibrillation; CVD – cardiovascular disease; mBPMs – modified blood pressure monitors; NNS-Rx - number needed to screen to identify one treatable 'new' AF case; OAC – oral anticoagulant; PAF – paroxysmal AF; QOF – quality and outcomes framework; QOL – quality of life; SEE – systemic embolic event; SLECG – single-lead electrocardiogram.

Wilson and Jungner's Screening Criteria	Applicability to AF Screening
1. The condition sought should be an important health problem.	• Increasing prevalence worldwide; up to 10% of ≥ 65-year-olds in England • Morbidity (stroke, heart failure, reduced QOL) and mortality leading to unnecessary human resources and costs
2. There should be an accepted treatment for patients with recognised disease.	• Rate/rhythm control may reduce symptoms, slow down/reverse the progression of disease and improve QOL • Reduction in stroke/SEE/mortality with OAC therapy outweighs the risks in most AF patients.
3. Facilities for diagnosis and treatment should be available.	• Widespread availability of 12LECG and oral pharmacological therapies • GP surgeries provide a universal access to screening; treatment encouraged by QOF scheme • Established shared care arrangements with tertiary/secondary care.
4. There should be a recognisable latent (asymptomatic) or early symptomatic stage.	Understanding of PAF as an early, symptomatic and possibly lower-risk phase of the disease.
5. There should be a suitable test or examination.	Introduction of modern SLECG devices and mBPMs that are more accurate than pulse palpation.
6. The test should be acceptable to the population.	SLECG devices and mBPMs offer rapid and non-invasive testing that is well accepted by service users.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.	• Detailed knowledge of aetiology, epidemiology and pathophysiology leading to complications • Recognised progression from PAF to permanent disease.
8. There should be an agreed policy on whom to treat as patients.	Established guidelines for diagnosis/treatment, including different disease patterns and patients with/without symptoms or comorbidities.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.	• Single time point screening identifies 'new' AF in 1.4% of ambulant ≥ 65s (NNS-Rx 83) • Opportunistic and systematic AF screening cost-effective compared to no screening.
10. Case-finding should be a continuing process and not a "once and for all" project.	NHS Long-term Plan supports effective AF detection and treatment within the CVD agenda.

The widespread availability of $_{12L}$ECG machines and oral pharmacological therapies means that the majority of AF patients may be successfully diagnosed and managed in a primary care setting (Bajorek *et al.* 2015; Taggar *et al.* 2016b). Primary care has been traditionally defined as *'integrated, accessible healthcare services by clinicians who are accountable for addressing a large majority of personal health care needs, developing a sustained partnership with patients, and practicing in the context of family and community'* (Donaldson et al. 1996). General practice forms the backbone of primary care services. General practitioner (GP) surgeries provide individuals with a universal first port of call and medical records, and deliver more than 300 million consultations per annum (NHS Digital 2009; NHS Digital 2020), thus offering an ideal setting and infrastructure to implement routine AF screening. GPs, practice-based nurses and healthcare assistants (HCAs) work increasingly more closely with other primary care healthcare professionals (HCPs), such as community pharmacists, who help share their workload within the integrated clinical services (NHS England 2016a; Department of Health and Social Care 2019), and may be in a position to facilitate AF detection and/or management. These partnerships have been brought even closer together by new Primary Care Networks (PCNs), the multidisciplinary structures introduced in the *'NHS Long-term Plan'*, which are focused heavily on CVD case-finding amongst the other Government's priorities (NHS England and BMA 2019c; The King's Fund 2019b). Collaborations between primary and secondary (hospital and community) or tertiary (highly specialised) care formed as part of Sustainability and Transformation Partnerships or Integrated Care Systems in England, provide a unique opportunity to establish combined AF detection and management pathways (The King's Fund 2017; NHS England 2020e), that may be effectively supported by cardiology and stroke specialists (Stewart *et al.* 2015; Kirchhof *et al.* 2016; Chahal *et al.* 2019; van den Dries *et al.* 2020).

The AF diagnosis and management are also encouraged by the Quality and Outcomes Framework (QOF), a system designed to financially remunerate GP surgeries for high-quality care (NHS England and BMA 2019a). As part of the QOF scheme, practices are required to report the quality-indicator data pertaining to the maintenance of the AF register, stroke risk assessment and initiation of OAC therapy (NHS England and BMA 2019a). Together with novel audit and decision-support mechanisms, such as the **G**uidance on **R**isk **A**ssessment and **S**troke **P**revention in the **A**trial **F**ibrillation (GRASP-AF) tool (Shantsila *et al.* 2015), the QOF scheme facilitated the prescribing of appropriate OAC therapy in > 85% of eligible individuals with AF across England in 2019 (NHS Digital 2019c).

Despite the significant progress in AF diagnosis and management, up to an estimated one in three (or > 400,000) patients with AF in England remain undiagnosed (Public Health

England 2017a; Public Health England 2019f). Since patient awareness of AF appears to be influenced by the presence of symptoms (Sabater-Hernandez *et al.* 2018), most of those undiagnosed are undoubtedly individuals with asymptomatic AF who could present with stroke as the first symptom (Sposato *et al.* 2015). The bulk of AF cases are accompanied by comorbidities, such as heart failure or IHD (Weijs *et al.* 2012; Oldgren *et al.* 2014), therefore the majority of those with incidentally detected AF, and certainly individuals aged ≥ 65, have a sufficiently high CHA_2DS_2-VASc score to benefit from OAC therapy (Lowres *et al.* 2014; Svennberg *et al.* 2015; Orchard *et al.* 2016; Chan & Choy 2016). A recent systematic review and meta-analysis found that single time point screening of the general ambulant population may help detect a previously undiagnosed AF in 1.4% of ≥ 65-year-olds regardless of the screening method, and that over 80% of those identified may qualify for OAC therapy (Lowres *et al.* 2019). A separate systematic review by Welton *et al.* (2017) demonstrated that, owing to the pronounced effects of stroke prevention, pro-active AF screening of ≥ 65s is also highly cost-effective compared to the *status quo* of routine practice, or no screening.

The detection of silent AF has been facilitated by the advent of modern tools, such as modified blood pressure monitors (mBPMs) or hand-held mobile single-lead ECG ($_{SL}$ECG) devices, which are discussed in more detail in the following section. These tools deliver rapid, automated AF screening in a cost-effective manner and are well-accepted by both patients and HCPs for their convenience (Orchard *et al.* 2014; Lowres *et al.* 2015; Halcox *et al.* 2017; Duarte *et al.* 2019; Lown *et al.* 2020). Perhaps due to convenience of AF screening using either simple pulse checks or modern devices, the average uptake of AF screening programmes in the general population may be at least 50% and possibly ≥ 70% (Welton *et al.* 2017), thus satisfying the 70% threshold for effective screening set by the WHO (2020).

1.2.2 AF screening tools and methods

According to Wilson & Jungner (1968), a suitable screening test for a particular disease should be '*cheap*, '*easy and quick to perform'*, *'acceptable to population'* and produce a sufficient *'yield'* of previously undiagnosed disease whilst remaining *'valid'* (i.e. accurately identifying those with and without the disease) and *'reliable'* (i.e. relatively unaffected by variations in the method or the observer/operator of the test). The validity or accuracy of the diagnostic test under evaluation (also referred to as the *'index test'*) is established in comparison with the accepted "gold" standard (also referred to as the *'reference standard'*) (Wilson & Jungner 1968; Cohen *et al.* 2016). The diagnostic accuracy is commonly expressed as *'sensitivity'* (test's ability to correctly identify the proportion of those with the

disease; 0-100%) and *'specificity'* (test's ability to correctly identify the proportion of those without the disease; 0-100%) (Cohen *et al.* 2016). Other measures of diagnostic accuracy, such as the positive predictive value (PPV; proportion of those with index test-positive diagnosis who have the disease; 0-100%), negative predictive value (NPV; proportion of those with index test-negative diagnosis who do not have the disease; 0-100%) and the overall accuracy/correct classification rate, may also be reported alongside and are described in more detail in section **2.7.2** (Baratloo *et al.* 2015; Trevethan 2017).

The systematic review by Taggar *et al.* (2016a) grouped AF screening tools or diagnostic tests into four major categories: pulse palpation, mBPMs, non-$_{12L}$ECG methods and smartphone applications. The heterogenous group of non-$_{12L}$ECG primarily included modern $_{SL}$ECG devices, although Taggar *et al.* (2016a) appraised several studies from the pre-mobile ECG era, which investigated AF detection using a varying number of limb or precordial leads (e.g. six-lead ECG ($_{6L}$ECG) using limb electrodes). Considering its role as a definitive test in the confirmation of AF diagnosis (NICE 2014a; Kirchhof *et al.* 2016), $_{12L}$ECG recording interpreted by at least one cardiologist/heart rhythm specialist is widely accepted as a reference standard for use by AF screening programmes evaluating the diagnostic accuracy of AF screening tools (Taggar *et al.* 2016a; Welton *et al.* 2017). However, the recognition that delayed $_{12L}$ECG referrals may prevent the timely diagnosis of PAF (which may last only 30 seconds) and the inception of rapid $_{SL}$ECG diagnostics, has recently encouraged several studies to utilise $_{SL}$ECG interpretation by a cardiologist as an alternative reference standard (Lowres *et al.* 2014; Orchard *et al.* 2016; Chan & Choy 2016). Similarly, a number of diagnostic accuracy studies utilised a continuous Holter monitor either as an alternative or a complementary reference standard to $_{12L}$ECG recordings (Hindricks *et al.* 2010; Quinn *et al.* 2018).

These variations in AF screening and diagnostic practice are reflected in the heterogeneity surrounding the modern definition of the screening yield, which may be used as one of the indicators of the screening effectiveness, and was originally defined by Wilson & Jungner (1968) as *'the measure of previously unrecognised disease (whether overt or latent), diagnosed as the result of screening and brought to treatment'*. A number of AF screening programmes followed this classic definition and reported the yield of 'new' AF diagnoses as % of participants whose diagnosis was confirmed by $_{12L}$ECG, including the % of those initiated on OAC therapy (Rhys *et al.* 2013; Lowres *et al.* 2014; Orchard *et al.* 2016). Other studies reported the yield of screening as the % yearly incidence of 'new', $_{12L}$ECG-confirmed AF (Hobbs *et al.* 2005; Fitzmaurice *et al.* 2007) or as the % of individuals with a 'new' diagnosis confirmed by non-$_{12L}$ECG methods, such as $_{SL}$ECG devices, also referred to as

the prevalence of previously undiagnosed or 'unknown' AF (Morgan & Mant 2002; Svennberg *et al.* 2015; Kaasenbrood *et al.* 2016; Halcox *et al.* 2017). Fewer screening programmes reported the yield or prevalence of 'actionable AF', defined as either a newly diagnosed AF or a previously diagnosed AF in individuals who are not prescribed the OAC therapy despite their eligibility (Sandhu *et al.* 2016; Quinn *et al.* 2018). Studies involving continuous or prolonged AF detection strategies (e.g. Holter monitoring) typically report the incremental yield over a period of time (%), which by some sources is also quoted as the cumulative AF detection rate or cumulative incidence (Gladstone *et al.* 2014; Sanna *et al.* 2014). Regardless of the definition, the selection of screening tests or tools does not generally appear to influence the yield of 'new' AF cases, which is instead more heavily influenced by the duration and intensity of the programme as well as the population screened (Lowres *et al.* 2019; Mairesse *et al.* 2017). The choice of the AF screening test is therefore largely driven by user convenience, the cost and differences in diagnostic accuracy rather than the output of 'new' AF cases.

Historically, AF case-finding had been undertaken using pulse palpation (often referred to as 'pulse checks') (NICE 2014a) (**Figure 1.4**). This is commonly performed by placing a few fingers over one of the arteries of the wrist for 20-60 seconds in order to feel the regularity of the pulse and to estimate the HR (Hill & Smith 1990; Yang & Chung 2018). Although not currently a part of a formal AF screening programme, this simple, quick and generally painless test has been successfully integrated into primary care NHS Health Checks and routine BP monitoring, referring those with irregular pulse to their GP for further investigation (Public Health England 2019d; NICE 2019a). Pulse palpation is also promoted as a method for AF self-detection amongst the general public by professional patient organisations (PPOs), such as the AF Association (AF Association 2020). In turn, most early studies evaluating the effectiveness of AF screening strategies utilised pulse palpation as the primary index test for AF detection amongst the ≥ 65s in general practice. Depending on the methodology and duration of the test, the diagnostic accuracy of pulse palpation in these studies varied considerably, with a sensitivity of 54-100% and a specificity of 71-98% (Sudlow *et al.* 1998a; Somerville *et al.* 2000; Morgan & Mant 2002; Hobbs *et al.* 2005). The UK-based RCT by Morgan & Mant (2002) found that the sensitivity of pulse palpation was the greatest when the nurse performing the check used *'any irregularity'* as the criteria for AF (91%), however declined to 72% and 54% where the screening criteria was *'frequent or continuous irregularity'* and *'continuous irregularity'*, respectively. The specificity of the test displayed an inverse relationship with the screening criteria, increasing from 74% with *'any irregularity'* to 94% and 98% with *'frequent or continuous irregularity'* and *'continuous irregularity'*, respectively (Morgan & Mant 2002).

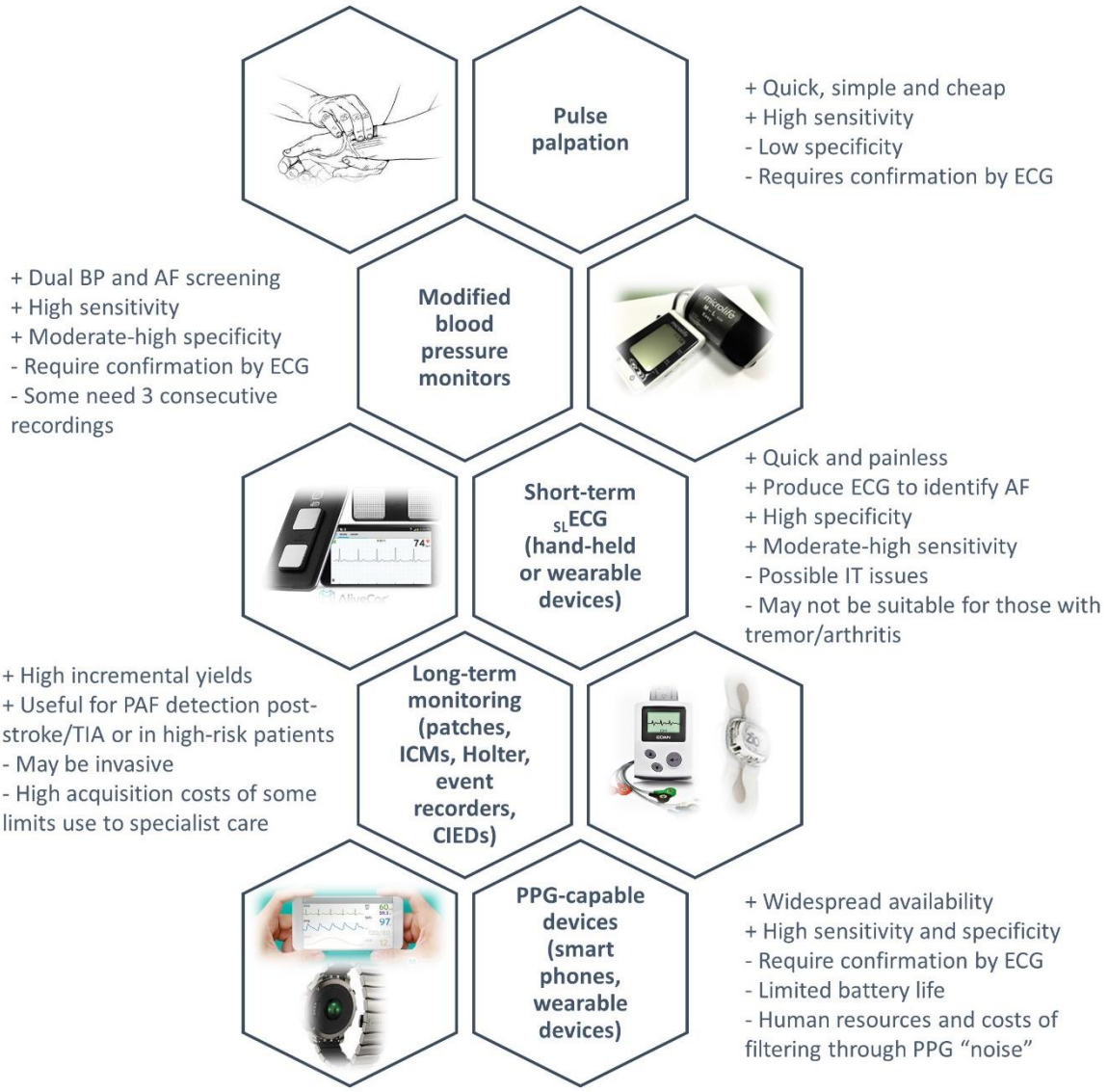


Figure 1.4 AF detection tools and methods

Adapted from: Andrade et al. (2015); Kirchhof et al. (2016); Taggar et al. (2016b); Mairesse et al. (2017); Welton et al. (2017); Orchard et al. (2019a); O'Sullivan et al. (2020); Pereira et al. (2020). All images obtained from the Microsoft online image library filtered for Creative Commons licence only. The image of pulse palpation adapted from: Hill & Smith (1990). Abbreviations: AF – atrial fibrillation; BP – blood pressure; ECG – electrocardiogram; ICM – insertable cardiac monitor; CIED - cardiac implantable electronic device; IT – information technology; PAF – paroxysmal AF; PPG – photoplethysmography; $_{SL}$ECG – single-lead ECG; TIA – transient ischaemic attack.

This variation in the sensitivity and specificity with changes in AF screening criteria may be explained by the occurrence of ectopic beats (either atrial or ventricular (VEBs)), which may

be confused with the pulse irregularity of AF (Cooke *et al.* 2006; Taggar *et al.* 2016a). The flexible criteria of *'any irregularity'* with pulse palpation captures most of those with AF, resulting in high sensitivity, yet at an expense of an excessive false positive rate of individuals with AEBs/VEBs, which produces a low specificity (Cooke *et al.* 2006).

Automated BP measurements using the mBPMs may be a viable, high-accuracy alternative to conventional AF detection by pulse palpation. An array of mBPMs possess an integrated algorithm which may detect pulse irregularities by analysing the intervals between the heart beats during the automatic deflation of the cuff (Wiesel *et al.* 2004; Stergiou *et al.* 2009). The most common and well-studied devices include those of Omron® and Microlife® brands (e.g. Omron M6® and Microlife BP A200 AFIB®), which produce either one or three sequential blood pressure measurements to detect AF (Marazzi *et al.* 2012; Kane *et al.* 2016). Whilst most mBPMs are routinely used in outpatient or primary care settings (Marazzi *et al.* 2012; Kearley *et al.* 2014; Chan *et al.* 2017b), they can also constitute an option for patients self-testing at home (Wiesel *et al.* 2013; Kollias *et al.* 2018). The systematic review by Welton *et al.* (2017) found that the use of mBPMs for AF screening in primary care was slightly more cost-effective than screening using pulse palpation. Recent systematic reviews also showed that, compared to pulse palpation, mBPMs displayed both a superior diagnostic sensitivity (92% vs. 96-98%, respectively) and specificity (79-82% vs. 92%, respectively) (Taggar *et al.* 2016a; Welton *et al.* 2017). Similar to pulse palpation, the moderate specificity of some mBPMs may be a consequence of false positive diagnoses due to ectopic beats, which may otherwise be ruled out by the interpretation of ECG (Chan *et al.* 2017b; Kollias *et al.* 2018; Lown *et al.* 2018). Indeed, any rhythm abnormalities detected by pulse palpation or mBPMs would warrant a further ECG confirmation prior to initiating the treatment (NICE 2014a; Kirchhof *et al.* 2016).

In 2004, the medical world saw an introduction of the first portable $_{SL}$ECG device (Zenicor-ECG®), which was able to record an interpretable ECG trace in 30 seconds (Zenicor Medical Systems 2020). Over the next few decades, short-term $_{SL}$ECG machines evolved as a diverse family of gadgets which today consists of standalone hand-held mobile appliances, watches and add-on features for existing devices (Ramkumar *et al.* 2018; Apple 2018; Rajakariar *et al.* 2020). Four commercially available hand-held $_{SL}$ECG devices, namely the Kardia Mobile® device (KMD), Zenicor-ECG® , MyDiagnostick® and Omron HeartScan®, have been studied the most (Bansal & Joshi 2018; Ramkumar *et al.* 2018). More recently, the family of $_{SL}$ECG devices has been expanded to include wearable tools, such as the Kardia Band®, which clips onto an Apple Watch®, or the Apple Watch® (Series 4 and above) itself (Apple 2018; Samol *et al.* 2019; Rajakariar *et al.* 2020).

$_{SL}$ECG devices are typically capable of recording and storing multiple (usually bipolar lead I) ECG traces which are then interpreted by an automated algorithm or are transmitted to a data-secure web-server and/or a mobile phone application for interpretation by a qualified individual, such as a cardiologist (Bansal & Joshi 2018; Ramkumar *et al.* 2018). The automated algorithms of $_{SL}$ECG devices are based on the detection of irregular R-R intervals and (in some cases) the absence of P waves, thus distinguishing between the $_{SL}$ECG traces corresponding to normal SR, AF, and for some devices, other rhythm abnormalities that may produce an inconclusive test result (Doliwa *et al.* 2009; Friberg *et al.* 2013; Lau *et al.* 2013; Vaes *et al.* 2014; Orchard *et al.* 2016). The ECG trace produced by a $_{SL}$ECG device also allows the interpreter to distinguish the non-AF rhythm or cardiac conduction abnormalities, such as frequent AEBs/VEBs or an AVB, which is not possible with pulse palpation or mBPMs (Svennberg *et al.* 2017; Himmelreich *et al.* 2019).

The in-built memory and mobile connectivity means that $_{SL}$ECG devices may either be operated by trained staff as part of a single-time point AF screening strategy (Kearley *et al.* 2014; Kaasenbrood *et al.* 2016), or may alternatively be given to patients to pursue repeated self-testing over a period of time at home (Svennberg *et al.* 2015; Halcox *et al.* 2017). Most $_{SL}$ECG devices, and certainly the KMD, demonstrate a high user acceptability, both amongst patients and HCPs, although less tech-savvy operators may struggle to connect these tools to their mobile phones or may experience other information technology (IT) issues (Orchard *et al.* 2014; Lowres *et al.* 2015; Halcox *et al.* 2017; Orchard *et al.* 2019a; Wessex AHSN 2019). Furthermore, the interpretation and referral of inconclusive test results generated by $_{SL}$ECG devices may be resource- and time-demanding, which may be an issue for time-pressured practice nurses or GPs (Orchard *et al.* 2014; Orchard *et al.* 2019a; Wessex AHSN 2019). The cost of human resources and devices themselves means that AF screening using $_{SL}$ECG is marginally less cost-effective than the conventional pulse palpation (Welton *et al.* 2017; Duarte *et al.* 2019), albeit still substantially below the price that NICE is typically willing to pay for a new healthcare intervention (i.e. the willingness-to-pay (WTP) threshold, usually ≈ £20,000/quality-adjusted life year (QALY) gained) (NICE 2012a). Lastly, the use of hand-held and even wearable $_{SL}$ECG devices may be limited in patients with certain comorbidities, such as arthritis or Parkinson's disease, which may prevent them from maintaining an effective contact with the device to produce a sufficiently high-quality ECG trace (Orchard *et al.* 2019a; Wessex AHSN 2019; Rajakariar *et al.* 2020). The relatively stable mBPMs may constitute an alternative to mobile $_{SL}$ECG devices in such patients (Wiesel & Salomone 2017).

The technical disadvantages and costs incurred by $_{SL}$ECG devices are offset by their superior diagnostic accuracy. According to Welton *et al.* (2017) and Taggar *et al.* (2016a), AF screening using modern $_{SL}$ECG devices in primary care might display a diagnostic sensitivity (91-96%) that falls between that of pulse palpation (92%) and mBPMs (96-98%). Their specificity (94-95%) is however greater than either of the other two methods (79-82% and 92% for pulse palpation and mBPMs, respectively), showcasing the potential to filter out additional false positive diagnoses. Recent studies of the Kardia Band® reported a sensitivity of 93-94% and a specificity of 82-84% (Bumgarner *et al.* 2018; Rajakariar *et al.* 2020), which were both under the respective 98% and 97% values seen in the validation study of the parent KMD device (Lau *et al.* 2013), possibly due to motion-related ECG noise with a wearable device. More detailed ECG data obtained with a novel $_{6L}$ECG Kardia Mobile 6L® may in the future help further refine the existing diagnostic algorithm (Stavrakis *et al.* 2017; AliveCor 2020), for instance by an easier discrimination of p waves.

The classic short-term single- or multiple-lead ECG devices, such as the KMD, provide a snapshot of the individual's heart rhythm and may overlook some of the patients experiencing asymptomatic PAF that may otherwise be detected using a continuous Holter monitor or an event recorder ECG (Andrade *et al.* 2015). In order to circumvent this problem and to minimise the use of relatively invasive multi-lead external ECG recorders, recent years have observed an introduction of several ambulatory devices capable of continuous $_{SL}$ECG monitoring (Fung *et al.* 2015; Hickey *et al.* 2018). The ZioPatch® line of devices is perhaps the most widely investigated and clinically used. Each device is a lightweight, water-proof adhesive patch which enables non-invasive $_{SL}$ECG recording (with an option to indicate the presence of symptoms by the patient) over a period of up to 14 days, and is then posted to the ECG lab for data analysis (Fung *et al.* 2015; Hickey *et al.* 2018). ZioPatches® are able to detect a suspected PAF with a greater efficiency than traditional Holter monitors, reducing the need for repeat testing and producing possible cost-savings (Barrett *et al.* 2014; NICE 2017; Kaura *et al.* 2019). The non-invasive nature and ability to detect a high incremental yield of PAF episodes beyond 48 hours may ultimately make such extended cardiac patch monitoring a preferred means of secondary AF detection post-cryptogenic stroke or TIA (Ackermans *et al.* 2012; Tung *et al.* 2014) – an area where Holter monitors or triggered ECG event recorders have traditionally been used (NICE 2014a; Kirchhof *et al.* 2016). Small subcutaneous insertable cardiac monitors (ICMs), such as Reveal LINQ® (former Reveal XT®), offer yet another alternative to external continuous ECG detection of PAF post-cryptogenic stroke (NICE 2018b). With reference to Holter monitors, this device records a relatively accurate automated or patient activated $_{SL}$ECG trace (sensitivity 96%, specificity 85%), corresponding to both symptomatic and asymptomatic

episodes of AF for up to three years (Hindricks *et al.* 2010). The Reveal LINQ® however carries a significantly greater acquisition cost than the classic Holter monitors, and similar to the ZioPatch®, in the foreseeable future is more likely to be restricted to selected patients with PAF managed by secondary or tertiary specialists (NICE 2017; NICE 2018b).

Besides the novel ECG recorders, some individuals at risk of AF (e.g. those with heart failure) may be offered CIEDs which are equipped with a lead allowing a continuous monitoring of atrial rhythm (Ponikowski *et al.* 2016; Kirchhof *et al.* 2016). The regular interrogation of these devices (check-up and retrieval of data) may therefore enable a detection of atrial high rate episodes (AHREs; > 180 bpm for > 5-6 minutes), which occur in up to 10% of patients with such devices and are associated with an elevated risk of AF, ischaemic stroke/SEE and all-cause mortality (Glotzer *et al.* 2003; Healey *et al.* 2012; Brambatti *et al.* 2014; Kirchhof *et al.* 2016). The latest ICMs or CIEDs may also possess a remote monitoring functionality facilitating the timely AF diagnosis and initiation of OAC therapy (Martin *et al.* 2015; Sanders *et al.* 2016).

Whilst the routine adoption of continuous $_{SL}$ECG monitors may remain limited to specialist recommendations, the role of relatively inexpensive and widely available personal devices, including smart watches and mobile/smart phones, in AF detection is likely to expand (Giebel & Gissel 2019). The key milestone in the evolution of such personal devices as mobile diagnostic tools for AF screening in primary care or community settings was the integration of photoplethysmography (PPG) technology (Mairesse *et al.* 2017). PPG-capable devices use a light-emitting diode to flash repeatedly onto the individual's skin in order to detect the propagation of BP pulses (i.e. blood flow) along the arterial walls, thus helping determine the HR and heart rhythm (Shelley 2007; Fantini *et al.* 2019). A number of contemporary smartphones contain an in-built ability to use their camera to generate a PPG trace that may detect pulse irregularities, such as AF (McManus *et al.* 2013). This process is facilitated by a selection of highly accurate software applications with automated diagnostic algorithms, which according to a recent meta-analysis display a pooled 94.2% sensitivity and 95.8% specificity for AF compared to $_{12L}$ECG (O'Sullivan *et al.* 2020).

As noted for short-term ECG monitors above, short, user-activated PPG recordings may overlook individuals with PAF. The development of smart wearable devices capable of recording passive intermittent or continuous PPG waveforms, such as watches or fitness trackers, may therefore be yet another major stepping-stone for the inception of affordable, population-wide AF detection (Pereira *et al.* 2020). A multitude of such devices had become available for AF detection in recent years (Pereira *et al.* 2020), however the Apple Watch®,

the Huawei Honor Band 4® and Huawei Watch GT® had been subject to two largest investigations to date, namely the Apple Heart Study and the Huawei Heart Study (Perez *et al.* 2019; Guo *et al.* 2019). The former involved over 400,000 participants who wore an Apple Watch® collecting passive intermittent PPG data every 2 hours for an average of 117 days. ECG-confirmed AF was detected in 0.04% of the group, with a PPV of 71% (Perez *et al.* 2019). Somewhat more promising results were obtained in the Huawei Heart Study whereby the two Huawei wearables (collecting passive PPG data every 10 minutes for ≥ 14 days) identified ECG-confirmed AF in 0.1% of > 180,000 participants, with a PPV of 92% (Guo *et al.* 2019). The level of PPV observed during these studies was somewhat similar to or higher than those of $_{SL}$ECG devices (74-83%) (Quinn *et al.* 2018; Himmelreich *et al.* 2019) and certainly above the PPV of pulse palpation (8-61%) (Sudlow *et al.* 1998a; Morgan & Mant 2002). The smaller diagnostic accuracy study in GP surgeries by Lown *et al.* (2018) found that two PPG-capable wearable devices (Polar H7® and Firstbeat Bodyguard 2®) displayed an identical diagnostic sensitivity for AF as the WatchBP® mBPM (96.3%), and a higher sensitivity than the KMD algorithm (87.8%). The wearables also showed a KMD-comparable specificity (98.2-98.5% compared to 98.8%) that was greater than the one of the WatchBP® device (93.5%) (Lown *et al.* 2018).

Despite a substantial diagnostic accuracy, most PPG-capable wearable devices remain limited by their inability to record ECG. This issue may be overcome by some newer devices, such as the Apple Watch® (Series 4 and above) or the Samsung Galaxy Watch Active 2®, which possess a dual passive PPG- active $_{SL}$ECG functionality (Samol *et al.* 2019; Apple 2018; Samsung 2020). Instant $_{SL}$ECG recordings following a rhythm irregularity detected by PPG waveforms may also resolve the possible follow-up delays which produced low yields of 'new' AF in the Apple Heart or Huawei studies (0.04-0.1%) – currently substantially below the 1.4% average yield computed for non-PPG methods by Lowres *et al.* (2019). The limited battery life of most PPG-capable devices poses yet another challenge for "true" continuous home monitoring to detect AF (Pereira *et al.* 2020). Last but not least, the ample amount of recordings and possible false positive results (only 34% of pulse irregularities detected by the Apple Watch® may actually be AF) (Perez *et al.* 2019) warrant a further development of current diagnostic algorithms and/or substantial human resources to filter through the "noise" of continuous PPG data, such as the motion artefacts (Pereira *et al.* 2020).

1.2.3 AF screening strategies

Apart from the selection of appropriate AF screening tools, the success of AF screening programmes depends on the screening strategy (Kirchhof *et al.* 2016; Freedman *et al.* 2017;

Mairesse *et al.* 2017). The National Institute for Health Research (NIHR)-commissioned systematic review distinguished between the three main strategies for the screening of asymptomatic AF:

- *Systematic population screening*, i.e. general screening of a defined population, e.g. individuals aged ≥ 65 years.
- *Systematic targeted screening*, i.e. screening of individuals at a higher risk of AF, e.g. those with risk factors such as heart failure, hypertension, IHD, diabetes, stroke or TIA.
- *Systematic opportunistic screening*, i.e. when a HCP takes an opportunity to screen an individual for AF during an unrelated consultation (Welton *et al.* 2017). Opportunistic AF screening strategy should be distinguished from *'opportunistic case-finding'* which is currently recommended by NICE (2014a) and involves a clinical assessment of symptomatic individuals using pulse palpation.

The first two strategies are commonly combined under the umbrella of *'systematic screening'* whereas the latter category may be referred to as *'opportunistic screening'* (Kirchhof *et al.* 2016; Freedman *et al.* 2017; Mairesse *et al.* 2017). During this thesis, for simplicity, systematic population screening is at times referred to as '*population-based screening'* whereas systematic targeted screening – as *'targeted screening'*. As may be seen from the description of various AF screening methods, AF detection may be implemented as a single time point (cross-sectional), intermittent (repeated) or continuous screening. The yields of newly detected AF typically increase with prolonged and/or more frequent testing as well as with the age and the burden of comorbidities within the target population (Andrade *et al.* 2015; Freedman *et al.* 2017; Mairesse *et al.* 2017). Finally, AF screening approaches may be sub-divided into primary (detecting AF before a stroke/TIA/SEE) and secondary (identifying AF after a thromboembolic event to prevent future events) (Andrade *et al.* 2015; Mairesse *et al.* 2017). Most of the clinical and scientific interest had been centred around the former approach (Freedman *et al.* 2017; Mairesse *et al.* 2017).

Four RCTs to date had evaluated primary AF detection using either opportunistic or systematic screening strategies. Three of them were conducted in the UK and recruited individuals aged ≥ 65 years attending the participating GP surgeries (Morgan & Mant 2002; Hobbs *et al.* 2005; Halcox *et al.* 2017). The study by Morgan & Mant (2002) randomised 3001 participants from four GP surgeries to undergo either systematic population (postal/telephone invitation) or opportunistic (flagged medical records during another

consultation) single time point AF screening by a trained practice nurse or GP using pulse palpation. The trial found that significantly more patients in the systematic screening arm had their pulse assessed compared to the opportunistic AF screening strategy (73% vs. 29%), leading to a slightly higher yield of new, lead II ECG-confirmed AF (0.8% vs. 0.5%) (Morgan & Mant 2002). The **S**creening for **AF** in the **E**lderly (SAFE) RCT randomised 50 GP surgeries (with > 14,000 participants) to either the control (routine care) or intervention (AF screening) arms (Hobbs *et al.* 2005; Fitzmaurice *et al.* 2007). Individuals in the intervention arm underwent either systematic screening (postal invitation to nurse-led pulse palpation and $_{12L}$ECG clinics) or opportunistic screening (flagged medical records for practice staff-led pulse palpation followed by nurse-led $_{12L}$ECG clinic if irregular). Those in the systematic screening arm with pre-existing risk factors for AF/stroke (e.g. IHD) were also distinguished from the rest of the group in order to compare the systematic population and targeted screening approaches. The incidence of 'new' AF cases was 1.63% and 1.04%/year in the intervention and control arms, respectively, with a similar screening outcome in opportunistic and systematic groups (1.64% and 1.62%/year, respectively) (Hobbs *et al.* 2005; Fitzmaurice *et al.* 2007). Approximately 46% and 28% of 'new' AF cases in the systematic group were detected through targeted and population-based screening strategies, respectively, with the rest detected outside the screening programme. The less-resource intensive opportunistic strategy was the most cost-effective option for annual AF screening of ≥ 65s-year-olds, with a cost of £363/'new' AF case detected compared to no screening, and a 60% likelihood of cost-effectiveness under the WTP threshold of £20,000/QALY gained (Hobbs *et al.* 2005). These findings were largely verified by the subsequent cost-effectiveness analysis which ascertained that opportunistic screening was more cost-effective than the systematic approach, although either of the two strategies using a variety of methods (such as pulse palpation, PPG, mBPMs or $_{SL}$ECG devices), and repeated every five years remained economically viable in ≥ 65s at least until the age of 80 years (Welton *et al.* 2017).

In contrast to the first two RCTs, the **Re**mote **He**art **R**hythm **S**ampling Using the Aliv**e**Cor Heart Monitor to Screen for **AF** (REHEARSE-AF) study exploited an intermittent, targeted AF screening strategy, recruiting individuals aged ≥ 65 years with a CHA_2DS_2-VASc score of ≥ 2 who did not have a recorded history of AF (Halcox *et al.* 2017). A total 1001 individuals were randomised to either routine care or the KMD arm which required them to record twice-weekly 30-second $_{SL}$ECGs (with additional recordings if symptoms occurred) at home over a period of 12 months. At the end of the study, the yields of 'new' AF confirmed by cardiologist's interpretation of $_{SL}$ECG were 1.0% (0% PAF or asymptomatic) and 3.8% (2.4% PAF; 1.6% asymptomatic) in the routine care and intervention arms, respectively,

with a screening cost of £8,255/diagnosis. All individuals with 'new' AF diagnoses in the screening arm were initiated on appropriate OAC therapy. Whilst the yield of this intermittent screening strategy was undoubtedly higher than observed with two single time point AF screening approaches above, the incidence of strokes/TIAs/SEEs and all-cause mortality were comparable between the control and intervention arms, thus questioning the "true" value of AF screening (Halcox *et al.* 2017). The **E**arly diagnosis of **A**F: a **R**andomized tria**L** in primar**Y** care (EARLY) pilot in Spanish general practice utilised a mixed targeted AF screening approach consisting of a baseline nurse-led $_{12L}$ECG at the surgery followed by six-monthly $_{12L}$ECGs appointments and once monthly pulse palpation by participants at home over a period of two years (Benito *et al.* 2015). A total of 928 individuals without a prior AF but with ≥ 1 risk factor(s) for stroke were randomised to either the intervention or routine care arms, and after a two-year period, 'new' AF was diagnosed in 2.4% (2.2% anticoagulated) and 1.3% (0.4% anticoagulated) of each group, respectively. Crucially, Benito *et al.* (2015) demonstrated that AF screening helped achieve a more timely diagnosis, with a median time to AF diagnosis of only seven days compared to 277 days in the control group.

A briefer but more intensive home-based systematic intermittent AF screening strategy was investigated by the STROKESTOP study in Sweden (Svennberg *et al.* 2015). This initiative recruited > 7,000 participants aged 75-76 years without a history of AF from the general population to undergo twice daily self-screening using the Zenicor-ECG® for a period of 14 days. At the end of the 28-month period, 3.0% of participants were diagnosed with a new, $_{SL}$ECG-confirmed AF (2.8% started on OAC therapy). Only 0.5% of them had AF on the first ECG showcasing the advantage of prolonged intermittent AF screening. A further 2.1% of the group with incidentally found 'known' AF received no OAC therapy prior to screening, and half of these benefitted from the programme by being offered an appropriate stroke prevention (Svennberg *et al.* 2015). This systematic AF screening strategy was highly cost-effective compared to no screening, at a cost of €6583 per stroke avoided and a near-100% likelihood of cost-effectiveness under the WTP threshold of < €30,000/QALY gained (Aronsson *et al.* 2015). A recent initiative by the same research group implemented a three-times daily, 14-day-long self-screening strategy using pulse palpation and Zenicor-ECG® within a Swedish general practice population aged ≥ 65 years. A total of 1,010 individuals were screened over 18 months, yielding new, $_{SL}$ECG-confirmed AF diagnoses in 2.7% of the sample (2.5% PAF; 1.6% asymptomatic; 0.5% detected by first ECG; 2.6% initiated on OAC therapy) (Ghazal *et al.* 2020). The preliminary findings of the ongoing STROKESTOP II study suggested that the yield of 'new' AF may be increased further (to approximately 4.4%) with four times daily intermittent $_{SL}$ECG recordings and by targeting 75-76-year-olds

with elevated blood levels of N-terminal prohormone of brain natriuretic peptide (NT-proBNP) (Kemp Gudmundsdottir *et al.* 2019), which may be an independent predictor of incident AF and stroke (Patton *et al.* 2009; Hijazi *et al.* 2012). The RCT element of this study at 5-year follow-up is expected to show whether or not the proposed approach could improve the clinical endpoints, for instance by reducing the risk of ischaemic stroke/SEE (Engdahl *et al.* 2017).

Even greater yields of 'new' AF are detected with continuous ECG monitoring. The conventional continuous 24-hour ECG monitor (Holter) detects AF (primarily PAF) in approximately 4% of patients post-cryptogenic stroke or TIA (Andrade *et al.* 2015). This detection rate may however be increased substantially up to 13.4% where the duration of ECG monitoring is extended to seven days or where the monitoring targets higher-risk individuals (Stahrenberg *et al.* 2010; Kishore *et al.* 2014). Similar principles apply to secondary AF detection following ablation, in which case a seven-day Holter monitor may detect up to 14% more AF recurrences than the classic 24-hour observation (Kottkamp *et al.* 2004). Prolonged monitoring using external triggered event recorder ECGs or ICMs may be yet more effective. The **E**vent **M**onitor **B**elt for **R**ecording **A**F after a **C**erebral ischaemic **E**vent (EMBRACE) trial randomised 572 patients aged ≥ 55 years with a six-month history of stroke/TIA to either a 24-hour Holter monitor or a 30-day event recorder ECG arms, detecting AF in 3.2% and 16.1% of each group, respectively (Gladstone *et al.* 2014). The **C**ryptogenic **S**troke and **U**nderlying **AF** (CRYSTAL AF) study recruited 441 participants aged ≥ 40 years with a record of cryptogenic stroke/TIA in the previous 90 days, randomising them to either routine care or three-year monitoring with the aforementioned Reveal® ICM (Sanna *et al.* 2014). At the end of three years, the 'new' AF detection rate in the Reveal® arm was 30% (27% prescribed OAC therapy) compared to 3% in the routine care group (Sanna *et al.* 2014; Brachmann *et al.* 2016). A recent study by Reiffel *et al.* (2017) used Reveal® devices to monitor 446 high-risk participants (with or without previous stroke), identifying incremental 'new' AF cases in an unprecedented 40% of individuals at 36 months. Since the likelihood of asymptomatic AF increases post-ablation, long-term surveillance using this diverse ICM detects up to 12% more AF recurrences than self-reported symptoms alone (Verma *et al.* 2013). Continuous ECG monitoring using a 14-day ZioPatch® may also be helpful post-cryptogenic stroke/TIA and may increase the incremental yield of PAF to 16.3% compared to 2.1% with traditional Holter monitoring (Kaura *et al.* 2019). AHREs detected by continuous CIED monitoring may predict AF in as many as 90% of patients (Martin *et al.* 2015; Healey *et al.* 2012). The clinic or remote interrogation of these devices is therefore likely to constitute an effective primary AF

screening strategy, detecting 'new' AF in ≥ 20% of these generally high-risk patients (Ricci *et al.* 2009; Lorenzoni *et al.* 2014; Noseworthy *et al.* 2019).

Several studies evaluated the economic value of continuous and/or long-term ECG monitoring. Kamel *et al.* (2010) suggested that the outpatient monitoring using a Holter or an event recorder ECG to detect AF post-cryptogenic stroke may be cost-effective at a cost of $13,000/QALY gained, which was largely unaffected by variations in AF yield. Time considerations may however be crucial for this approach because the cost of a 'new' AF diagnosis using an event recorder ECG increases from approximately $600 in week 2 to over $5,000 in week 3 (Zimetbaum *et al.* 1998) – a marked difference from £363 per 'new' AF case with single-time point opportunistic pulse checks in the SAFE trial (Hobbs *et al.* 2005). The NIHR health technology assessment of ICMs for AF detection post-cryptogenic stroke concluded that these devices would likely bring value for money with an incremental cost < WTP of £20,000/QALY gained (Edwards *et al.* 2020). Similarly, prolonged monitoring using Reveal® devices may be cost-effective in the primary detection of AF amongst individuals with one or more risk factors for stroke (Rinciog *et al.* 2019).

As shown by multiple AF screening initiatives discussed above, the yield and hence the (cost)-effectiveness of the AF screening strategy are influenced heavily by the selection of appropriate target population. The age of 65 years has been the common threshold for opportunistic and systematic AF screening strategies in primary care settings (Kirchhof *et al.* 2016; Freedman *et al.* 2017), owing to the increased likelihood of such individuals benefitting from OAC therapy should a 'new' AF be detected (Lip *et al.* 2011). Whilst the classic ("flagged records") opportunistic or population-based screening of ≥ 65s attending GP surgeries may indeed constitute an effective AF detection strategy (Welton *et al.* 2017), an even more efficient method may include combining the screening with another healthcare intervention that applies to the same age group. Seasonal influenza vaccination clinics are attended by 70% of eligible ≥ 65-year-olds and may thus provide a regular annual access to this at-risk group of individuals (Public Health England 2019g). The study by Rhys *et al.* (2013) delivered a one-off GP and medical student-led opportunistic pulse palpation programme amongst a group of 573 ≥ 65s attending seasonal influenza vaccination clinics in UK general practice, and discovered 'new', $_{12L}$ECG-confirmed AF in 0.4% of the sample (all qualified for OAC therapy) over a single vaccination season. An equivalent study in Australian GP surgeries utilised 30-second KMD recordings produced by a nurse to opportunistically screen 972 individuals aged ≥ 65 years at seasonal influenza vaccination appointments, detecting a $_{12L}$ECG-confirmed 'new' AF in 0.8% of the group (0.3% started on an OAC) (Orchard *et al.* 2016). An even higher yield of 'new' AF diagnoses (1.1%; 78%

qualified for OAC therapy) was reported by Kaasenbrood *et al.* (2016) who conducted single time point opportunistic screening of more than 3,000 ≥ 60s receiving seasonal influenza vaccinations in Dutch GP surgeries using a MyDiagnostick® device. Although the yield derived by this study was not verified by $_{12L}$ECG, the screening strategy proposed was highly economical, with a cost-effectiveness probability of 99.8% under a WTP threshold of €20,000/QALY gained (Jacobs *et al.* 2018).

Apart from ambulatory/home-based monitoring or AF screening in GP surgeries, a number of research groups investigated the less common approaches to AF detection, such as screening in public places or community locations. Proietti *et al.* (2016) exploited the opportunity posed by the *'Belgian Heart Rhythm Week'* to conduct population-based, nurse-led AF screening using the Omron HeartScan® device amongst more than 65,000 individuals aged ≥ 20 years (median age 58 years) who were visiting one of the 89 national hospitals. A surprising 1.1% of this relatively young sample were found to have a previously undiagnosed AF and 57% of these had a CHA_2DS_2-VASc score ≥ 2 demonstrating the potential of population-based screening outside the primary care (Proietti *et al.* 2016). Similarly, Battipaglia *et al.* (2016) utilised a MyDiagnostick® device to screen 855 individuals in a busy UK shopping centre during a single-day arrhythmia specialist-led heart rhythm awareness event, identifying new, $_{SL}$ECG-confirmed AF in 0.8% of the group. The study was however limited by excessive noise within the supermarket setting, leading to unreadable $_{SL}$ECGs in 7% of the sample (Battipaglia *et al.* 2016). A recent initiative by Gwynn *et al.* (2020) conducted population-based AF screening using the KMD in a community of 619 Aboriginal Australians aged ≥ 45 years. The screening led by health workers and nurses from the same community was well-accepted by patients and helped detect 'new' AF in 0.6% of the sample, mostly those under 65 years of age, suggesting that certain high-risk population groups may benefit from a lower age threshold for AF detection (Macniven *et al.* 2019; Gwynn *et al.* 2020).

1.2.4 Current recommendations and policies

In 2015, recognising the global risks posed by undiagnosed and/or undertreated AF, and appreciating the potential benefits of proactive AF detection, the international medical and scientific community established the AF-Screen collaboration (AF-Screen 2020). The work of this group culminated in a white paper supporting the case for opportunistic screening of asymptomatic AF in individuals aged ≥ 65 years (Freedman *et al.* 2017). In parallel, the evidence favouring opportunistic AF screening in this age group was reviewed by the ESC, which recommended or indicated (Class I recommendation) primary opportunistic screening for AF by pulse taking or an ECG rhythm strip in patients > 65 years of age

(Kirchhof *et al.* 2016). Similarly, opportunities for AF detection posed by routine CIED monitoring (Ricci *et al.* 2009; Lorenzoni *et al.* 2014; Noseworthy *et al.* 2019) encouraged ESC to recommend the regular interrogation of these devices to detect AHREs, which may be confirmed as AF following an ECG (Class I recommendation). The systematic screening of AF may be considered in population groups where it is supported by adequate evidence, such as individuals aged > 75 years (Svennberg *et al.* 2015; Aronsson *et al.* 2015) or those at high risk of stroke (Benito *et al.* 2015; Halcox *et al.* 2017) (Class IIb recommendation). Due to high yields of AF detection after cryptogenic thromboembolic events (Andrade *et al.* 2015), ESC also recommended secondary AF screening with short-term ECG recordings followed by continuous ECG monitoring for at least 72 hours in individuals post-ischaemic stroke or TIA (Class I recommendation). In order to document silent AF in these patients, clinicians should consider long-term monitoring using devices, such as ICMs (Sanna *et al.* 2014; Brachmann *et al.* 2016; Kirchhof *et al.* 2016) (Class IIa recommendation).

The recommendations for AF screening laid out in the ESC guidelines have been largely endorsed by the European Heart Rhythm Association consensus document (Mairesse *et al.* 2017). Besides the general support for AF screening in selected groups of individuals, this report emphasised the significance of appropriate stakeholder engagement to raise AF awareness and to fast-track its timely management: from patients and PPOs to GPs and other primary care HCPs (Mairesse *et al.* 2017). The recent industry-driven white paper consolidated some of these ideas, calling on European governments to develop formal strategies aimed at reducing the impact of AF-related stroke, particularly by improving its early detection and the uptake of OAC therapies (The Health Policy Partnership 2018). Perhaps due to ongoing scientific, medical and industrial efforts, the need to improve AF detection has also been recognised by the UK Government (referred to as *'the Government'* throughout this report) which included this condition as one of the top three CVD priorities in the *'NHS Long-term Plan'* alongside hypertension and dyslipidaemia (also dubbed by the term *'cardiovascular ABC'*, i.e. **A**F, high **B**P and high **C**holesterol) (NHS England 2019d; Public Health England 2019c). The 10-year ambitions outlined in this plan include the timely diagnosis of 85% of all AF cases and the initiation of OAC therapy in 90% of all eligible patients, which overall may help prevent up to 150,000 strokes, MIs and dementia cases by 2029 (NHS England 2019d; Public Health England 2019c).

A number of policy-driven initiatives had been organised to assist the Government in achieving these ambitious targets. The *'Detect, Protect and Perfect'* programme by the Academic Health Science Network (AHSN) distributed close to 6,000 AF detection devices to GP surgeries, community pharmacies and other primary care institutions across the 15

AHSNs in England, encouraging HCPs and support staff to opportunistically check their patients for AF. This initiative detected 5,586 cases of AF (6.8% of general population screened) over a period of 14 months, preventing an estimated 187 strokes (The AHSN Network 2019a; Wessex AHSN 2019). The collaborative project between the NHS Lothian and the Digital Health Institute in Scotland utilised KMDs to opportunistically screen high-risk individuals aged ≥ 65 years attending their annual long-term condition reviews across five of the fourteen Scottish regions. This one-year-long initiative detected AF in an estimated 5.5% of the group, with an 80% probability of cost-effectiveness (< WTP of £30,000/QALY gained) (Tassie *et al.* 2015). *'A Focus on AF in Scotland'* report that followed built on the evidence provided by this programme, appealing to the Scottish Government to encourage AF screening of at-risk population groups and to invest in novel technology for AF detection (Cross-Party Group on Heart Disease and Stroke 2018).

Despite the favourable international scientific-medical consensus, and the recognition of AF as a national CVD priority, the population-wide screening for this condition is not currently endorsed by the UK National Screening Committee (UK NSC 2019). The latest NICE guidance also does not recommend routine screening for asymptomatic AF, and instead supports opportunistic case-finding in symptomatic individuals referred to above (NICE 2014a). A similar lack of nationwide endorsement of systematic AF screening may be encountered in other countries, such as France or US (Haute Autorité de Santé 2014; U. S. Preventive Services Task Force 2018). One of the arguments underlying these recommendations is the fact that the yields and cost-effectiveness of systematic population or targeted screening approaches are likely inferior to opportunistic AF detection (Hobbs *et al.* 2005; Welton *et al.* 2017). More importantly, none of the AF screening studies to date had demonstrated any palpable effect on clinical endpoints, especially a reduction in ischaemic stroke or all-cause mortality without an excess of OAC-related bleeding, which had otherwise been shown in a general AF population (Hart *et al.* 2007; Ruff *et al.* 2014). As such, the economic evaluations of AF screening strategies (Lowres *et al.* 2014; Aronsson *et al.* 2015; Welton *et al.* 2017; Jacobs *et al.* 2018) were conducted under an assumption that patients with screening-detected AF had the same risk profile as more symptomatic and possibly higher-risk individuals identified through routine care (Flaker *et al.* 2005; Rienstra *et al.* 2014). The results of the cohort study by Martinez *et al.* (2014) were indeed promising, nevertheless further adequately-powered RCTs are required to prove the effectiveness of OAC therapy in screening-detected AF, and to convince the sceptics, including the UK NSC, that widespread AF screening would help achieve a favourable benefit-to-risk balance (Lown *et al.* 2017a; Jones *et al.* 2019). A number of such initiatives evaluating different AF screening methods and strategies are currently on the way, both in

the UK and elsewhere (Engdahl *et al.* 2017; ISRCTN Registry 2019; SAFER study 2020; ClinicalTrials.gov 2020b; ISRCTN Registry 2020; ClinicalTrials.gov 2020a).

1.3 Pharmacist-led AF screening in primary care: a scoping review

1.3.1 Background

The quality of health screening programmes, including the diagnostic accuracy of selected index tests, may be influenced by observer or operator-specific factors, such as their level of training and expertise (Schmidt & Factor 2013; Cohen *et al.* 2016). The vast majority of AF screening programmes to date had been conducted in general practice and had therefore been facilitated by either GPs or practice nurses (Welton *et al.* 2017; Mairesse *et al.* 2017). Most GPs, nurses and practice-based HCAs are confident undertaking AF screening using either conventional pulse palpation or modern tools, such as $_{SL}$ECG devices (Taggar *et al.* 2016b; Orchard *et al.* 2019a). In recent years however, the NHS and general practice in particular fell under a considerable strain due to the ever-worsening GP and nurse workforce crisis (The King's Fund 2019a; NHS Digital 2019b). According to recent estimates, an additional 7,000 full-time equivalent (FTE) GPs would be required to match the clinical demand across NHS England by 2024, which may be a challenging target considering that over 50% of them are close to retirement age (Gibson *et al.* 2017; Buchan *et al.* 2019). More than 90% of GPs are also adversely affected by increasing workload (Gibson *et al.* 2017) – a key barrier to AF screening in primary care identified by both GPs and practice nurses in a recent survey by Taggar *et al.* (2016b). Whilst a continuing fall in the workforce of these HCPs may be partially compensated by the rising numbers of advanced nurse practitioners, a broader multidisciplinary approach is warranted to sustain high-quality primary care for the future (The King's Fund 2019a; Buchan *et al.* 2019). The need to improve the utilisation of other primary care professionals, such as social workers or therapists, was recognised by the *'NHS Five Year Forward View'* (NHS England 2014). A year later, the *'new ways of working'* within the 10-point action plan for general practice placed allied healthcare professionals at the heart of the agenda to resolve the ongoing workforce crisis (Snow-Miller 2015a).

Pharmacists were amongst a number of other HCPs referred to in this report (Snow-Miller 2015a). Throughout the history, most pharmacists have been based in community pharmacies, which have served as the first port-of-call for minor health issues or healthcare advice for centuries, possibly since ancient Greece (Kremers *et al.* 1976; Murray 2016). The introduction of the NHS in 1948 led to a substantial rise in GP prescriptions, meaning that community pharmacists had to spend an increasing amount of time dispensing medicines,

making them less visible to the general public (Anderson 2007). This was not helped by public confusion concerning the professional boundaries between pharmacists and pharmacy technicians whose roles emerged to assist pharmacists with the growing volume of work (Kelly *et al.* 2014; Boughen *et al.* 2017). Add to this the retail nature of community pharmacy business, and the public perception of pharmacists as trusted frontline HCPs was replaced by that of dispensers and shopkeepers – a perception that has extended into the 21st century (Anderson *et al.* 2004; Gidman *et al.* 2012). It was not until the late 1970s and 1980s that policymakers and commissioners began to realise the potential of community pharmacists to provide extended clinical public health services, such as contraception or BP monitoring (Anderson 2007). The Nuffield report was the key catalyst for this process, recognising that education and training received by pharmacists could help them play a *'unique and vital role'* in the provision of community healthcare. It also encouraged a closer collaboration between community pharmacists and GPs, and proposed a shift from pure dispensing to formalised clinical services, including health education/advice for patients, domiciliary visits as well as long-term patient care (Turner 1986).

Fast-forward to early 2000s, in order to meet the training demands of these new clinical roles, the classic three-year Bachelor of Science (BSc) in pharmacy degree was replaced by a five-year Master of Pharmacy (MPharm)-pre-registration model, covering a diverse range of relevant topics from drug design, pharmacology and pathophysiology to diagnosis, clinical therapeutics and healthcare economics (Sosabowski & Gard 2008; General Pharmaceutical Council 2011). In turn, the 2005 NHS community pharmacy contract extended the range of clinical community pharmacy services, focusing on public health interventions, such as the minor ailments scheme and smoking cessation, amongst the pharmaceutical services, for instance the newly-introduced medicines use reviews (Bond *et al.* 2008; Richardson & Pollock 2010). Following the CVD prevention-orientated report and the white paper in 2008, community pharmacies who met the defined requirements were also encouraged to provide an enhanced (additional) service of NHS Health Checks (Department of Health 2008b; Department of Health 2008a). This service was received favourably by patients and helped improve the identification of individuals at risk of IHD or stroke (Corlett & Krska 2016). Some pharmacies developed locally commissioned INR monitoring services for patients receiving warfarin (Ingram *et al.* 2018). Another milestone in expanding the umbrella of pharmacist-led public health services was the 2015 introduction of the community pharmacy seasonal influenza vaccine service, which allowed trained pharmacists to administer influenza vaccines to selected population groups under a patient group direction (PSNC and NHS England 2019). The recent *'NHS Long-term Plan'* and the new *'Community Pharmacy Contractual Framework'* have placed an even greater

emphasis on community pharmacies becoming a crucial partner for local PCNs in order to promote healthy lifestyle and disease prevention, and to support urgent care by accepting referrals from GP surgeries or local hospitals (NHS England 2019d; Department of Health and Social Care 2019). The inception of pharmacist independent prescribing qualification empowered these practitioners to help GPs by managing patients with specific long-term illnesses as part of targeted clinical medication reviews, or by assisting those with acute symptoms, such as ear, nose and throat infections (Baqir *et al.* 2012; Wilson & Falconer 2019; PSNC 2020b).

The rapid evolution of clinical and/or public health services in community pharmacies redefined the concept of *'clinical pharmacy'*, which had traditionally related to pharmaceutical services, such as medicines information or therapeutic drug monitoring, in a hospital pharmacy setting (Turner 1986; Hepler 2004). The modern definition of clinical pharmacy is much broader, describing it as a *'health science discipline in which pharmacists provide patient care that optimises medication therapy and promotes health, and disease prevention'* (American College of Clinical Pharmacy 2015). As such, most practising pharmacists that are involved in the provision of clinical services could be defined as clinical pharmacists (CPs) regardless of the care setting. Indeed, besides community pharmacies, CPs have also provided specialist clinical services in other primary care settings, particularly general practice – probably from late 1990s. Clinical medication reviews delivered by CPs in GP surgeries were evaluated as part of early RCTs in the North of England and Scotland, demonstrating their ability to conduct consultations with complex patients whilst identifying drug-related problems and producing cost savings for surgeries involved (Krska *et al.* 2001; Zermansky *et al.* 2001; Zermansky *et al.* 2002). More recently, several studies showed that CP-led interventions in general practice may also reduce the number of GP appointments (Bush *et al.* 2017), improve patient adherence to treatment (Tan *et al.* 2014a), optimise the use of national guidance (Virdee & Stewart 2017) and help control a variety of chronic long-term conditions, including hypertension, diabetes, CVD (Tan *et al.* 2014b), asthma and/or COPD (Khachi 2014). Perhaps due to their integration within the practice infrastructure, CP services in this setting are well-accepted by both patients and HCPs (Ryan *et al.* 2018; Wilcock & Hughes 2015; Tinelli *et al.* 2015), including GPs, who had in the past described competitive or tense relationships with community pharmacists (Hughes & McCann 2003; Hindi *et al.* 2019).

Recognising the breadth and added value of CP-led primary care services, in 2015 NHS England launched the *'Clinical Pharmacists in General Practice'* (CPGP) pilot (Snow-Miller 2015b). As part of this programme, approximately 1,000 CPs were deployed across

England to help improve the general practice workforce capacity by reviewing patients with long-term illnesses, addressing repeat prescription requests and managing the transfer of care (Mann *et al.* 2018; NHS England 2020a). The development of pharmacy roles in general practice was facilitated further by the introduction of an additional 180 pharmacist and 60 pharmacy technician posts to deliver medicines optimisation in care homes (NHS England 2018b). Following the success of these pilots, NHS England have pledged to integrate CPs into the emerging PCNs, providing at least one FTE of CPs per population of 50,000 people (NHS England and BMA 2019c). Within their areas of expertise, these prescribing practitioners are expected to lead on the primary care medicines optimisation agenda, including the management of patients with polypharmacy or long-term conditions, anticoagulation, the implementation of the QOF scheme and the development of shared clinical protocols with the wider healthcare team, such as their community/hospital pharmacy counterparts (NHS England and BMA 2019c). Recent surveys suggest that the range of services provided by CPs and/or pharmacy technicians in GP surgeries may be even wider and somewhat comparable to clinical or public health services delivered in community pharmacies: from the management of common or acute illnesses and domiciliary visits to administration of vaccines, travel medicine, substance misuse services and health screening (Bradley *et al.* 2018; Savickas *et al.* 2020a).

The expansion of CP-led services in primary care settings showcases their professional capability to deliver public health interventions beyond the traditional scope of pharmaceutical expertise, either in community pharmacies or GP surgeries. The professional focus on identification and management of individuals with modifiable CVD risk factors or those with established long-term illnesses (Corlett & Krska 2016; Murray 2016; Bradley *et al.* 2018), places pharmacists practising in both of these settings in a convenient position to facilitate opportunistic or systematic AF screening programmes. As an example, both pharmacists based in community pharmacies and GP surgeries may be involved in delivering seasonal influenza vaccinations, which amongst others involve individuals aged ≥ 65 years (Public Health England 2020a) – the primary target population for pro-active AF detection (Kirchhof *et al.* 2016). Specialised primary care pharmacists also possess in-depth knowledge of stroke prevention and OAC therapies (Virdee & Stewart 2017; Ingram *et al.* 2018; Chahal *et al.* 2019), providing them with an opportunity to deliver convenient and potentially time-saving AF screening and management clinics in conjunction with local GPs and cardiology/stroke specialists. This therapeutic expertise offers pharmacists an advantage over the HCAs or practice nurses who may display more advanced clinical assessment skills, yet often lack the confidence to manage those with newly diagnosed AF (Taggar *et al.* 2016b). The willingness and capacity of primary care pharmacists to become

more involved in AF detection was witnessed by the evaluation of the AHSN programme whereby each participating pharmacist screened an average of 57 individuals compared to 36, 38 and 42 screens by GPs, registered nurses and HCAs, respectively (Wessex AHSN 2019).

This literature review aimed to identify and map the research evidence pertaining to pharmacist-led AF screening or detection in primary care settings, including community pharmacies and GP surgeries. It was anticipated that this process would help assess the amount and quality of current clinical evidence supporting the delivery of pharmacist-led AF screening programmes in primary care and would determine the areas for further research.

1.3.2 Methods

Considering the explorative nature of the research aim, this study adapted a methodology of a scoping review (Arksey & O'Malley 2005). This increasingly more common and flexible methodology charts the available evidence from studies of varying designs and methods, and helps reveal the gaps in literature, which may then warrant further research or a more stringent systematic review (Colquhoun *et al.* 2014; Buckingham *et al.* 2020; Lenton-Brym *et al.* 2020). In order to define a research question and to facilitate a sensitive literature search, a facet analysis was conducted using a *'Population, Concept, Context'* (PCC) framework, which is a tool for scoping reviews recommended by the Joanna Briggs Institute (JBI) of evidence-based research (Peters *et al.* 2020), and is a less restrictive alternative to *'Population, Intervention, Control, Outcomes'* (PICO) mnemonic employed by systematic reviews (Thomas *et al.* 2020) (**Table 1.2**). The literature search strategy involved three independent searches of MEDLINE, CINAHL and Cochrane Library on the 20th of August 2020. The search terms included both the relevant subject headings and keywords, with truncations applied to selected keywords to ensure that alternative endings were covered by the search. Boolean operators 'OR' and 'AND' were used to combine individual searches in each facet category and searches across the facets, respectively (see **Appendices 1, 2 and 3** for a complete search history).

Table 1.2 Literature search strategy and facet analysis using the Population, Concept, Context framework

	Population		**Concept**		**Context**
Facets	General adult population (any age or sex) in primary care		Atrial fibrillation (AF) screening		AF screening by pharmacists
Subject Headings	Pharmacies OR Primary Health Care OR General Practice		Atrial Fibrillation AND Mass Screening		Pharmacists
	OR	AND	OR	AND	OR
Keywords	Community pharmac* OR General practice OR GP surger* OR GP practice* OR Primary care		Atrial fibrillation OR AF AND Screening OR Detect*		Pharmacist*

In order to retrieve the most contemporary and relevant results, the search was limited to studies in humans published in English between January 2000 and August 2020. Primary or secondary research studies of all designs and research methods were eligible for inclusion provided they related to the aim of the review and the research question defined by the PCC framework. The titles and abstracts of all results from the database search were initially screened to identify potentially eligible studies. Full-text manuscripts, or where unavailable, abstracts of eligible studies were then obtained and screened for inclusion into the study. The reference lists of studies identified during the search and those of recent systematic reviews/meta-analyses were screened alongside for additional eligible studies (Welton *et al.* 2017; Duarte *et al.* 2019; Lowres *et al.* 2019).

The characteristics and relevant findings of studies selected for inclusion were extracted and charted using the criteria for scoping reviews adapted from Arksey & O'Malley (2005) (**Appendix 4**). Due to the breadth of research identified, a narrative approach was then taken to summarise and present the findings pertaining to studies of different designs and methodologies. Although scoping reviews generally do not seek to provide a detailed assessment of methodological research quality (Arksey & O'Malley 2005), each study

included in this review was broadly appraised using the critical appraisal checklists for respective study designs developed by the JBI as previously described (Buckingham *et al.* 2020; JBI 2020) (**Appendices 5, 6, 7 and 8**). The key limitations or biases ascertained during this process were charted alongside the other study characteristics and helped identify the gaps in high-quality evidence that might drive future research.

1.3.3 Results

The initial database search retrieved a total of 92 relevant records, with a further seven studies identified through the review of reference lists (**Figure 1.5**). The removal of duplicates followed by the title and abstract screening step excluded 78 records, resulting in 21 studies which were considered for inclusion into the review. The subsequent full-text and, where unavailable, abstract analysis excluded a further eight studies, yielding 13 records dated between 2014 and 2020 (**Appendix 4**). Eleven records included full-text manuscripts and two related to conference abstracts (Antoniou *et al.* 2017; Antoniou *et al.* 2019). The studies identified overall fell into four main categories: cross-sectional (prevalence) studies (n = 10), diagnostic accuracy studies (n = 4), economic evaluations (n = 2) and qualitative research (n = 3). One manuscript incorporated the prevalence, diagnostic accuracy and economic components (Lowres *et al.* 2014). A further three articles reported the analyses of AF prevalence and diagnostic accuracy (Sandhu *et al.* 2016; Zaprutko *et al.* 2019; Cunha *et al.* 2020). One mixed-methods study included a prevalence investigation and a qualitative research element (da Costa *et al.* 2020).

None of the studies included in the review aimed to ascertain the impact of AF screening programmes on clinical endpoints or long-term outcomes beyond three months. Most studies were conducted in either Europe (n = 5), North America (n = 3) or Australia (n = 3), although two records pertained to the same global initiative that involved 5-10 countries and covered all habitable continents except South America (Antoniou *et al.* 2017; da Costa *et al.* 2020). UK was amongst the countries covered by these two studies and was also the location of two additional independent screening programmes (Twigg *et al.* 2016; Antoniou *et al.* 2019). The studies involved between 205 (Cunha *et al.* 2020) and 3,071 participants (Bacchini *et al.* 2019). Twelve studies related to AF screening initiatives in community pharmacies whilst one US-based study was conducted at health fairs held at community centres, festivals/carnivals, senior centres, state capital buildings, pharmacy meetings and religious venues (Anderson *et al.* 2020). Two of the community pharmacy-based studies also described additional AF screening in other care settings, such as community centres, hospital outpatient clinics and a nursing home (Cunha *et al.* 2020; da Costa *et al.* 2020).

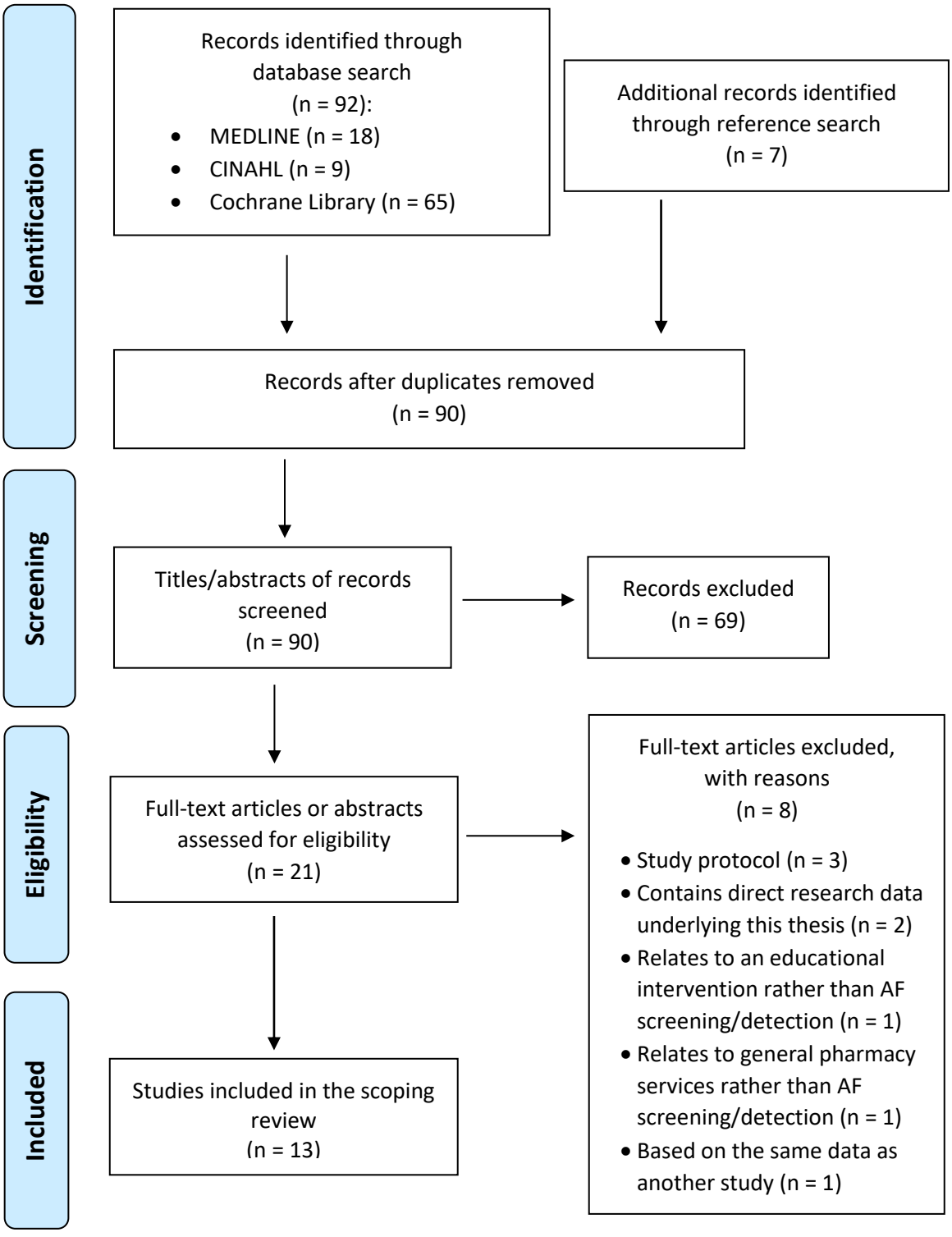


Figure 1.5 Flow-chart presenting the literature search and study selection process

Adapted from: Moher et al. (2009). Abbreviations: AF – atrial fibrillation.

Cross-sectional (prevalence) and diagnostic accuracy studies

All 10 cross-sectional studies included in this review employed single time point AF screening strategies, either population-based (n = 7), opportunistic (n = 2) or mixed opportunistic-targeted (n = 1) approaches. Two of the opportunistic AF screening strategies involved combined AF and CVD risk factor screening sessions (Sandhu *et al.* 2016; Twigg *et al.* 2016) whereas the third one related to opportunistic AF detection using an mBPM (Bacchini *et al.* 2019). Four of the population-based AF screening strategies were branded by authors as opportunistic (Lowres *et al.* 2014; Zaprutko *et al.* 2019; Cunha *et al.* 2020; da Costa *et al.* 2020), however it was not possible to establish whether or not AF screening was consistently combined with another consultation on such occasions. Half of all AF screening strategies recruited individuals aged ≥ 65 years (Lowres *et al.* 2014; Sandhu *et al.* 2016; Twigg *et al.* 2016; Zaprutko *et al.* 2019; Antoniou *et al.* 2019) whereas the rest included either younger participants aged ≥ 18 (Antoniou *et al.* 2017), ≥ 40 (Cunha *et al.* 2020; da Costa *et al.* 2020), ≥ 50 years (Bacchini *et al.* 2019), or all individuals regardless of their age (Anderson *et al.* 2020). The targeted screening by Twigg *et al.* (2016) involved individuals aged 50-64 years who had pre-existing CVD risk factors, such as heart failure or high BMI.

In the majority of studies (n = 6), pharmacists were solely responsible for conducting AF screening whereas fewer initiatives utilised either trained volunteers (Sandhu *et al.* 2016), trained and pharmacist-supervised pharmacy students (Zaprutko *et al.* 2019; Anderson *et al.* 2020) or pharmacists/other pharmacy staff (Twigg *et al.* 2016). Eight AF screening programmes were conducting using $_{SL}$ECG devices, which predominantly included the KMD enabled by an automated AF detection algorithm (n = 6). The **S**creening **E**ducation **A**nd **R**ecognition in **C**ommunity p**H**armacies of **AF** (SEARCH-AF) study was conducted before the inception of the KMD algorithm, therefore pharmacists were originally responsible for the interpretation of $_{SL}$ECG recordings which were then retrospectively subjected to the algorithm interpretation for diagnostic accuracy purposes (Lowres *et al.* 2014). The **P**rogram for the **I**dentification of '**A**ctionable' **AF** in the **P**harmacy (PIAAF-Pharmacy) study utilised the HeartCheck® device-based $_{SL}$ECG recordings interpreted by technicians (Sandhu *et al.* 2016). In the screening programme by Twigg *et al.* (2016), KMD-based $_{SL}$ECG was only recorded if the patient tested positive following a check with a Microlife WatchBP Office AFIB® mBPM. The MicrolifeAFIB® device was the sole test for AF used by Bacchini *et al.* (2019). Conventional pulse palpation as a single method for AF detection was performed by one study (Antoniou *et al.* 2017) however was more commonly undertaken alongside the KMD recordings (Lowres *et al.* 2014; Antoniou *et al.* 2019; da Costa *et al.* 2020).

The prevalence of $_{SL}$ECG-confirmed AF at the time of screening varied from 1.5% in the study by Twigg *et al.* (2016) which recruited participants aged ≥ 65 years without a prior history of AF to 6.7% in the study by Lowres *et al.* (2014) which included population of the same age threshold with and without AF (**Figure 1.6**). The prevalence of AF was somewhat lower in studies that recruited participants < 65 years of age (2.3-4.5%) (Anderson *et al.* 2020; da Costa *et al.* 2020). The yield of $_{SL}$ECG-confirmed new possible AF ranged from 1.3% in the study by Zaprutko *et al.* (2019) to 4.5% in the study by da Costa *et al.* (2020), although the latter was skewed by high yields of new cases detected outside the community pharmacy setting (1.8%), such as care homes (13.0%) or day centres (7.2%). The study by Sandhu *et al.* (2016) also reported the $_{SL}$ECG-based yield of 'actionable AF' (2.5%), i.e. new and known AF cases unless on OAC therapy, whereas Antoniou *et al.* (2019) referred to the yield of $_{SL}$ECG-confirmed 'actionable AF' as the yield of known AF cases not on OAC therapy (1.2%). The proportion of individuals with screening-detected AF eligible for OAC therapy (CHA_2DS_2-VASc score of ≥ 2 or ≥ 1 if male) was reported by five studies, and ranged from 69.0% in the younger health-fair sample (Anderson *et al.* 2020) to 100% in the ≥ 65s attending community pharmacies (Lowres *et al.* 2014; Zaprutko *et al.* 2019). Where stated (n = 4), $_{12L}$ECG yields of 'new' AF varied between 0.3% (Sandhu *et al.* 2016) and 6.3% (Cunha *et al.* 2020), yet similar to da Costa *et al.* (2020), only 1.0% of new cases identified by the latter multi-setting programme originated in a community pharmacy. The proportion of 'new' AF cases initiated on OAC therapy at follow-up ranged from 0.3% (20.0% of 'new' AF) in the study by Lowres *et al.* (2014) to 1.6% (100% of 'new' AF) in the initiative by Antoniou *et al.* (2019) which was facilitated by a referral pathway from community pharmacies to a one-stop arrhythmia and OAC clinic. Besides the screening outcomes, the other key findings of studies included in the review were the low public awareness of AF (56-60%) and the significant improvement in pharmacists' knowledge pre- versus post-AF screening (Lowres *et al.* 2014; Anderson *et al.* 2020). The programmes by Sandhu *et al.* (2016) and Twigg *et al.* (2016) also demonstrated that a combined AF-CVD screening service delivered by community pharmacy teams might not only be feasible but might also help identify individuals with sub-optimal blood pressure control (≤ 55% of participants), those with excessive alcohol consumption (≤ 22%) and those at risk of diabetes (≤ 90% of participants) who may benefit from further interventions.

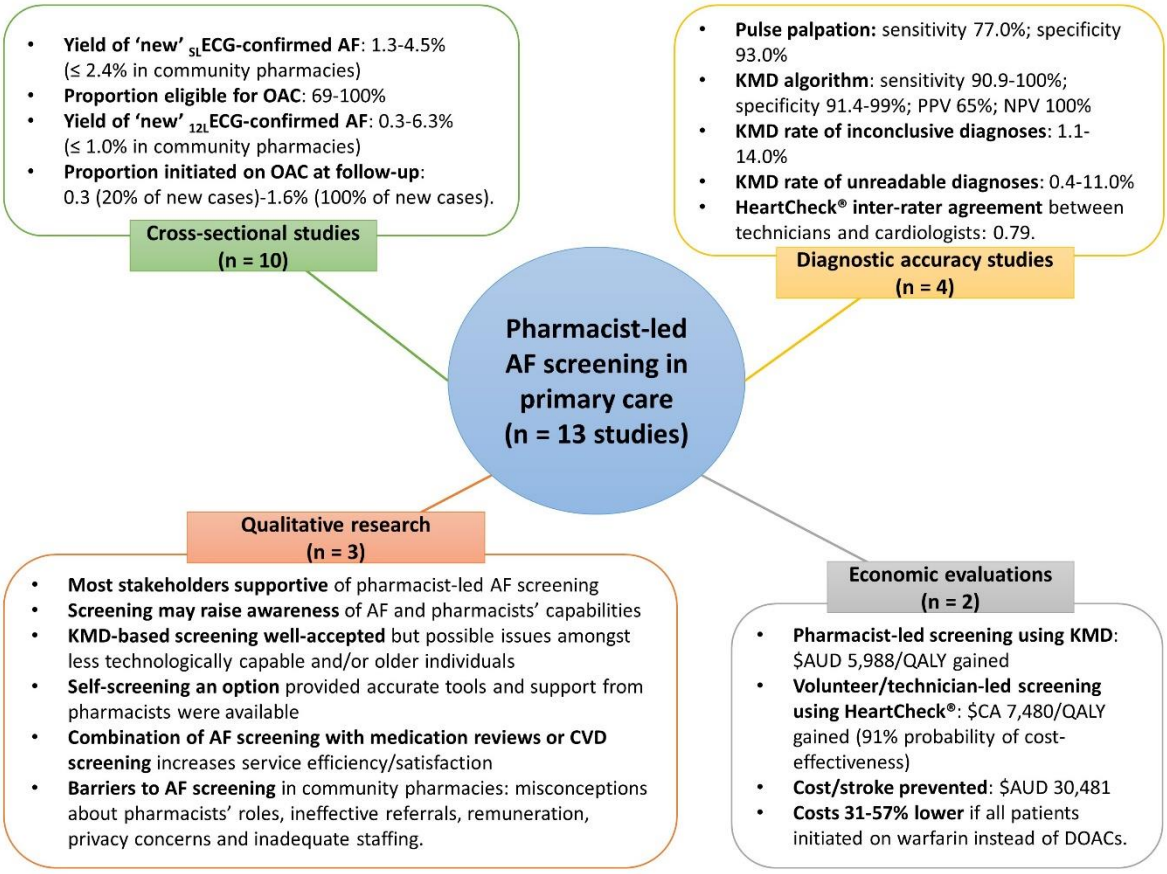


Figure 1.6 The map of studies and key findings identified during the scoping review

Abbreviations: $AUD – Australian dollars; $CA – Canadian dollars; 12LECG – 12-lead electrocardiogram; AF – atrial fibrillation; CVD – cardiovascular disease; DOAC – direct-acting oral anticoagulant; KMD – Kardia Mobile® device; OAC – oral anticoagulant; QALY – quality-adjusted life year.

Four of the prevalence studies investigated the diagnostic accuracy of AF detection using either the automated KMD algorithm (n = 3), the manual SLECG interpretation by pharmacists (n = 1) or technicians (n = 1), or pulse palpation (n = 1). Three of the four studies used the cardiologist's interpretation of SLECG as a reference standard for diagnostic accuracy measures whilst the study by Cunha *et al.* (2020) employed the cardiologist-interpreted 12LECG recordings. The SLECG-based reference standard during the SEARCH-AF study was also complemented by 12LECG recordings whenever they were available (Lowres *et al.* 2014). Compared to cardiologist's interpretation, the sensitivity and specificity of the automated KMD algorithm were 90.9-100% and 91.4-99.0%, respectively (Lowres *et al.* 2014; Zaprutko *et al.* 2019; Cunha *et al.* 2020) whereas the PPV and NPV were 65.0% and 100%, respectively (Zaprutko *et al.* 2019). During the SEARCH-AF study,

the sensitivity and specificity of pharmacist-interpreted $_{SL}$ECGs were below those of the KMD algorithm at 77.0% and 87.0%, respectively (Lowres *et al.* 2014). Pharmacist-performed pulse palpation had a comparable to KMD algorithm specificity (93.0%) but significantly lower sensitivity (77.0%). The inter-rater agreement between the pharmacist's and cardiologist's interpretations of $_{SL}$ECG was moderate (0.42), and lower than either that of pulse palpation (0.52) (Lowres *et al.* 2014) or technician's interpretation of $_{SL}$ECG produced by HeartCheck® device (0.79) (Sandhu *et al.* 2016). Considering the other prevalence studies, the rate of inconclusive ('Unclassified') diagnoses produced by the automated KMD algorithm was 1.1-14.0%, and 0.4-11.0% of $_{SL}$ECGs were unreadable or non-interpretable (Zaprutko *et al.* 2019; Cunha *et al.* 2020; Anderson *et al.* 2020; da Costa *et al.* 2020).

Reflecting the methodological and reporting heterogeneity, the quality of studies included in this review varied substantially (**Appendix 5**). With an exception of the conference abstract by Antoniou *et al.* (2017), all studies provided a comprehensive account of research participants and the AF screening setting. All initiatives were also conducted with an appropriate statistical analysis for a cross-sectional study design, although the complete details of statistical analyses were not provided by the two conference abstracts (Antoniou *et al.* 2017; Antoniou *et al.* 2019). Despite the generally detailed description of eligibility criteria, none of the studies indicated a sampling method, increasing the risk of selection bias (Delgado-Rodriguez & Llorca 2004). The self-reported medical history was relied upon by six of the studies (Sandhu *et al.* 2016; Twigg *et al.* 2016; Bacchini *et al.* 2019; Cunha *et al.* 2020; Anderson *et al.* 2020; da Costa *et al.* 2020), raising concerns over the recall bias (Delgado-Rodriguez & Llorca 2004) which may affect the validity of AF or CVD/risk factor prevalence reported in the manuscripts. These outcomes might have also been modified by an additional selection bias (Delgado-Rodriguez & Llorca 2004) in studies that utilised self-completed questionnaires to recruit individuals without a prior history of AF (Sandhu *et al.* 2016; Twigg *et al.* 2016). Furthermore, only two initiatives conducted an appropriate sample size calculation (Lowres *et al.* 2014; Sandhu *et al.* 2016), questioning whether or not the outcomes derived during the other studies were a reliable estimate of the population values. Most screening programmes included the recruitment and participant exclusion flow charts, yet only the multinational initiative by da Costa *et al.* (2020) provided the response or the screening uptake rate (65.9%, 2,762/4,193 of individuals attending the AF awareness event). Nevertheless, similar to the other study conducted during an AF awareness campaign (Cunha *et al.* 2020), this initiative was predominantly based in community pharmacies limiting the generalisability of data to other settings, such as nursing homes, which formed only 0.8% of the total sample (da Costa *et al.* 2020). The generalisability of

findings beyond individual studies was also limited for programmes conducted within a single geographical region (Lowres *et al.* 2014; Twigg *et al.* 2016).

Nine out of 10 studies included in this review followed the international recommendations (Kirchhof *et al.* 2016) and confirmed AF diagnoses by ECG traces, generally interpreted by cardiologists (**Appendix 6**). The remaining study relied entirely on mBPM recordings and did not confirm AF by ECG, thus raising doubts over the validity of the reported AF prevalence (Bacchini *et al.* 2019). The guideline-recommended $_{12L}$ECG recordings (NICE 2014a; Kirchhof *et al.* 2016) were clearly performed and reported by only four studies (Lowres *et al.* 2014; Twigg *et al.* 2016; Sandhu *et al.* 2016; Cunha *et al.* 2020). The $_{SL}$ECG-$_{12L}$ECG combination reference standard used by Lowres *et al.* (2014) may have increased the risk of a partial/differential verification bias leading to the misclassification of diagnoses (Schmidt & Factor 2013). Similarly, the misclassification and over- or under-estimation of AF prevalence may have also occurred in studies where pulse palpation and KMD were applied inconsistently (da Costa *et al.* 2020) or where the use of such dual tests was not adequately described (Antoniou *et al.* 2019). None of the four diagnostic accuracy studies indicated the blinding status of either the observers performing the index tests or cardiologists interpreting the findings, predisposing the diagnostic accuracy data to a diagnostic review bias (Schmidt & Factor 2013), particularly where manual tests such as pulse palpation were performed. The interval between the index test and the reference standard was also indicated by a single diagnostic accuracy study (Zaprutko *et al.* 2019), with the rest subjected to disease progression bias, for instance by overlooking individuals with PAF (Whiting *et al.* 2013).

Economic evaluations

The two manuscripts which incorporated an economic evaluation related to either the SEARCH-AF or PIAAF-Pharmacy research programmes in Australian and Canadian community pharmacies, respectively (Lowres *et al.* 2014; Tarride *et al.* 2017). Both economic evaluations focused on the cost-utility (cost per QALY gained) of AF screening interventions with $_{SL}$ECG devices operated by pharmacists (Lowres *et al.* 2014) or trained volunteers/technicians (Tarride *et al.* 2017), compared to the alternative of routine care (or no screening) amongst individuals aged ≥ 65 years. Each evaluation was built using a popular Markov model (Sonnenberg & Beck 1993; Welton *et al.* 2017) accompanied by either 1,000 or 100,000 Monte Carlo simulations, which generated the average incremental costs, outcomes and utilities in the AF screening cohort vs. the routine care (this model is described in more detail in section **2.8**). The economic evaluation by Lowres *et al.* (2014) also included an element of cost-effectiveness analysis by estimating the cost of stroke

prevented as a result of AF screening (Jakubiak-Lasocka & Jakubczyk 2014). The time horizon for the economic model simulation was 10 years in the study by Lowres *et al.* (2014) and lifetime in the study by Tarride *et al.* (2017). The SEARCH-AF programme (Lowres *et al.* 2014) assumed that all eligible patients with AF were initiated on warfarin therapy at base case whereas the PIAAF-Pharmacy study split the individuals prescribed warfarin and DOACs into the 52:48 ratio (Tarride *et al.* 2017).

The results of both economic evaluations suggested that the two AF screening interventions were likely to offer value for money at a cost of 5,988 Australian dollars ($AUD)/QALY (≈ £1,932/QALY) gained for the SEARCH-AF programme (Lowres *et al.* 2014) and 7,480 Canadian dollars ($CA)/QALY (≈ £4,589/QALY) gained for the PIAAF-Pharmacy initiative (Tarride *et al.* 2017). The cost of each stroke prevented as a result of AF screening was $AUD 30,481 (≈ £18,852) (Lowres *et al.* 2014). The AF screening intervention by Tarride *et al.* (2017) had a 91% probability of being cost-effective at a WTP threshold of $CA 50,000/QALY (≈ £30,000/QALY) gained, and remained cost-effective unless < 20% of 'new' AF cases received OAC therapy, the PPV of the device fell ≤ 20% or ≥ 50% of AF cases were diagnosed through routine care. Further variations of model parameters during each sensitivity analysis demonstrated that the costs of AF screening could be 31-57% lower if all individuals with newly detected AF were initiated on warfarin rather than the DOAC therapy (Lowres *et al.* 2014; Tarride *et al.* 2017). Similarly, Lowres *et al.* (2014) ascertained that the costs of pharmacist-led AF screening could be reduced by another 35% where adherence to OAC therapy was maximised from 55% to 80%.

The quality of the two economic evaluations was overall largely comparable (**Appendix 7)**. Both studies provided a well-defined question and a comprehensive description of the economic model, including the alternative scenario, relevant costs, parameters and outcomes, which were evaluated during multiple sensitivity analyses. Neither of the studies appeared to consider the additional costs of inconclusive or unreadable diagnoses produced by $_{SL}$ECG devices, which may warrant unnecessary $_{12L}$ECG appointments, thereby likely underestimating the real-world cost of each intervention. The study by Lowres *et al.* (2014) did not specify the costs of OAC-related haemorrhages or the overall likelihood of cost-effectiveness. It was also limited by the non-inferiority assumption concerning the clinical effects of DOACs vs. warfarin. This may explain a larger gap between the costs of DOAC- and warfarin-dominated models (57%) than observed in the study by Tarride *et al.* (2017) (31%), which was built using the contemporary data displaying the clinical benefits of DOACs over warfarin (Ruff *et al.* 2014). The latter economic evaluation however did not consider the sensitivity or specificity of the $_{SL}$ECG device, which were taken into account by

Lowres *et al.* (2014), and instead relied heavily on the PPV value derived from unpublished data. This may have overlooked the rate of false negative AF diagnoses, thus potentially overestimating the economic benefits. Tarride *et al.* (2017) also did not account for the costs of manual $_{SL}$ECG interpretation by technicians, nor did it report the costs of follow-up appointments with GPs and clinical specialists. The probabilities of clinical events (ischaemic stroke/major bleeding) included in this study were extracted from the general AF population (Friberg *et al.* 2012) and might not have accurately reflected those amongst individuals with incidentally detected AF which were considered by Lowres *et al.* (2014).

Qualitative research

Two out of three manuscripts with a qualitative research component evaluated the aforementioned AF screening programmes (Lowres *et al.* 2014; da Costa *et al.* 2020). The qualitative evaluation by Lowres *et al.* (2015) conducted individual semi-structured interviews with nine pharmacists from 10 community pharmacies participating in the SEARCH-AF initiative in order to ascertain their experience of implementing the novel AF screening service. Similarly, the mixed-methods study by da Costa *et al.* (2020) carried out the interviews with all co-ordinators of the early AF detection programme in multiple countries and across several settings to explore the enablers and barriers to the initiative undertaken during the AF awareness campaign. The third article utilised individual semi-structured and focus group interviews with multiple stakeholders (service users, pharmacists/pharmacy owners, non-pharmacist HCPs and PPO representatives; n = 19) to facilitate the co-design of a new community pharmacy service for the self-monitoring/screening of AF and hypertension using a mBPM (Sabater-Hernandez *et al.* 2018). All three studies followed a standard protocol to audio-record and transcribe the interviews. Qualitative data was then analysed by two to three researchers using the inductive grounded theory (Lowres *et al.* 2015; da Costa *et al.* 2020) or thematic analysis (Sabater-Hernandez *et al.* 2018) approaches, which are commonly employed in the development and evaluation of new health services or practices (Benzer *et al.* 2012; Valley & Stallones 2018). In each case, the final themes/sub-themes were discussed and agreed by at least three authors.

All three qualitative data analyses suggested that pharmacists were comfortable and willing to engage in AF screening as an enhanced role within the existing community pharmacy service bundle. Most stakeholders, including patients (customers) and GPs, were supportive of pharmacist-led AF screening in community pharmacies – a crucial facilitator of successful AF screening programmes mentioned by all three studies. A minority of pharmacists interviewed by each of the studies reported or predicted a degree of scepticism

and resistance from patients, GPs or cardiologists with regards to their unconventional, non-pharmaceutical role of AF screening. Adequate professional relationships between pharmacists and GPs were therefore deemed by all studies to be of paramount importance in ensuring effective referrals and follow-up care of individuals with screening-detected abnormalities. Two qualitative evaluations suggested that AF screening initiatives themselves may help improve the relationships between pharmacists and patients/GPs whilst raising the profile of community pharmacy services amongst the general public (Lowres *et al.* 2015; da Costa *et al.* 2020). According to stakeholders interviewed by Lowres *et al.* (2015) and Sabater-Hernandez *et al.* (2018), proactive AF screening initiatives by pharmacists may also increase the inadequate public awareness of AF and its risks. A *'layered approach'* to AF and screening promotion were proposed by these two studies generally consisting of the distribution of cardiovascular organisation-approved advertising materials, a direct contact with pharmacy staff and health promotion events. Stakeholders involved in all three studies highlighted the importance of providing clear and simple explanations regarding AF and the screening process, for instance by avoiding text-dense booklets or medical jargon. The educational role of pharmacists was valued by themselves and other stakeholders in this context and as an asset to explaining the AF screening results, particularly where initial screening was to take place at home. This model of self-monitoring or screening for AF and hypertension using an mBPM (over 2-4 weeks) was generally welcomed by patients who were unafraid of obtaining a positive diagnosis at home, although some HCPs raised their concerns over the inaccuracy of currently available mBPMs and the need for a further ECG (Sabater-Hernandez *et al.* 2018). Screening with the KMD was perceived as a quick and simple option by pharmacists who were motivated by the identification of 'new' AF cases (da Costa *et al.* 2020), and also used the instant trace as an engaging educational tool for individuals participating in the service (Lowres *et al.* 2015). A number of less tech-savvy pharmacists experienced difficulties getting used to the technology (Lowres *et al.* 2015) which was more positively received by younger, technologically aware individuals than the older and possibly more at-risk population (da Costa *et al.* 2020).

In two studies, AF screening was trialled by community pharmacists as an add-on service to medication reviews or the CVD risk factor screening package, for instance the checks for hypertension or hypercholesterolaemia, which increased the service efficiency and patient/pharmacist satisfaction (Lowres *et al.* 2015; da Costa *et al.* 2020). Similarly, stakeholders interviewed by Sabater-Hernandez *et al.* (2018) supported the combined AF-hypertension self-screening/monitoring service (with pharmacy/GP follow-up) which should prioritise individuals aged ≥ 65 years with hypertension (with/without AF or previous stroke).

The role of the *'local champion'* was perceived by country co-ordinators of the early AF detection programme as *'instrumental'* to the design and development of such combined AF screening-CVD services in community pharmacies (da Costa *et al.* 2020). The primary barrier which might prevent the future implementation of pharmacist-led AF screening in community pharmacies and was mentioned by stakeholders of all three studies included the lack of appropriate remuneration or financial constraints. Lowres *et al.* (2015) and Sabater-Hernandez *et al.* (2018) also identified the possible issues of excessive workload/inadequate staffing levels and, for some pharmacies, the lack of private consultation area. The upskilling of other pharmacy staff, such as pharmacy technicians or assistants, to lead the service promotion and initial screening was seen as a possible workforce solution (Lowres *et al.* 2015), however stakeholders interviewed by Sabater-Hernandez *et al.* (2018) did not support this model and instead suggested involving a pharmacy-visiting nurse practitioner.

The quality of all three qualitative investigations included in this review was similar (**Appendix 8**). All three studies were designed and executed using the appropriate, aforementioned qualitative research methodologies, accompanied by the frequently used data collection methods of individual semi-structured and focus group interviews (Breen 2006; Adams 2015). They also provided a comprehensive description of the ethical approval, research question/aims, data analysis/interpretation and relevant conclusions. None of the articles indicated the philosophical perspective or epistemological position underlying their respective studies which may have steered their analysis and conclusions in different directions (Giddings & Grant 2006), although da Costa *et al.* (2020) shared the details of the theoretical hypothesis that guided data analysis. Despite the detailed outline of data collection and analysis, none of the studies described the specific cultural/theoretical perspectives of researchers involved or provided any information about their reflexive accounts. Considering the professional background or other characteristics of researchers participating in each study, this deficiency might have introduced a bias into data analysis and limited the confirmability of findings by other researchers (Lincoln & Guba 1985b; Tong *et al.* 2007). The studies Lowres *et al.* (2015) and da Costa *et al.* (2020) also focused entirely on the qualitative evaluation of pharmacists' perspectives and did not interview any other stakeholders, such as patients or GPs, thereby limiting the value of feedback from these two stakeholder groups which was instead indirectly voiced by pharmacists. Sabater-Hernandez *et al.* (2018) provided a triangulated account of qualitative interviews with multiple stakeholder groups. Nevertheless, the qualitative data derived from a heterogeneous multi-stakeholder focus group interview was limited by the risk of power or hierarchical relationships, either between different HCPs or between them and service

users, which might have prevented some of the less confident individuals from expressing their true views or opinions (Krueger & Casey 2000c; Hofmeyer & Scott 2007). This study also involved only one GP, nurse practitioner and cardiologist each, and whilst the sample size may not be as crucial in qualitative research, an adequate caution should be applied when transferring the findings of this study to a wider context of population-wide service development (Lincoln & Guba 1985b).

1.3.4 Discussion and rationale for the enquiry

This scoping review aimed to retrieve and depict the evidence pertaining to pharmacist-led AF screening or detection in primary care settings, focusing on community pharmacies and general practice. The literature search and review identified a total of 13 records, all published in the last six years, which could be further subdivided into cross-sectional, diagnostic accuracy, economic and qualitative research studies. The majority of these studies were conducted in the developed, ageing Western societies of Europe, North America and Australia where AF and its consequences had been identified as a growing public health epidemic (Chugh *et al.* 2014b), and where pharmacists may provide additional workforce to alleviate the pressures faced by other primary care HCPs, such as nurses or GPs (NHS England and BMA 2019c). Most evidence generated by studies included in this review supported AF screening in community pharmacies and by community pharmacists, which is in line with the Government's focus to establish community pharmacies as centres of healthy living and CVD prevention (NHS England 2019d; Department of Health and Social Care 2019). The AF screening strategies were typically either single time point opportunistic or population-based, and were aimed at individuals aged ≥ 65 years (with or without risk factors), thus mostly conforming with international medical/scientific consensus (Kirchhof *et al.* 2016; Freedman *et al.* 2017). Nearly all studies utilised modern AF detection methods, such as $_{SL}$ECG devices and mBPMs, showing a clear shift in practice from earlier GP surgery-based AF screening initiatives (Morgan & Mant 2002; Hobbs *et al.* 2005) which employed historic and possibly less accurate pulse palpation (Taggar *et al.* 2016a). During the diagnostic accuracy studies appraised here, pharmacist- or student-operated KMD algorithm showed both high sensitivity (91-100%) and specificity for AF detection (91-99%) which were not far from the 98% and 97% respective values observed in the algorithm validation study (Lau *et al.* 2013), and were overall above those for pulse palpation (77% and 93%, respectively) (Lowres *et al.* 2014; Zaprutko *et al.* 2019).

Whilst affected by significant methodological heterogeneity, the prevalence data overall demonstrated that pharmacists or pharmacy students/other pharmacy staff were capable of effectively using modern technology to identify 'new' AF in approximately 1.3-2.4% of

individuals undergoing single time point screening in community pharmacies (Lowres *et al.* 2014; Sandhu *et al.* 2016; Twigg *et al.* 2016; Zaprutko *et al.* 2019; da Costa *et al.* 2020). This range of $_{SL}$ECG-confirmed yields was somewhat below the 2.6-3.8% reported for intermittent AF screening strategies in primary care or community settings (Halcox *et al.* 2017; Svennberg *et al.* 2015; Kemp Gudmundsdottir *et al.* 2019), however reflected the 1.4% yield of 'new' AF with single time point screening computed by Lowres *et al.* (2019) and the 1.1-1.5% $_{SL}$ECG yields of AF detected by nurses or GPs in general practice (Kearley *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019b). The yields of 'new' AF were even higher in a nursing home (13.0%), hospital outpatient clinics (7.2-9.9%) or day care centres (7.2%), possibly reflecting the overall older and/or higher-risk populations (Cunha *et al.* 2020; da Costa *et al.* 2020).

More important than the yield itself was the fact that most individuals with 'new' AF identified through pharmacist-led screening initiatives displayed a sufficiently high risk of stroke to benefit from OAC therapy (Lowres *et al.* 2014; Zaprutko *et al.* 2019; Anderson *et al.* 2020). The SEARCH-AF and PIAAF-Pharmacy screening programmes in community pharmacies were also cost-effective at a cost of approximately £1,900-4,600/QALY gained (Lowres *et al.* 2014; Tarride *et al.* 2017), placing them below the commonly used WTP thresholds (NICE 2012a). Besides the quantitative considerations, the concept of community pharmacist-led AF screening was widely welcomed by all stakeholder groups, including the prospective service users, other HCPs and pharmacists themselves (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020). The educational skillset of pharmacists appeared to be particularly valuable in raising the inadequate public awareness of AF and in explaining the test results at the time when modern technology could otherwise enable self-screening (Lowres *et al.* 2015; da Costa *et al.* 2020). The success of pharmacist-led AF screening during AF awareness campaigns (Antoniou *et al.* 2017; Cunha *et al.* 2020; da Costa *et al.* 2020) suggests that these HCPs could successfully combine the health awareness and testing responsibilities, and that PPOs and professional organisations may indeed have a role in promoting the service as well as the public health profile of pharmacists (Mairesse *et al.* 2017).

Few of the initiatives included in this review reported follow-up data which was overall defined by relatively low yields of AF after a $_{12L}$ECG (0.3-1.0%). This may reflect deficiencies in the referrals from community pharmacies to GP surgeries, which appear to occur in only 20-24% of the referred participants (Sandhu *et al.* 2016; da Costa *et al.* 2020). The inadequate follow-up may in turn be a consequence of either intrinsically poor communication between GPs and community pharmacists or the lack of an established

referral pathway, which were both highlighted as potential barriers to effective AF screening in community pharmacies by qualitative studies (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020). It was therefore not surprising that the one-stop clinic approach, incorporating a clear referral pathway from community pharmacies to specialists, produced perhaps the most promising yield of 'new' and anticoagulated AF (1.6%) (Antoniou *et al.* 2019). This initiative also ensured that a further 1.2% of individuals with known AF who were not receiving OAC therapy were prescribed the treatment accordingly, demonstrating the role of community pharmacists in simultaneous AF screening and medicines optimisation (Antoniou *et al.* 2019). Four of the AF screening programmes discussed here reported at least some success of combining opportunistic AF detection with either medication reviews or the wider CVD screening approach (Lowres *et al.* 2015; Sandhu *et al.* 2016; Twigg *et al.* 2016; da Costa *et al.* 2020). This model ties in well with the Government's *'cardiovascular ABC'* agenda (Public Health England 2019c), and as proposed by da Costa *et al.* (2020), may be facilitated by strong leadership from *'local champions'*. Similar concepts of the AF *'screening champion'* had previously been proposed in general practice, where the leadership of GPs and senior nurses, had led to increased practice engagement with the initiative (Orchard *et al.* 2016; Orchard *et al.* 2019b; Orchard *et al.* 2019a).

Apart from the classic resistance to new services in clinical settings (LeTourneau 2004), AF screening in community pharmacies may face numerous other barriers which were identified by stakeholders of qualitative studies captured by this review: from public misconceptions about the role of pharmacists and privacy concerns to financial constraints, a high dispensing workload and inadequate staffing (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020). Financial constraints may be overcome through appropriate funding schemes, such as the local commissioning of NHS Health Checks in community pharmacies (PSNC 2020a), although a centralised approach, perhaps similar to pharmacy-led seasonal influenza vaccinations may ensure a consistent service provision (PSNC and NHS England 2019). In turn, the rapid development of pharmacy technicians' roles (Boughen *et al.* 2017; Savickas *et al.* 2020a) may help address the workload concerns through a two-step AF screening service, whereby the initial screening is performed by technical support staff followed by a consultation with the pharmacist. On the other hand, as shown by Sabater-Hernandez *et al.* (2018) this model may not necessarily be viewed favourably by other HCPs or the public due to concerns about the qualifications of non-pharmacist staff. It may also exacerbate the pre-existing confusion about the roles of pharmacists and other community pharmacy personnel, which

is already affecting the public's trust in clinical community pharmacy services (Gidman *et al.* 2012; Kelly *et al.* 2014; Lowres *et al.* 2015).

Overall, whilst limited by its scoping methodology and the lack of detailed synthesis, cumulative evidence presented by this review suggested that pharmacists (and in some cases other pharmacy staff/students) were capable of conducting opportunistic or population-based AF screening in community pharmacies and possibly other primary care or community settings. The screening was largely enabled by modern AF detection tools, such as $_{SL}$ECG devices, which facilitated accurate, effective, cost-effective and well-accepted AF services, offering opportunities for patient education and raising the profile of pharmacists as clinically qualified HCPs. The barriers to AF screening in community pharmacies identified here may be addressed through the improved utilisation of pharmacy support staff and the concerted effort of local champions and the Government. They also urge a further qualitative exploration involving a larger number of non-pharmacist stakeholders, such as service users, GPs, nurses and cardiologists, to help understand the mechanisms underlying each barrier, and to facilitate the future development of pharmacist-led AF screening programmes.

The findings of this scoping review raised several other questions for future research. First of all, as is generally the case for AF screening, none of the studies analysed here had investigated the direct impact of pharmacist-led screening interventions on clinical endpoints, such as all-cause mortality or stroke. Additional adequately powered studies are therefore warranted to determine the long-term clinical and economic value of pharmacist-led AF screening programmes in primary care. The conduct of a full systematic review targeting this area of research may be delayed until the results of such studies become available. Although most studies evaluated during this review focused on AF screening in community pharmacies, a number of recent pharmacist-led initiatives were conducted in other settings (Cunha *et al.* 2020; da Costa *et al.* 2020; Anderson *et al.* 2020), suggesting that pharmacists or other pharmacy staff may be equally able to deliver AF screening outside the traditional retail environment. The numbers of participants recruited in these settings, particularly care homes, have however to date been limited and further larger-scale investigations with adequate follow-up are required to ascertain the benefits and risks of pharmacist-led AF detection outside community pharmacies.

The England-wide integration of practice-based CPs within the PCNs (NHS England and BMA 2019c) offers them access to several population groups who may be at risk of AF and stroke, such as those with long-term illnesses (Ball *et al.* 2013) and/or care home residents

(Gordon *et al.* 2014). An enquiry into this rapidly evolving role of primary care pharmacists and the feasibility of them conducting AF screening in GP surgeries, care homes or other primary care/community settings as part of their service portfolio may therefore be both timely and valuable. Following an example set by the SEARCH-AF study in Australia (Lowres *et al.* 2014; Lowres *et al.* 2015), such a UK-based enquiry should involve a mixed-methods approach to determine the recruitment success, the screening effectiveness/cost-effectiveness and the acceptability of the CP-led intervention. A qualitative research component involving different stakeholder groups may provide a comparison of facilitators and barriers to community pharmacist-led AF screening outlined above, and may give an indication of whether or not any of them are transferrable to other primary care settings, such as GP surgeries. A number of possible options for the design of the AF screening service may be evaluated during the enquiry, either involving a combined opportunistic/targeted AF-CVD screening approach (Lowres *et al.* 2015; da Costa *et al.* 2020) or an opportunistic/population-based AF detection during the age-matched seasonal influenza vaccinations as previously described (Orchard *et al.* 2016; Kaasenbrood *et al.* 2016). A comparison of AF detection rates and diagnostic accuracy using different methods, including the conventional pulse palpation and $_{SL}$ECG devices, may provide additional feasibility data and may help determine the most optimal tool for the future routine AF screening in different primary care settings.

1.4 Overview and aims of the thesis

This PhD enquiry builds on the gaps of research evidence delineated above and explores the role of UK primary care CPs in the screening and detection of AF outside the community pharmacy setting. The thesis is divided into eight chapters. It began with an introduction to the enquiry set out above (**Chapter 1**) which is followed by the outline and appraisal of the underlying research methods (**Chapter 2**). The subsequent five chapters provide both quantitative and qualitative research evidence in support of CP-led AF screening services. **Chapters 3-5** relate to the mixed methods **P**harmacists **D**etecting **AF** (PDAF) study which was conducted in GP surgeries (**Chapters 3 and 4**) and care homes (**Chapter 5**), and evaluated the effectiveness, cost-effectiveness and acceptability of CP-led AF screening of the ≥ 65-year-old population eligible for seasonal influenza vaccinations. **Chapter 6** describes a study which investigated the feasibility of an AF screening intervention delivered by pharmacy students under the supervision of CPs within a South Asian community setting. **Chapter 7** includes the results of a qualitative study with GPs which aimed to ascertain their views about the national AF screening programme, thereby providing a broader perspective of how CP-led AF screening services may be developed and integrated within the existing healthcare infrastructure. The final **Chapter 8** offers a summary of key

findings in light of pre-existing literature whilst considering the implications of the enquiry for clinical practice, policy and future research.

The overarching aim of this thesis was to investigate the role of primary care CPs in the detection and screening of AF outside the community pharmacy setting. With reference to the results chapters described above, this aim was split into five aims corresponding to individual chapters:

1) To assess the feasibility, accuracy and economic impact of CP-led AF screening in GP surgeries using either pulse palpation or $_{SL}$ECG during the influenza vaccination season (**Chapter 3**).
2) To explore the facilitators and barriers to the development and implementation of the CP-led AF screening strategy in GP surgeries from the perspectives of patients, CPs and general practice staff (GPS) participating in the PDAF study (**Chapter 4**).
3) To assess the feasibility, accuracy and economic impact of CP-led AF screening in care homes using either pulse palpation or $_{SL}$ECG during the influenza vaccination season (**Chapter 5**).
4) To assess the feasibility, accuracy and economic impact of AF screening using $_{SL}$ECG delivered by trained pharmacy undergraduates under the supervision of a CP at places of worship of a selected South Asian community (**Chapter 6**).
5) To explore the perspectives of UK-based GPs in relation to the national AF screening programme, focusing on the facilitators and barriers to its development and implementation (**Chapter 7**).

The objectives underlying each of these aims are provided in respective chapters.

Chapter 2: Methods

2.1 Introduction

This chapter provides an overview of general materials and methods employed during the component research studies of this thesis in order to address the aims and objectives outlined in section **1.4**. It begins with an introduction to health services research and the underpinning Medical Research Council's (MRC) guidance for *'Developing and evaluating complex interventions'* (MRC 2006), explaining its application to this research project. That is followed by an overview of the component study design, sampling and data collection alongside the methods for data analysis, economic modelling and ethical considerations. The rationale for each method is provided with reference to pre-existing research evidence, while critically appraising the selection of other alternative options. The summary of methods used during each of the component studies of this enquiry is provided in **Table 2.1**. The detailed materials and methods, including the specific participant eligibility criteria or outcome measures, are discussed under the Methods section of each subsequent chapter.

2.2 Health services research and MRC guidance for complex interventions

The fundamental methodologies and underlying methods utilised during this project were constructed around the broad definition of research compiled by Bowling (2014) as follows:

'The systematic and rigorous process of enquiry which aims to describe phenomena and to develop and test explanatory concepts and theories' […] 'to contribute to a scientific body of knowledge.'

The key phenomenon investigated by this enquiry included the role of primary care CPs in the detection of AF. In turn, several broad explanatory concepts or theories were developed and tested as part of constituent studies:

- The feasibility, accuracy and economic impact AF detection by CPs in general practice (**Chapter 3**) or care home (**Chapter 5**) settings
- The facilitators and barriers to AF detection by CPs in general practice setting from the perspectives of multiple stakeholders (**Chapter 4**)
- The diagnostic accuracy of $_{SL}$ECG devices over conventional pulse palpation in the detection of AF (**Chapters 3 and 5**)
- The feasibility, accuracy and economic impact of AF detection by non-pharmacist staff (pharmacy undergraduates) under the CP's supervision (**Chapter 6**)

- The feasibility of AF detection within a South Asian community by individuals of South Asian ethnicity (**Chapter 6**)
- The facilitators and barriers to the development of the national AF screening programme from the perspectives of GPs (**Chapter 7**).

It was anticipated that the findings would contribute towards the evidence base to support the development of a national AF screening or detection programme.

In order to focus on the development and evaluation of health services, this enquiry strived to investigate *'the relationship between the provision, effectiveness and efficient use of health services and the health needs of the population'* (Bowling 2014). The sheer complexity of this aim means that research into health services often employs a *'mixed-methods'* approach consisting of quantitative and qualitative research methods (O'Cathain *et al.* 2007; Zhang & Creswell 2013). Methodologies utilising the quantitative and qualitative research methods historically stemmed from two main philosophical perspectives or epistemological positions of positivism and interpretivism/constructivism, respectively (Giddings & Grant 2006). The positivist paradigm is concerned with objective reality and causal relationships, thus typically matching the hypothesis-testing questions of quantitative research (Sale *et al.* 2002). In contrast, the interpretivist/constructivist paradigm assumes a subjective reality, and aims to understand the individual's experience thereby fitting the exploratory profile of qualitative research (Sale *et al.* 2002).

The comprehension of these two philosophical positions enables an appreciation of how quantitative and qualitative research methods may complement each other in helping understand the research phenomenon, such as a complex health service (Giddings & Grant 2006; O'Cathain *et al.* 2007), through the process referred to as the methods triangulation (Patton 1999). For instance, patients suffering from depression may show a promising improvement in their depression or anxiety scores following a mindfulness course (quantitative/positivist component), however semi-structured interviews with them may reveal that treatment could be even more effective if a follow-up appointment was arranged (qualitative/interpretivist component) (Finucane & Mercer 2006).

Table 2.1 Summary of methods used during each component study of this enquiry

Abbreviations: PDAF – Pharmacists Detecting Atrial Fibrillation; GP – general practitioner; AF – atrial fibrillation; CP – clinical pharmacist; ECG – electrocardiogram; TDF – theoretical domains framework, CCG – clinical commissioning group.

Study (chapter)	Aims	Research method (epistemological position)	Study design	Sampling frame	Data collection methods (instruments)	Data analysis
PDAF in GP surgeries (Chapter 3)	Feasibility, accuracy and economic impact of CP-led AF screening in GP surgeries	Quantitative (positivism)	Cross-sectional diagnostic accuracy study	GP records of individuals aged ≥ 65 in participating surgeries	Pulse palpation, single-lead ECG and feedback questionnaires	Demographic analysis, diagnostic accuracy analysis, descriptive and content analysis of questionnaires, Markov economic model
PDAF in GP surgeries (Chapter 4)	Facilitators and barriers to development/ implementation of CP-led AF screening strategy from multi-stakeholder perspectives	Qualitative (interpretivism/ constructivism)	TDF-based qualitative study	All individuals participating in PDAF screening	Focus group interviews	TDF-based data analysis of facilitators and barriers

PDAF in care homes (Chapter 5)	Feasibility, accuracy and economic impact of CP-led AF screening in care homes	Quantitative (positivism)	Cross-sectional diagnostic accuracy study	List of care home residents aged ≥ 18 registered with surgeries participating in PDAF study	Single-lead ECG	Demographic analysis, diagnostic accuracy analysis, Markov economic model
AF screening with a South Asian community (Chapter 6)	Feasibility, accuracy and economic impact AF screening delivered by pharmacy undergraduates under CP's supervision within a South Asian community	Quantitative (positivism)	Cross-sectional diagnostic accuracy study	British Indian individuals ≥ 18 years attending selected Gurdwaras	Single-lead ECG and feedback questionnaires	Demographic analysis, diagnostic accuracy analysis, descriptive and content analysis of questionnaires, Markov economic model
Perspectives of GPs on AF screening programme (Chapter 7)	Facilitators/barriers to development/ implementation of national AF screening programme from GP perspectives	Qualitative (interpretivism/ constructivism)	TDF-based qualitative study	List of GPs reachable via the research team contacts in GP surgeries and CCGs	Individual semi-structured interviews	TDF-based data analysis of facilitators and barriers

The widely-accepted triangulation of mixed methods has also been advocated for in the MRC guidance for complex interventions (MRC 2006), which applies to the majority of health services research (Craig *et al.* 2008). The MRC defines *'complex interventions'* as *'interventions that contain several interacting components'* which may have *'several dimensions of complexity'* for example *'the range of possible outcomes, or their variability in the target population'* (MRC 2006; Craig *et al.* 2008). An intervention such as AF detection or screening service can be considered complex due to the presence of multiple possible outcomes (e.g. SR, AF or other diagnoses), the multitude of detection methods or their administration by different types of staff, the variability in the nature of consultations with patients, the dynamic environment of the intervention delivery or the selection of the target population itself (e.g. those aged ≥ 65 compared to those aged < 65 years). The recognition of this complexity has led to a shift in the MRC stance towards complex intervention research from the linear model of design and evaluation commonly used by RCTs of medicines (Campbell *et al.* 2000) to a semi-flexible cyclical framework, placing a greater emphasis on the *'early phase piloting and development work'* (MRC 2006; Craig *et al.* 2008). The purpose of this relatively fluid approach is to refine the intervention in an appropriate context by moving between the initial development, feasibility/piloting and evaluation stages, therefore maximising the likelihood of real-life success and minimising the risk of failure upon implementation (MRC 2006; Craig *et al.* 2008).

As recommended by the MRC guidance, this enquiry began with the development of the intervention (AF detection using pulse palpation/$_{SL}$ECG by CPs), which included identifying the best available evidence or gaps in such evidence through a comprehensive literature review (**Chapter 1**), followed by the modelling of process for AF detection and measures of possible outcomes to design a fundamental study protocol (Veale *et al.* 2018) (**Figure 2.1**). The feasibility/piloting and initial evaluation stages of quantitative or positivism-driven research then ensued to test the protocol, to estimate the recruitment rate/efficiency/sample size and predicted outcomes, and to evaluate the preliminary effectiveness and economic impact of the intervention in various care settings (**Chapters 3, 5 and 6**). This was accompanied by the qualitative or predominantly interpretivist components of the enquiry in either concurrent/convergent (**Chapter 4**) or sequential (**Chapter 7**) manner (Giddings & Grant 2006; Tariq & Woodman 2013) to help understand the processes or behaviours involved and to assess the acceptability of the intervention from the perspectives of multiple stakeholders. The findings of each component study were iteratively used to refine the intervention (for example, by optimising the AF detection protocol), and to identify the key areas for future research, thus repeatedly returning back to the development element of the MRC framework.

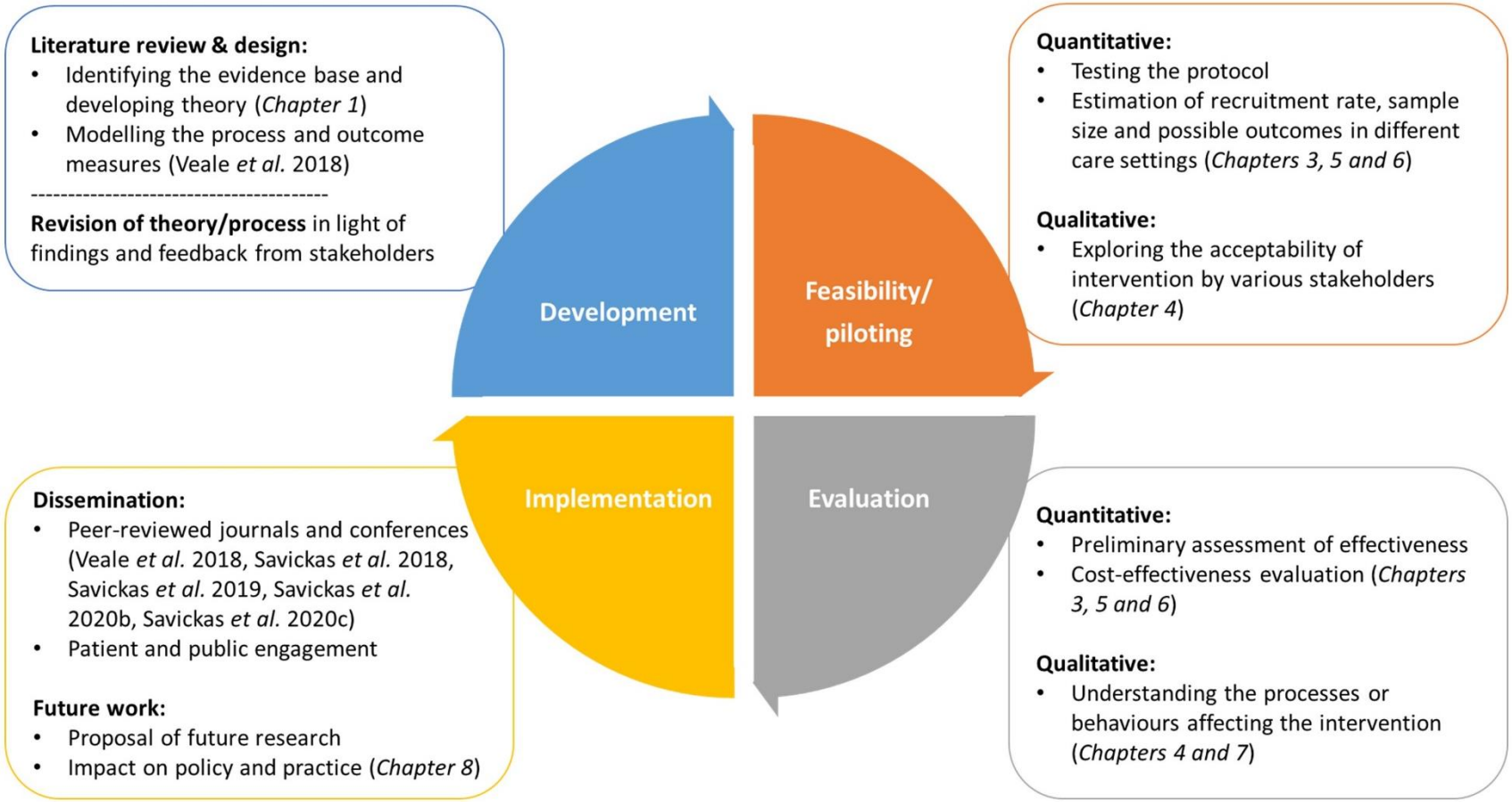


Figure 2.1 Mixed research methods employed in the development and evaluation of the complex intervention at the centre of this research enquiry/thesis

The figure is mapped onto the four elements of the Medical Research Council's (MRC) guidance for complex interventions (MRC 2006; Craig et al. 2008). References are made to each chapter of the thesis under the relevant elements of MRC guidance.

The implementation element of this enquiry involved an active dissemination of the protocol and findings through scientific journals and international conferences (Veale *et al.* 2018; Savickas *et al.* 2018; Savickas *et al.* 2019; Savickas *et al.* 2020b; Savickas *et al.* 2020c). The study documentation and results of the project were also regularly presented to lay audiences and the Medway School of Pharmacy (MSOP) Patient Involvement in Pharmacy Studies (PIPS) group, the feedback of which together with scientific peer-review, facilitated the ongoing element of development. It was anticipated that this MRC guidance-driven approach, which places a significant focus on the development and feasibility of the intervention, will provide the necessary, in-depth evidence base for a future large-scale, effectiveness-focused RCT (discussed in more detail in section **8.5**).

2.3 Research quality

In order to ensure the quality of research, all studies were designed, delivered and reported in line with appropriate guidelines and checklists for respective study designs provided by the internationally-recognised **E**nhancing the **QUA**lity and **T**ransparency **O**f health **R**esearch (EQUATOR) network (EQUATOR Network 2020). All three quantitative studies (**Chapters 3, 5 and 6**) were carried out according to the **S**tandards for **R**eporting of **D**iagnostic **A**ccuracy **S**tudies (STARD) guidelines (Cohen *et al.* 2016). The two qualitative studies (**Chapters 4 and 7**) were conducted in conjunction with the **Co**nsolidated Criteria for **Re**porting **Q**ualitative (COREQ) studies (Tong *et al.* 2007).

Apart from considerations included in the guidelines, each aspect of quantitative research methods was critically appraised for potential sources of bias and their impact on internal or external validity of study findings (Delgado-Rodriguez & Llorca 2004):

- *Internal validity* is concerned with the accuracy of statements about causal relationships between the variables, and is an extent to which study results represent the truth and are not due to methodological errors or bias (Leighton 2010b; Patino & Ferreira 2018).
- *External validity* or generalisability relates to an extent to which study findings are generalisable beyond the study sample, especially with regards to the target population it should represent (Leighton 2010a; Patino & Ferreira 2018).

The strategies for addressing some of the threats to internal or external validity that were applied during this enquiry are summarised in **Table 2.2**, and are discussed in relevant sections below. In addition, the concept of reliability, which relates to the precision or consistency of repeated measurements and is a prerequisite to adequate internal validity

(Gushta & Rupp 2010), is referred to when reflecting on various aspects of statistical analyses. The concept of content validity is in turn referred to when discussing the development of study documentation and feedback questionnaires, and may be defined as an assessment of *'whether or not the content of the manifest variables'* (e.g. questionnaire items) are *'right to measure the latent concept'* (e.g. GP views about AF detection) (Muijs 2011). The sub-concept of content validity described as face validity, or the assessment of *'whether the instrument or test looks valid'*, is referred to alongside (Muijs 2011).

The methodological rigor of qualitative research methods was maintained by applying the widely-used Lincoln and Guba's evaluative criteria for qualitative research (Lincoln & Guba 1985b; Nowell *et al.* 2017; Forero *et al.* 2018). These standards emphasise the trustworthiness of research which is defined as a way for a researcher to *'persuade his or her audiences (including self) that the findings of an inquiry are worth paying attention to'* (Lincoln & Guba 1985b). In turn, the trustworthiness is described as a composite of the four-dimensional criteria:

- *Credibility* – confidence that the results are true, credible and believable (an equivalent of internal validity)
- *Confirmability* – an extent to which researcher's interpretations and findings are clearly derived from the data and could be confirmed by other researchers
- *Dependability* – consistency or repeatability of findings in the same cohort of participants, researchers and context (an equivalent of reliability) and
- *Transferability* – a degree to which the findings can be generalised or transferred to other contexts or settings (an equivalent of external validity) (Lincoln & Guba 1985b; Nowell *et al.* 2017; Forero *et al.* 2018).

Similar to quantitative studies, these criteria are referred to when appraising the selection of methods for qualitative research below. The strategies used to ensure that qualitative research methods addressed these criteria are discussed where appropriate.

Table 2.2 Strategies used to ensure the quality of research included in this enquiry

Adapted from: Lincoln & Guba (1985b); Patton (1999); Delgado-Rodriguez & Llorca (2004); Currivan (2004); Leighton (2010a); Leighton (2010b); Whiting et al. (2013); Schmidt & Factor (2013); Krueger & Casey (2015); Nowell et al. (2017); Forero et al. (2018); Waterfield (2018); Patino & Ferreira (2018); DeJonckheere & Vaughn (2019).

Quality Criteria	Strategies Applied
Quantitative research studies (Chapters 3, 5 and 6)	
Internal validity	Adjustment for confounding factors (e.g. age)
	Single reference standard for all diagnostic accuracy studies to reduce partial/differential verification bias
	Timely reference standard to reduce disease progression bias
	Process/documentation training to reduce observer/interviewer bias
	Index test training to reduce misclassification bias
	Piloting study documentation to ensure face validity
External validity (generalisability)	Selection of sampling frame to maximise the coverage
	Recruitment in multiple areas or sites
	Multiple promotion/recruitment strategies to reduce non-response bias
	Recruitment of groups with limited access to conventional healthcare (care home residents and South Asian individuals)
	Use of appropriate written or spoken language/translation
Qualitative research studies (Chapters 4 and 7)	
Credibility	Training of interview facilitators
	Piloting topic guides
	Maintaining field notes (source triangulation)
	• Data from multiple stakeholders (source/theory triangulation) • Data analysis by multiple researchers with different perspectives (analyst/theory triangulation)
Confirmability	
	Audit trail (field notes, reflexive account, intermediate themes)
Dependability	Use of pre-established protocols
	Training of researchers to become familiar with study protocols
	Systematic approach to data collection and analysis
Transferability	Description of phenomenon from several dimensions ('thick description')
	Reaching data saturation

2.4 Summary of study design

Considering the MRC guidance (MRC 2006; Craig *et al.* 2008), this enquiry placed a heavy emphasis on establishing and exploring the feasibility of the intervention proposed, i.e. AF detection by primary care CPs. For the purpose of this enquiry, the definition of a *'feasibility study'* was adapted from the NIHR guidance as *a 'study done in anticipation of a full-scale clinical trial, to test out different components of the methods or to provide information that will help with the trial's design* (NIHR 2019b). As recommended by the NIHR, the constituent feasibility studies included in this project were used *'to estimate important parameters that are needed to design the main study'*, such as the recruitment rate/sample size, the prevalence of the condition, the accuracy or anticipated economic impact of the diagnostic tests and the acceptability of the intervention in several care settings (NIHR 2019a). The qualitative and quantitative study designs selected to achieve these aims and objectives are presented and appraised below.

2.4.1 Quantitative studies

Cross-sectional study design

All three feasibility studies employing quantitative research methods (**Chapters 3, 5 and 6**) were based on the protocol for the PDAF study in GP surgeries developed by Veale *et al.* (2018). As such, all of them adopted a prospective, cross-sectional diagnostic accuracy study design (Thiese 2014), and a single-time point, systematic population AF screening strategy (Welton *et al.* 2017). The PDAF study in general practice (**Chapter 3**) targeted all individuals aged ≥ 65 years whereas the PDAF study in care homes (**Chapter 5**) and the study within the South Asian community setting (**Chapter 6**) screened those aged ≥ 18 years. In addition, some participants of the PDAF study in GP surgeries and care homes were offered opportunistic screening before or after their seasonal influenza vaccinations (Welton *et al.* 2017). Both single time point opportunistic and population-based screening strategies are equally as effective in identifying individuals with 'new' AF and are highly likely to be cost-effective (Welton *et al.* 2017).

During the PDAF studies in general practice and care homes, after cross-sectional screening participants with suspected AF or inconclusive diagnoses were also referred to their GP and actively followed up by the research team. The equivalent sub-groups of patients identified during the AF screening study within a South Asian community were given a referral letter and an optional follow-up outcomes form to post back but were not actively followed-up. One may postulate that this longitudinal element of the three studies concerned resembled that of a prospective cohort study design (Thiese 2014; Quinn *et al.*

2018). Contrary to “classic” cohort studies (Schnabel *et al.* 2009; Martinez *et al.* 2014), however only selected participants were followed-up for a short duration and at *ad hoc* times. Therefore, the format of data analysis during all three studies generally followed that of a cross-sectional study (Thiese 2014; Lowres *et al.* 2014).

As shown in **Table 2.3**, cross-sectional study design is an ethically-sound and inexpensive means of determining the point prevalence of a disease whilst enabling a simultaneous assessment of multiple outcomes (Thiese 2014; CEBM 2020). It is therefore an ideal study design for initial feasibility or pilot studies. Nevertheless, whilst less expensive and time-consuming than either RCTs or cohort studies, cross-sectional research is unable to demonstrate temporality (time-dependent, causal relationships) (Tripepi *et al.* 2010; Thiese 2014; CEBM 2016) and suffers from the prevalence-incidence (or Neyman’s) bias (Delgado-Rodriguez & Llorca 2004). This may for instance include a misleadingly low prevalence of short-lived conditions, such as paroxysmal AF (PAF), which may be undetected using a one-off screening approach. The cross-sectional prevalence of the condition may be further skewed by the non-response bias, for example the well-known *‘healthy volunteer’* effect whereby study participants are healthier and not representative of the less engaged but potentially more ill population (Delgado-Rodriguez & Llorca 2004; Froom *et al.* 1999). The two types of selection biases mentioned above may limit both internal validity and generalisability of study findings to the wider population (Leighton 2010b; Kalaian & Kasim 2011). Furthermore, the absence of randomisation in cross-sectional study design means that the internal validity of findings may be affected by the unequal distribution of confounders across the groups (e.g. participants with and without AF) (Delgado-Rodriguez & Llorca 2004; CEBM 2020). The correction for certain confounders may alleviate this shortcoming and was undertaken during a sub-group analysis of comorbidities pertaining to South Asian participants (**Chapter 6**).

Besides the general considerations of study design, the internal validity of cross-sectional demographic and feedback questionnaires completed during the three quantitative studies were subject to a degree of recall and reporting biases (Raphael 1987; Delgado-Rodriguez & Llorca 2004). For instance, some participants may have not recalled their comprehensive past medical history whereas others may have underreported their level of alcohol consumption leading to a potential under-representation of CVD risk factors.

Table 2.3 Advantages and disadvantages or biases of cross-sectional study design compared to randomised controlled trials and cohort studies

Adapted from: Raphael (1987); Froom et al. (1999); Delgado-Rodriguez & Llorca (2004); Tripepi et al. (2010); Thiese (2014); CEBM (2016); CEBM (2020). Abbreviations: CEBM - Centre for Evidence-Based Medicine; RCT – randomised controlled trial.

Study design	Advantages	Disadvantages/Biases
Cross-sectional studies	• simple and inexpensive • ethically safe • timely • determines point prevalence • can assess multiple outcomes	• no temporality • Neyman's bias • non-response bias • confounders may be unequally distributed • group sizes may be unequal • not ideal for rare diseases or those of short duration • recall bias • observer/interviewer bias
Randomised controlled trials (RCTs)	• capable of proving cause-effect relationships • unbiased distribution of confounders • blinding more likely • randomisation facilitates statistical analysis	• ethically problematic at times • expensive and time-consuming
Cohort studies	• administratively easier and cheaper than RCTs • ethically safe • subjects can be matched • can establish timing and directionality of events • can assess multiple exposures and outcomes	• controls may be difficult to identify • exposure may be linked to a hidden confounder • blinding is difficult • randomisation not present • not ideal for rare diseases

Last but not least, the fact that researchers assisted some of the participants when completing their questionnaires, reduced the internal validity of findings by introducing an observer/interviewer bias (Delgado-Rodriguez & Llorca 2004). As an example, this may have involved subconsciously placing an emphasis on certain questions of interest to the researcher, thus influencing the participants' responses to feedback questionnaires. Relevant training in completing study documentation which is discussed in section **2.6.1**, and in individual chapters, may have reduced the likelihood of such effects.

Diagnostic accuracy study design

The "sub-design" of a diagnostic accuracy study may be attached to either cross-sectional research (Lowres *et al.* 2014; Orchard *et al.* 2016; Chan *et al.* 2016), cohort studies (Quinn *et al.* 2018; Tison *et al.* 2018) or RCTs (Morgan & Mant 2002; Hobbs *et al.* 2005). Whilst affected by individual characteristics of these study designs critiqued above, diagnostic accuracy studies possess a number of distinct features which are presented in the STARD guidelines and should be considered alongside (Schmidt & Factor 2013; Cohen *et al.* 2016).

The first consideration relates to the appropriate selection of index tests and the reference standard (Cohen *et al.* 2016). The "parent" PDAF study in GP surgeries (**Chapter 3**) and care homes (**Chapter 5**) measured the diagnostic accuracy of two main index tests recommended for opportunistic screening of AF by the ESC (Kirchhof *et al.* 2016): the conventional pulse palpation and an ECG strip (in this instance, a $_{SL}$ECG). Similar to the Australian feasibility study in community pharmacies (Lowres *et al.* 2014), pulse palpation was administered first before proceeding with the $_{SL}$ECG recording which was then interpreted by an automated algorithm and CPs. The predicted diagnostic superiority of $_{SL}$ECG devices over pulse palpation indicated by the PDAF study (Savickas *et al.* 2020b) led to the exclusion of the latter test from the subsequent study within the South Asian community (**Chapter 6**). The reference standard selected for all three diagnostic accuracy studies was the cardiologist's interpretation of $_{SL}$ECG traces, which was previously utilised by numerous studies investigating the diagnostic accuracy of $_{SL}$ECG devices in the detection of AF (Lowres *et al.* 2014; Orchard *et al.* 2016; Chan & Choy 2016). Although in ideal circumstances, a cardiologist-interpreted $_{12L}$ECG recording would have been considered a perfect "gold" standard for the diagnosis of AF (Kirchhof *et al.* 2016; Welton *et al.* 2017), the interpretation of $_{SL}$ECG was chosen as a reference standard due to the limited research budget and the feasibility nature of study design. The interpretation of $_{SL}$ECG also helped minimise the impact of the disease progression bias which could have otherwise led to the attrition of individuals with screening-detected PAF by their $_{12L}$ECG appointments, potentially compromising the estimation of diagnostic accuracy measures

(Whiting *et al.* 2013). The risk of partial or differential verification biases, which may otherwise compromise the internal validity of diagnostic accuracy measures, was minimised by ensuring that all $_{SL}$ECG recordings were verified by the same study cardiologist (Delgado-Rodriguez & Llorca 2004; Schmidt & Factor 2013).

Considering the feasibility focus of all three quantitative studies in this enquiry, all diagnostic accuracy testing was carried out in an open-label manner. In contrast to other recent diagnostic accuracy studies of AF detection (Orchard *et al.* 2016; Chan *et al.* 2016; Desteghe *et al.* 2017; Quinn *et al.* 2018; Brasier *et al.* 2019), neither those performing the index tests nor the overreading cardiologist were blinded to provisional diagnoses derived through pulse palpation or the $_{SL}$ECG device's algorithm. In addition, the performers of index tests had access to patient-level data collected through demographic questionnaires, for example the participant's medical history. Whilst the lack of blinding is an indisputable limitation potentially introducing a diagnostic review bias and affecting the internal validity of diagnostic accuracy in any of the three studies (Schmidt & Factor 2013; Whiting *et al.* 2013), it is not too dissimilar to real-world clinical practice. A variety of in-built algorithms for the interpretation of single- or multiple-lead ECG exist and provide practitioners, such as GPs, nurses or pharmacists, with provisional diagnoses, which they may wish to accept or reject upon their own clinical judgement (Lau *et al.* 2013; Desteghe *et al.* 2017; Cairns *et al.* 2017; Smith *et al.* 2019b; AliveCor 2019b).

2.4.2 Qualitative studies

Framework approach and theoretical domains framework (TDF)

Apart from the underlying philosophical perspectives discussed in the first section of this chapter, qualitative research design and methodology are influenced greatly by the appropriate selection of the theoretical framework and methodological orientation (Tong *et al.* 2007). A variety of approaches or orientations, such as grounded theory, phenomenology or ethnography, exist and have been successfully exploited in health services research for numerous reasons, for example to explain the health behaviours or to study the quality of life of carers (Goodson & Vassar 2011; Foley & Timonen 2015; Rodriguez & Smith 2018). More recently, health services research and implementation science have seen an increased utilisation of the structured framework approach, which is largely dissociated from traditional epistemological positions or schools of qualitative research (Smith & Firth 2011; Gale *et al.* 2013). Originally developed to facilitate social policy research in the 1980s, the "classic" framework approach makes use of the predefined set of codes (called the analytical framework or coding guideline) to gather and chart

qualitative data onto the framework matrix, i.e. participant cases against the framework of codes, with cells of summarised data or quotes (Ritchie & Lewis 2003; Gale *et al.* 2013). Traditionally perceived as deductive, the framework approach may involve a mixture of deductive and inductive processes, for example deriving the initial analytical framework and interview topic guide from pre-existing literature (deductive) but then iteratively refining the framework matrix itself once preliminary themes begin to emerge (inductive) (Smith & Firth 2011; Gale *et al.* 2013). In this sense, the framework approach falls between the interpretivist and positivist paradigms (Sale *et al.* 2002; Giddings & Grant 2006) whereas its analytical process may resemble that of the constant comparative thematic analysis (Braun & Clarke 2006) or even grounded theory (Foley & Timonen 2015). In fact, Smith & Firth (2011) argued that the framework approach had an advantage over conventional thematic analyses due to tighter interconnections between the analytical stages, potentially making data analysis more transparent and producing what they referred to as the *'conceptual framework'* rather than a pure set of themes and sub-themes. This systematic, multifaceted approach may therefore be useful when developing or refining a complex intervention with a framework of possible parameters, such as the AF screening service.

One of the strategies to using a framework approach in this context would be to explore the facilitators and/or barriers to selected health behaviours or interventions, which can then be mapped onto the pre-defined dimensions, for example social or organisational domains (Kelleher *et al.* 2017; de Vos *et al.* 2017). Perhaps the most widely used methodology in this respect involves a Theoretical Domains Framework (TDF), which was initially validated to help study the HCP behaviour (Michie *et al.* 2005) but has since successfully branched out to qualitative investigations of patient behaviour (Nicholson *et al.* 2014; Baay *et al.* 2019) and healthcare interventions (Kolehmainen *et al.* 2011; Kirk *et al.* 2016; Debono *et al.* 2017; Hallsworth *et al.* 2019). This framework also appears to be easily-adaptable and may inform the design and delivery of qualitative research studies using either the methods of individual semi-structured interviews (Nicholson *et al.* 2014; Kirk *et al.* 2016; Debono *et al.* 2017; Hallsworth *et al.* 2019) or focus groups (Kolehmainen *et al.* 2011; Baay *et al.* 2019). The latest version of the TDF consists of 14 domains each of which may be further broken down into between three and 11 component constructs (Cane *et al.* 2012) (**Appendix 9**). These multiple dimensions provide TDF with a unique ability to capture the *'cognitive, affective, social and environmental influences on behaviour'* (Atkins et al. 2017) which may in turn influence the development or implementation of the new intervention or service.

Application of TDF to qualitative study design

During this enquiry, the TDF approach adapted from Atkins *et al.* (2017) was used at the study design, delivery and analysis stages of both multi-stakeholder focus groups of the PDAF study (**Chapter 4**) and individual semi-structured interviews with GPs (**Chapter 7**). In contrast to the approach described by Atkins *et al.* (2017), this project did not identify the specific set of target behaviours amongst the stakeholders, but instead focused on exploring the facilitators and barriers within the domains of the TDF which were the most likely to affect the development and/or implementation of the intervention (AF detection or screening service/programme). The domains and component constructs of the TDF were initially consulted when designing the topic guides for respective interviews and were subsequently utilised for a mixed inductive-deductive data analysis method (Atkins *et al.* 2017; Islam *et al.* 2012). The key facilitators and barriers derived through this analysis were then mapped back onto the TDF to highlight the domains which were the most likely to influence the development and/or implementation of the intervention and should therefore be a priority for future service developers or commissioners.

The qualitative component of the PDAF study (**Chapter 4**) was delivered in a concurrent or convergent fashion alongside the quantitative cross-sectional diagnostic component discussed above (**Chapter 3**) (Giddings & Grant 2006; Tariq & Woodman 2013), and used the widely-employed method of focus group interviews (Sabater-Hernandez *et al.* 2018; Lown *et al.* 2018; ISRCTN Registry 2019). Since the recruitment for focus group interviews failed to engage GPs from participating practices (**Chapter 4**), a separate qualitative study was designed to investigate their perspectives about the AF screening and detection programmes (**Chapter 7**). This individual interview-based study was delivered in a sequential manner with respect to the PDAF study, building on its cumulative quantitative and qualitative experience (Giddings & Grant 2006; Tariq & Woodman 2013). The successful implementation of the TDF approach during the PDAF study (Savickas *et al.* 2020c), led to its adoption to semi-structured interviews with GPs.

Research team

The appropriate selection of the research team, including the interviewers/facilitators is one of the most crucial elements of successful qualitative research execution (Breen 2006; Tong *et al.* 2007; Rudestam & Newton 2007; Krueger & Casey 2015). According to the COREQ checklist, the range of personal characteristics which may influence the conduct of qualitative research include the researchers' gender, occupation, credentials, experience and training, relationship(s) with participants and any other qualities which may introduce bias, for instance interests in the research topic (Tong *et al.* 2007). The selection of

researchers for qualitative components of this enquiry therefore aimed to balance the specialist expertise of qualitative research and pharmacy practice with the less biased views from those outside each field for analyst or theoretical triangulation purposes (Patton 1999; Krueger & Casey 2015).

For convenience, all researchers were sampled from the PDAF study team and included three pharmacists and two electrophysiologists. Two of the three pharmacists were academic researchers with extensive qualitative research experience. One of them (SC) acted as the Principal Investigator (PI) for both qualitative research components (HRA 2020c) whereas the other reviewed the accuracy of qualitative data analysis (SB). The third pharmacist was a PhD researcher (VS) who also acted as one of the seven CPs during the quantitative component of the PDAF study. They had some prior qualitative research experience involving focus groups and semi-structured interviews, and together with SC, led the design, delivery and analysis of all qualitative research. The two electrophysiologists (EV and AM) had limited qualitative research experience and provided support for data analysis by reviewing the themes derived. One of the electrophysiologists, who acted as the PI for the quantitative component of the PDAF study (EV), also contributed to the content of the topic guides, delivered technical assistance during all focus group interviews and reviewed the audio transcripts.

To ensure the dependability of findings, both qualitative studies were conducted using pre-established protocols and all researchers were aware of their responsibilities (Nowell *et al.* 2017; Forero *et al.* 2018). In addition, VS underwent self-directed learning to become familiar with relevant moderating or facilitation techniques for respective methods of interviewing (Krueger & Casey 2015; DeJonckheere & Vaughn 2019). He was also provided with developmental feedback by SC following each focus group interview to uphold the credibility of data collection and analysis (Forero *et al.* 2018). Both VS and SC maintained a reflexive account to sustain the confirmability of findings by acknowledging the influence of their professional background and involvement in the PDAF study on qualitative data collection and analysis (Stewart *et al.* 2007; Hiller & Vears 2016; Forero *et al.* 2018).

2.5 Summary of sampling and recruitment

2.5.1 Quantitative studies

All three quantitative studies included in this enquiry employed a convenience sampling method, a type of non-probability sampling which is commonly used due its efficiency and

cost- or resource-effectiveness (Saumure & Given 2008b; Martínez-Mesa *et al.* 2016; Jager *et al.* 2017; Waterfield 2018). Convenience sampling exploits the accessibility of eligible participants as a result of geographical proximity or the available list of contacts (Saumure & Given 2008b; Waterfield 2018). Besides logistical benefits, convenience sampling is useful for both generating new hypotheses and addressing the specific research questions (Martínez-Mesa *et al.* 2016). It has therefore been commonly used by both initial feasibility and diagnostic accuracy studies investigating different AF detection strategies in primary care or community settings (Vaes *et al.* 2014; Orchard *et al.* 2014; Lowres *et al.* 2014; Orchard *et al.* 2016; Quinn *et al.* 2018; Perez *et al.* 2019). In contrast to probability sampling methods, such as the simple random or stratified sampling however, the convenience sampling recruits a non-random, typically consecutive sample of participants, who are not necessarily representative of the target population (Martínez-Mesa *et al.* 2016). This non-random sampling bias may add to other selection biases described for the cross-sectional study design above (section **2.4.1**), potentially compromising the statistical analysis and affecting the accuracy of disease prevalence or other effects in relation to the "true" parameters within the target population (Delgado-Rodriguez & Llorca 2004; Thiese 2014; Waterfield 2018).

Besides acknowledging the limitations of convenience sampling, a number of steps were taken to mitigate the impact of its shortcomings on the internal validity and generalisability of findings within each of the three studies (Martínez-Mesa *et al.* 2016; Waterfield 2018). First of all, an optimal sampling frame was selected in each instance to maximise the comprehensiveness or the coverage of the target population by the study sample (Currivan 2004). With reference to specific research aims and objectives, the target populations for each study were derived from the total population of England and Wales, and were defined as:

- All individuals aged ≥ 65 years during the PDAF study in GP surgeries (**Chapter 3**) (Office for National Statistics 2017a; Office for National Statistics 2017b; Office for National Statistics 2017c).
- Care home residents aged ≥ 18 years during the PDAF study in care homes (**Chapter 5**) (Office for National Statistics 2014). It was considered appropriate to include all residents regardless of their age because the study focused on AF detection in a care home setting rather than in an age-defined population.
- Asian/Asian British/Indian individuals (referred to as the 'British Indian') individuals aged ≥ 18 years during the study within the South Asian community (**Chapter 6**) (Office for National Statistics 2018c).

The eligibility criteria for PDAF studies in GP surgeries and care homes reflected these target populations and largely overlapped, with an exception of participants' age which was ≥ 18 and ≥ 65 years in the two settings, respectively. Considering the feasibility design, the sampling frame for both target populations was derived from a single county of Kent, using the list of medical records of individuals registered at GP surgeries participating in the PDAF study. The vast majority of the population are registered with a GP thereby providing a universal coverage (NHS Digital 2020), which may not be fully achieved by other sampling frames, for instance the community pharmacy records (Boardman *et al.* 2005; NHS Digital 2019a). The comprehensiveness of the sampling frame chosen was further improved by involving GP surgeries and care homes served by these surgeries in three different areas of Kent. The risk of non-response bias and the erroneous exclusion of prospective participants was reduced by using a multitude of recruitment strategies (Waterfield 2018; Stasny 2015; Currivan 2004): from research team or CPs approaching eligible participants on the day of their influenza vaccination to GP surgeries sending invitations via text messages and self-referral by participants themselves after noticing a promotional leaflet/poster or visiting the study website. The matching eligibility age of ≥ 65 years (NHS England 2019c) for influenza vaccinations and AF screening (Kirchhof *et al.* 2016) was expected to reduce the risk of erroneous inclusions from the sample frame (Stasny 2015), and increase the recruitment rate of the relevant study sample. The recruitment in GP surgeries was carried out over two influenza vaccination seasons and ended once the sample saturation or the minimum required sample size was reached (Martínez-Mesa *et al.* 2016). The recruitment in care homes took place over a single influenza vaccination season and ended once all interested and eligible residents were screened.

During the study within the South Asian community setting, the sampling frame was not attached to GP surgery records and instead included all adults attending the selected Sikh places of worship (Gurdwaras). Over 90% of the UK Sikh religious group consider themselves to be of British Indian ethnicity (British Sikh Report 2017), thereby providing access to a relatively homogenous community, which could be representative of the target population (Office for National Statistics 2018c). Most of the recruitment took place at a single Gurdwara in Kent thus possibly compromising the comprehensiveness of the sampling frame, although a demographic comparison was sought via a one-day recruitment at another Gurdwara in South Yorkshire. In addition to methods used during the PDAF study, the recruitment rate and comprehensiveness of the sampling frame were maximised through ethnicity and language concordance between the study participants and the research team (Laveist & Nuru-Jeter 2002; Ahmed *et al.* 2015; Waibel *et al.* 2018) (complete definitions of these terms are provided in section **6.1**). This included the utilisation of study

documentation translated in Punjabi, the common language of the Sikh community (British Sikh Report 2019), and the selection of front-line researchers of South Asian ethnicity, who were able to communicate in Punjabi or Hindi (detailed information about the translation process is provided in section **6.3.7**). As for PDAF recruitment in care homes, the setting-driven eligibility criteria for this study allowed for inclusion of anyone ≥ 18 years, however the data analysis focused on those individuals of British Indian origin. The sampling process and recruitment were conducted in two phases: over two weeks around the time of the *'Global AF Aware Week'* in Kent and at a single-day public health event in South Yorkshire.

2.5.2 Qualitative studies

Due to their focus on participants' views and experiences qualitative research studies usually use the non-probability sampling methods to include a deliberately diverse sample of participants, which helps saturate a concept until it is theoretically meaningful (Krueger & Casey 2000c; Rudestam & Newton 2007; Saumure & Given 2008b; DeJonckheere & Vaughn 2019). The purposive sampling technique is perhaps the most popular one and relies on recruiting information-rich participants whose qualities help address the research question, often from an array of perspectives (Rudestam & Newton 2007; Palys 2008; Guest *et al.* 2013). Other qualitative studies exploit a snowball sampling method whereby current participants refer prospective participants with similar characteristics to the research team (Saumure & Given 2008b; Morgan 2008). Neither of the two sampling methods are without drawbacks. Whilst providing holistic and in-depth qualitative data, purposive sampling may be logistically more complex or time-consuming than the convenience sampling approach, and may be biased by the subjective judgement of the research team (Palys 2008; Guest *et al.* 2013). Similarly, the snowball approach risks capturing only a specific subset of the population based on the contacts of original participants, thereby possibly limiting the diversity of views included in the study (Morgan 2008).

The somewhat less complex convenience sampling strategies may be used as an alternative but, as discussed for quantitative research methods above, display a limited degree of transferability of findings to other contexts (Saumure & Given 2008b; Waterfield 2018). This disadvantage on the other hand is substantially less significant when interpreting qualitative data which is concerned with an exploration of the process and meanings of individuals rather than the generalisation of findings as may be the case for quantitative research (Sale *et al.* 2002; Giddings & Grant 2006). Convenience sampling was therefore successfully used by the variety of qualitative studies exploring the perspectives of patients or HCPs with regards to either healthcare phenomena (Bösner *et al.* 2014; Gordon *et al.* 2017) or the delivery of healthcare interventions (Woodrow *et al.* 2006). It was

also previously utilised by several qualitative investigations into facilitators and/or barriers to health behaviours or healthcare interventions built around the TDF approach (Debono *et al.* 2017; Smith *et al.* 2019a).

Based on this successful experience, the convenience sampling method was used to recruit participants for both qualitative studies included in this enquiry. The sampling frame of the qualitative component of the PDAF study (**Chapter 4**) included all participants of AF screening recruited during the quantitative component (**Chapter 3**). The research team or CPs invited all eligible participants to take part in optional focus group interviews at the end of their screening appointments. Patients screened in care homes were not included in this study due to the high prevalence of mental incapacity (**Chapter 5**). Apart from patients, the research team also invited all GPS from participating practices and the six CPs who conducted the screening to take part via an email (*N.b.* the seventh clinical pharmacist was a part of the research team). All interested individuals were welcome to participate and formed a series of homogeneous focus groups as described in section **2.6.2** (Krueger & Casey 2000c).

During the qualitative study with GPs (**Chapter 7**), the sampling frame included a list of GPs in Medway and Kent reachable via the research team's contacts in GP surgeries and clinical commissioning groups (CCGs). The research team sent email invitations and relevant study information to the list of contact gatekeepers who agreed to forward them to eligible study participants. Semi-structured interviews were conducted with all eligible respondents to the initial round of invitations. Data saturation, defined as the point at which *'data collected do not contribute any new information about barriers and facilitators influencing the implementation problem'* (Atkins *et al.* 2017), was reached after the eight participant and no further invitations to take part were sent out.

2.6 Summary of research instruments and data collection

2.6.1 Quantitative studies

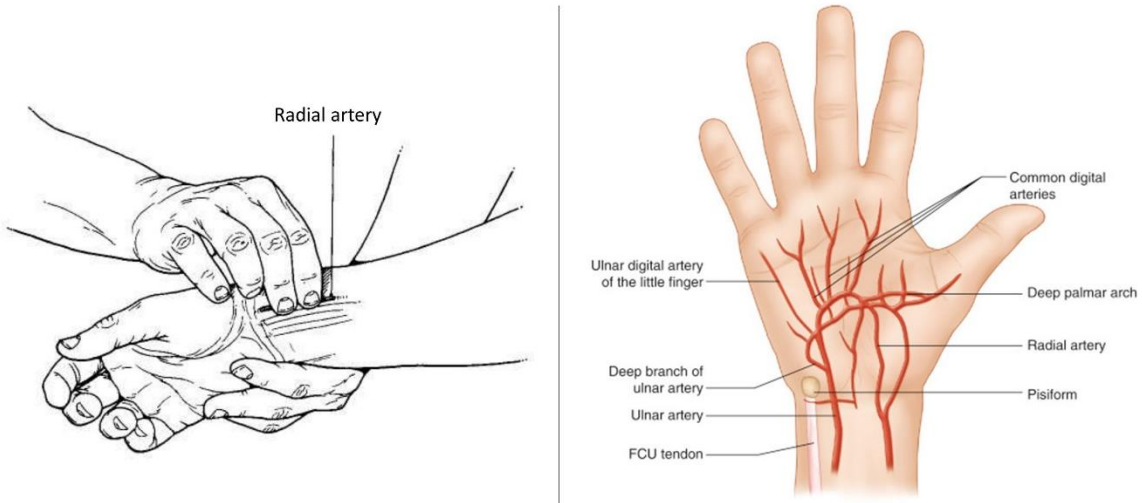
Pulse palpation

The method of arterial pulse palpation was selected as one of the index tests for use during the PDAF feasibility studies in GP surgeries (**Chapter 3**) and care homes (**Chapter 5**). The choice of this method was guided by its inclusion in the current NICE guidelines for the detection of AF in symptomatic individuals (NICE 2014a), and in the ESC guidelines for opportunistic screening of AF amongst the individuals aged ≥ 65 years (Kirchhof *et al.*

2016). Whilst recent years have seen an introduction of novel technologies (Lau *et al.* 2013; Chan *et al.* 2017a; Perez *et al.* 2019) (section **1.2.2**), pulse palpation remains a relatively quick, simple and generally painless procedure to detect AF, and is supported by extensive clinical research evidence and a favourable cost-effectiveness profile (Sudlow *et al.* 1998a; Somerville *et al.* 2000; Morgan & Mant 2002; Hobbs *et al.* 2005; Welton *et al.* 2017).

The technique may be applied to multiple arteries depending on the purpose and is based on the physical examination of arterial pulse (Moran 1990). The examination of peripheral radial pulse is carried out as shown in **Figure 2.2** and is routinely used to check for irregularity of the heart rhythm (Moran 1990). Similar to previous studies (Morgan & Mant 2002; Hobbs *et al.* 2005; Smyth *et al.* 2016), CPs performing AF screening in GP surgeries or care homes examined each participant's radial pulse using the fingertips of the second and third fingers aligned longitudinally over the course of the artery (Hill & Smith 1990; Yang & Chung 2018). Where impalpable or unclear, the CP then used the same technique to feel the participant's ulnar pulse (on the other side of the wrist) documenting the final result accordingly. The provisional diagnoses included either 'Normal SR' where no abnormalities were detected, 'Possible AF' where AF was suspected, 'Unclassified' where pulse indicated a non-AF abnormality or was inconclusive and 'Unreadable' if the pulse was impalpable.

Apart from multiple examination techniques, pulse palpation may vary in duration from as short as 20-30 seconds (Morgan & Mant 2002; Lowres *et al.* 2014; Quinn *et al.* 2018) to one minute or more (Somerville *et al.* 2000; Hobbs *et al.* 2005). To date, only the one-minute-long method, which delivers a mean of 87% sensitivity and 81% specificity for AF, has been ascertained as cost-effective in the ≥ 65-year-old group (Maeda *et al.* 2004; Hobbs *et al.* 2005; Moran *et al.* 2016), and was selected as an index test for both PDAF studies in general practice and care homes. It was also felt that one minute was an optimal duration to maximise the diagnostic accuracy of pulse palpation performed by rather inexperienced operators whilst maintaining the promptness of the test for study participants. In order to reduce the risk of misclassification due to other rhythm irregularities, such as AEBs/VEBs (Cooke *et al.* 2006; Schmidt & Factor 2013), and to improve the diagnostic accuracy of AF detection using pulse palpation, all participating CPs underwent a minimum of one-hour practical training with a cardiologist. This was followed by a practice ("mock") screening clinic and several optional drop-in sessions (a complete description of training is provided in section **3.3.3**).



Radial pulse palpation
(adapted from Hill & Smith 1990)

Anatomy of radial and ulnar arteries
(adapted from Yang & Chung 2018)

Figure 2.2 Radial pulse palpation and anatomy of radial/ulnar arteries
Adapted from: Hill & Smith (1990); Yang & Chung (2018).

$_{SL}$ECG and KMD

Despite the cumulative clinical experience and supporting research evidence, the reliability and accuracy of pulse palpation as a method for AF detection have been repeatedly questioned by several research groups (Cooke *et al.* 2006; Taggar *et al.* 2016a). In the systematic review by Taggar *et al.* (2016a), pulse palpation displayed up to 13% more false positive diagnoses compared to non-$_{12L}$ECG methods, such as $_{SL}$ECG devices. Together with an ability to identify non-AF rhythm abnormalities and the non-invasive nature of use, this potentially lower rate of false positives, has made newer $_{SL}$ECG devices attractive to researchers, clinicians and policy makers investigating, developing or commissioning the AF detection services (Kirchhof *et al.* 2016; Ramkumar *et al.* 2018; The Health Policy Partnership 2018; The AHSN Network 2019a). The KMD is the most widely studied instrument out of the $_{SL}$ECG device range (Duarte *et al.* 2019; Giebel & Gissel 2019; NICE 2019b), and has been selected for use during all quantitative studies of this enquiry (**Chapters 3, 5 and 6**). The device and its smartphone application are Conformitè Europëenne (CE)-marked, and are approved for AF detection both by the US Food and Drug Administration (FDA) and by the Australian Therapeutic Goods Administration (AliveCor 2019c). The KMD has also been reviewed by NICE for the detection of symptomatic AF, yet is not currently endorsed for clinical use (NICE 2015; NICE 2019b).

Despite this lack of approval, in 2017 the device was chosen as the primary method for opportunistic AF detection during the AHSN initiative in primary care (Wessex AHSN 2019).

The KMD consists of a plastic plate with two metal pads, which act as a bipolar lead I, and are activated by the placement of individual's fingers (Lau *et al.* 2013). To record an ECG, the user places two or more fingers from the left and right hand on each of the electrodes, as shown in **Figure 2.3.** The ECG is recorded for a requested period of time and is transmitted to a smartphone application via the ultrasound technology. The trace is then interpreted by an automated algorithm to determine whether an individual may have AF ('Possible AF'), is in 'Normal SR', presents with another irregularity ('Unclassified) or whether the ECG is of insufficient quality to be read reliably ('Unreadable') (Lau *et al.* 2013). These provisional results may be interpreted face-to-face or uploaded onto a secure online server for review and interpretation by individual's practitioner (Lau *et al.* 2013). The simplicity, convenience and efficiency of this AF detection process using KMD devices was overall positively appraised by patients and HCPs interviewed during the previous qualitative research studies (Orchard *et al.* 2014; Lowres *et al.* 2015; Orchard *et al.* 2016; Orchard *et al.* 2019a; da Costa *et al.* 2020) as well as by the evaluation of the AHSN initiative (Wessex AHSN 2019).

The aforementioned diagnostic categories, distinguished by the device's algorithm and CPs themselves, were utilised during the PDAF studies in general practice (**Chapter 3**) and care homes (**Chapter 5**). More recently, KMD has become the first $_{SL}$ECG device to receive the FDA clearance for the algorithm detection of 'Sinus Tachycardia' or 'Sinus Bradycardia' (AliveCor 2019a). These additional diagnostic categories were taken into account when analysing the data collected during the AF screening study within a South Asian community (**Chapter 6**). In this instance, the KMD was operated by pharmacy undergraduates under the supervision of a CP. The device's algorithm was followed to provide the patient with a provisional diagnosis, and no CP-led interpretation took place.

Much like with pulse palpation, the duration of $_{SL}$ECGs produced by the KMD may vary from 30 seconds to as long as 5 minutes (AliveCor 2019c). During the validation study, a 60-second recording by the device in a sample of cardiology patients displayed both a high sensitivity of 98% and a specificity of 97% against the $_{12L}$ECG interpretation by the cardiologist (Lau *et al.* 2013).

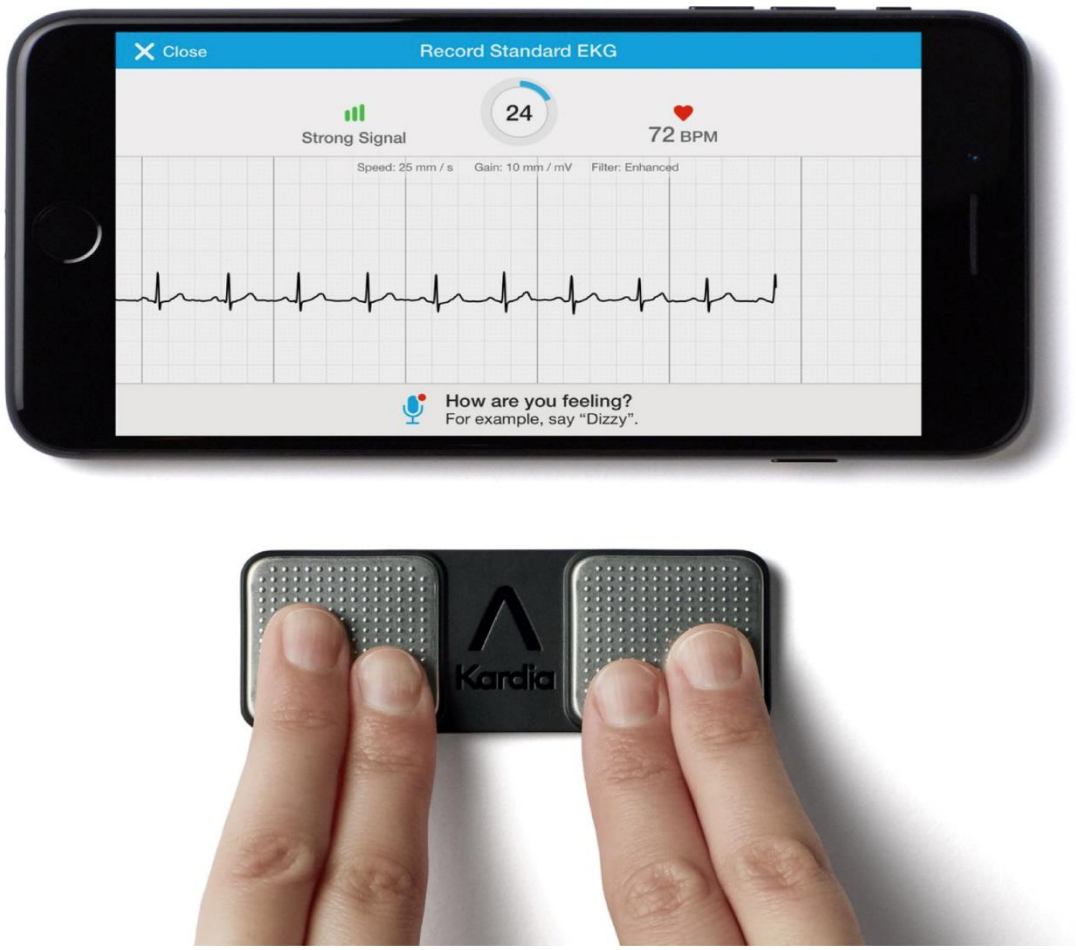


Figure 2.3 AliveCor® Kardia Mobile® single-lead, handheld electrocardiogram device
Image used by permission from AliveCor®.

Nevertheless, the subsequent diagnostic accuracy studies of KMD in primary and secondary/tertiary care settings (Lowres *et al.* 2014; Haberman *et al.* 2015; Chan *et al.* 2016; Chan & Choy 2016; Orchard *et al.* 2016; Desteghe *et al.* 2017) all adopted the method of a 30-second recording as recommended by the ESC (Kirchhof *et al.* 2016). The 30-second KMD-based screening of the ≥ 65-year-old Australian population in general practice (Orchard *et al.* 2016) or community pharmacies (Lowres *et al.* 2014) produced a sensitivity and specificity for AF detection against the cardiologist's interpretation of $_{SL}$ECG that were comparable to those in the original validation study (Lau *et al.* 2013). The use of 30-second KMD recordings in community pharmacies was also cost-effective (Lowres *et al.* 2014). In addition to ESC recommendations (Kirchhof *et al.* 2016), this promising cumulative evidence led to the adoption of a 30-second $_{SL}$ECG duration during all diagnostic accuracy studies of this enquiry.

As with pulse palpation, in order to optimise the diagnostic accuracy and ECG quality, CPs participating in the PDAF study underwent a minimum of one-hour practical training with the

study cardiologist to be able to operate the device and to interpret the $_{SL}$ECG traces for the diagnostic categories identified above. Similarly, pharmacy undergraduates underwent a two-hour training with a CP. Both groups of device operators were also given an opportunity to test their skills during a practice clinic and received regular feedback from either the cardiologist (for pharmacists) or the CP (for students) throughout the study (a complete description of relevant training is provided in sections **3.3.3** and **6.3.3**).

Case report forms and feedback questionnaires

During the PDAF study in GP surgeries and care homes (**Chapters 3 and 5**), every participant's case report form (CRF) consisted of the eligibility document, the demographic form and the pulse and ECG recording form (*N.b.* all forms and documentation are enclosed as appendices accompanying individual chapters). Following informed consent, these forms were completed by a CP with an assistance of the participant for the completion of the demographic form. Each participant screened in GP surgeries was also asked to complete an anonymous 17-item feedback questionnaire. Similarly, each CP performing AF screening in GP surgeries was asked to complete a 14-item study feedback and an eight-item training evaluation questionnaires. The views of GPs from participating surgeries were registered by inviting them to complete a tailored 14-item questionnaire. Lastly, the PhD researcher used an enhanced demographics form to capture additional demographic data of participants who required a follow-up action.

All CRF documentation and feedback questionnaires were developed jointly by the PIs for quantitative and qualitative components of the PDAF study (EV and SC). The content validity of each data collection instrument (Muijs 2011) was maximised by reviewing the outcome measures and qualitative themes derived from previous AF detection studies, which investigated AF screening in primary care using pulse palpation and/or $_{SL}$ECG devices (Sudlow *et al.* 1998a; Hobbs *et al.* 2005; Lowres *et al.* 2012; Lau *et al.* 2013; Lowres *et al.* 2014; Orchard *et al.* 2014; Lowres *et al.* 2015; Kaasenbrood *et al.* 2016; Orchard *et al.* 2016; Sandhu *et al.* 2016; Lown *et al.* 2017b). In order to ensure the face validity of each form and questionnaire (Muijs 2011), they were independently reviewed by the panel of another three researchers from the PDAF study team (VS, SB and AM). All patient-related documentation was also critically assessed by the MSOP's PIPS group to provide a non-specialist perspective for face validity (Muijs 2011). Afterwards, the CRF documentation and participant feedback questionnaire were piloted during the practice clinic which also served as a training session for participating CPs to become familiar with relevant study documentation. Minor amendments to the layout of the forms were introduced after the clinic.

Following the experience from the PDAF study, the CRF for AF screening study within a South Asian community (**Chapter 6**) was designed to incorporate the eligibility criteria, the participant demographic data (including some of the enhanced demographics) and the ECG data in a single document. The CRF was developed using the PDAF study documentation and the template of the data collection sheet provided by the AF Association (**Appendix 10**). In addition, the CRF aimed to capture the country of birth of each participant owing to pre-existing evidence which suggested that individuals born in South Asian countries may experience an increased risk of stroke mortality compared to the general UK population (Wild & Mckeigue 1997; Gunarathne *et al.* 2009). The optional, anonymous 17-item participant feedback questionnaire, which was offered to all study participants after their screening appointment, was adapted from the PDAF study by replacing the question pertaining to pulse palpation by another question aimed at ascertaining any barriers to South Asian engagement in health screening initiatives. This decision was guided by evidence underlying the study, which suggested that low South Asian engagement in healthcare and/or research may be influenced by various language, cultural, educational or socioeconomic factors (Greenhalgh *et al.* 1998; Ludwig *et al.* 2011; Palmer *et al.* 2015; Public Health England 2015; Emadian *et al.* 2017; Quay *et al.* 2017; Office for National Statistics 2018a; Ministry of Housing 2018).

All study documentation was developed by VS and the PI for the study (SB) who was of South Asian ethnicity and advised on the methods to overcome some of the barriers to South Asian engagement in research listed above. The CRFs were completed by aforementioned pharmacy undergraduates of South Asian ethnicity who also assisted participants filling in the demographic section of the CRF. The draft versions of all study documentation were piloted during a practice clinic within a purposively chosen group of South Asian students and academic staff, which also provided a training opportunity for pharmacy undergraduates. Similar to the PDAF study, slight formatting/layout changes were introduced to several forms based on the feedback from this session accordingly.

2.6.2 Qualitative studies

Focus group interviews

The qualitative research component of the PDAF study (**Chapter 4**) explored the facilitators and barriers to the development and implementation of the CP-led AF screening intervention using the method of focus group interviews with multiple stakeholders, including the patients, GPS and CPs. The focus group method involves one or more informal, up to two-hours-long, moderator-facilitated interviews with small groups of individuals (usually up

to 10), who share certain characteristics or experiences of interest (Wilkinson 1998; Krueger & Casey 2000a; Krueger & Casey 2000b; Breen 2006). The purpose of such interviews is to provide a platform for comparing individual perspectives, exploring common issues or developing/generating ideas within a social context (Breen 2006) (**Table 2.4**). The dynamic interaction between focus group participants helps reveal the shared views, priorities and insights into the problem, which may not have surfaced during the easier-to-organise but less-efficient and individual experience-driven one-to-one interviews (Breen 2006; Adams 2015). Therefore, despite being time-consuming and resource-intensive (Breen 2006), focus groups provide a large amount of rich qualitative data relating to a particular phenomenon, which may help explain or complement the quantitative research component (Krueger & Casey 2000a; Tariq & Woodman 2013; Tausch & Menold 2016).

Due to their informativeness and efficiency, focus group interviews have been widely and successful integrated into the development and evaluation of various health services for several decades (Wilkinson 1998; Kelly *et al.* 2006; Kayyali *et al.* 2016; NHS England 2016c; Mann *et al.* 2018). In recent years, the method of focus groups has also been employed by research groups seeking multi-stakeholder input into the development of AF detection services (Sabater-Hernandez *et al.* 2018; ISRCTN Registry 2019). The design of the qualitative element of the PDAF study, including the topic guide, built on the TDF (Atkins *et al.* 2017) and findings of earlier studies within the field, which utilised individual semi-structured interviews (Orchard *et al.* 2014; Orchard *et al.* 2016; Lowres *et al.* 2015), to further explore the themes derived in those studies using a homogeneous focus group method.

As implied by the term, this sub-type of focus group method involves interviewing a relatively homogeneous group of stakeholders or individuals, such as patients, excluding those who possess an opposing characteristic, for instance healthcare professionals, as may occur in mixed or heterogeneous focus groups (Krueger & Casey 2000c; Femdal & Solbjør 2018). This approach minimises the influence of hierarchical relationships, making sure that participants are able to share their honest views in an unrestricted environment which may otherwise be affected by the characteristics of others, for example a patient-doctor relationship (Krueger & Casey 2000c; Hofmeyer & Scott 2007). Furthermore, the relative homogeneity of interviewees facilitates the data analysis within each stakeholder group and a comparison of qualitative themes derived from different groups (Krueger & Casey 2000c), thereby providing a multidimensional view of key facilitators or barriers to health service development and implementation.

Table 2.4 Advantages and disadvantages of focus groups and individual interviews

Adapted from: Krueger & Casey (2000c); Breen (2006); Hofmeyer & Scott (2007); Vogl (2013); Adams (2015); DeJonckheere & Vaughn (2019).

Qualitative Method	Advantages	Disadvantages
Focus group interviews	• Facilitate the comparison of individual experiences • Reveal shared views or insights • Help generate ideas • Provide a large amount of rich data • Efficiency of multiple simultaneous interviews	• May be expensive • May be time-consuming • Organisational effort to get all participants to attend • Difficulties preventing particularly vocal participants from dominating • Risk of hierarchical relationships if non-homogeneous
Individual interviews	• Convenience of recruitment • Short duration (usually less than one hour) • Multiple formats (telephone, face-to-face, video) • Probe into deeper personal views or experiences • Useful for sensitive issues	• Telephone-based interviews may feel less personal (harder to build rapport) • Less efficient • Data not as rich as that from focus groups

Individual interviews

This component of the enquiry completed the triangulated approach of ascertaining the facilitators and barriers to AF screening from the perspectives of multiple stakeholders (Patton 1999; Rudestam & Newton 2007) (**Chapter 7**). Rather than focusing on the localised intervention delivered during the PDAF study, this project explored the broader perspectives of GPs with regards to the development and/or implementation of the national AF screening programme. The latter approach was chosen to encourage the engagement of GPs beyond those whose surgeries participated in the PDAF initiative. Building on the experience of the PDAF study (**Chapter 4**), in order to facilitate the recruitment of GPs, this

sequential qualitative research component utilised the data collection method of individual telephone-based interviews (Breen 2006; Adams 2015).

Individual semi-structured interviews are the most popular qualitative research method in health services research (DeJonckheere & Vaughn 2019) and involve short (usually up to one hour), one-to-one dialogues facilitated by a flexible topic guide (Adams 2015; DeJonckheere & Vaughn 2019). Although the data obtained may not be as rich as that from focus groups, individual interviews offer an opportunity to probe deeper into the independent views or experiences of an individual (Adams 2015; DeJonckheere & Vaughn 2019). That was desirable during this study when targeting peers (i.e. GPs) from a single region, who may not have wished to openly share their personal views about a relatively controversial topic, for instance the national AF screening programme (Lown *et al.* 2017a; UK NSC 2019).

Indeed, more than a few qualitative research studies concerned with AF detection employed a method of semi-structured interviews to explore the perspectives of different stakeholders including patients, general practice managers, receptionists, nurses, pharmacists or GPs (Orchard *et al.* 2014; Lowres *et al.* 2015; Orchard *et al.* 2016; Sabater-Hernandez *et al.* 2018; Orchard *et al.* 2019a). Together with qualitative findings of the PDAF study and the TDF approach (Atkins *et al.* 2017; Savickas *et al.* 2020c), this research informed the design of the topic guide and the delivery of semi-structured interviews with GPs presented in this enquiry. Whilst semi-structured interviews may be conducted face-to-face (Croxson *et al.* 2017; Debono *et al.* 2017) or even as a video call (NHS England 2017a), the mode of telephone interviews was selected for this study (Woodrow *et al.* 2006; Allen *et al.* 2019). This method lacks the visual element potentially turning the conversation less personal, yet it tends to make the participant feel more anonymous, which may help manage the power balance between the interviewer and the interviewee leading to a more open conversation (Vogl 2013). That may have been important during this study where the interviewer (VS) was often less clinically experienced than the GPs interviewed.

Facilitation and data collection

In order to ensure the credibility of data collection and findings (Forero *et al.* 2018), the interview process and topic guides for both focus groups and semi-structured interviews were tested during pilot interviews (described in individual chapters). A number of significant themes emerging from initial focus group interviews with patients and semi-structured interviews with GPs were further explored during the subsequent interviews, albeit in a less inductive manner than may occur with grounded theory studies (Foley & Timonen 2015), and without any formal amendments to each topic guide.

All focus group interviews were conducted at the venues convenient for prospective participants and were facilitated by VS and/or SC with assistance of EV to maximise the data collection (Krueger & Casey 2015). Telephone-based semi-structured interviews with GPs were facilitated by VS. During either focus groups or semi-structured interviews, the facilitator used a flexible topic guide and an appropriate moderating technique (Krueger & Casey 2015; DeJonckheere & Vaughn 2019) to ask a series of open-ended questions followed by either pre-determined (planned) or opportunistic (unplanned) prompts and questions to explore the key areas.

Both focus groups and individual interviews were audio-recorded using digital recorders and were transcribed verbatim by VS. Considering the focus of this enquiry on qualitative audio themes rather than the conversational aspects of the interviews, an orthographic method of transcription, which excludes non-linguistic observations, was used instead of the more paralinguistic approaches (Braun & Clarke 2013). The accuracy of transcription was confirmed by at least one other researcher (SC and/or EV). Apart from appropriate education/training of facilitators, this systematic approach to audio recording and transcription helped ensure the dependability of qualitative data obtained (Nowell *et al.* 2017; Forero *et al.* 2018). As is common during the qualitative data collection, in order to support the credibility of findings and to ease data analysis (Lincoln & Guba 1985b; Krueger & Casey 2015; DeJonckheere & Vaughn 2019), audio recordings were supplemented (or source-triangulated) (Patton 1999) by the diary of field notes which was maintained either by SC during the focus groups or by VS during semi-structured interviews. Lastly, to ensure the confirmability of findings, an audit trail of data collection and analytical process was maintained, including the raw audio data, the field and reflexive notes, and the intermediate themes/subthemes of the analysis (Nowell *et al.* 2017; Forero *et al.* 2018).

2.7 Statistical considerations and quantitative data analysis

2.7.1 Statistical considerations

All quantitative data input and analyses during the PDAF studies (**Chapters 3 and 5**) and the study within the South Asian community setting (**Chapter 6**) were conducted using the International Business Machines® (IBM) Statistical Package for Social Sciences (SPSS) (v25). This versatile software is employed universally for the analysis of quantitative outcome data across clinical studies of different designs (Hobbs *et al.* 2005; Lowres *et al.* 2014; Chan & Choy 2016; Halcox *et al.* 2017). Selected diagnostic accuracy and economic analyses used Microsoft Excel 2016 and are discussed under the separate headings below.

Descriptive statistical analysis was undertaken for all participant demographic variables, the quality of $_{SL}$ECGs and the breakdown of diagnostic categories derived using the index tests or the reference standard. Each continuous variable was tested for normality of distribution using the Shapiro-Wilk test (for sample sizes of ≤ 50 participants) or the Kolmogorov-Smirnov test (for sample sizes > 50 participants) (Yap & Sim 2011). All normally distributed continuous variables were expressed as mean ± standard deviation (SD) whereas all non-normally distributed ones were expressed as a median [interquartile range]. Unless indicated otherwise, nominal and ordinal (categorical) data appearing in the text were expressed as the % of the group accompanied by the number of participants/total number of participants, e.g. 30%, 30/100, and as the number of participants (% of the group), e.g. 30 (30%) in tables and figures. Participant cases containing missing data were included in the analysis, although individual missing data points were omitted without data imputation (Kang 2013). The exception to this were participants recruited during the study within the South Asian community whose gender and age were both missing in the demographic questionnaires leading to their exclusion from the dataset.

In case of inferential analyses, two-sided (tailed) tests were used to determine statistical significance, which was kept at the conventional 5% ($p < 0.05$). Following the guidance set out in the British Journal of General Practice (BJGP), P values were quoted to two significant figures down to $p = 0.01$. Any values below this were quoted to one significant figure down to $P = 0.001$, below which P values were indicated as < 0.001 (BJGP 2020). All tests were performed under the assumption that the sample in question was comparable to a random sample from the same population (Waterfield 2018). Pairwise deletion was used to exclude the missing data points for each pair of variables tested (Kang 2013). All variables compared during inferential statistical analyses were non-normally distributed. The continuous demographic variables of individuals in various study sub-groups (for instance, those with and without AF) were compared using a Mann Whitney U test, which is typically applied to determine any significant differences between the non-normal distributions of two independent samples (Hinton 2010). The between-group differences or associations for categorical variables were ascertained using the Pearson's Chi-square test, unless more than 20% of cells had expected frequencies of < 5, in which case the Fisher's exact test was performed instead (Kim 2017). The Freeman-Halton extension was applied to either Pearson's Chi-square or Fisher's exact tests involving contingency tables larger than two by two (2 x 2) to improve the accuracy of the test (Freeman & Halton 1951). In such cases, the Bonferroni correction for multiple comparisons was also applied to reduce the risk of type I statistical errors, i.e. rejecting the null hypothesis or erroneously discovering a

statistically significant result where one does not exist (McEwan 2017). Statistically significant, between-measurement differences of paired continuous variables (for example, HR readings derived through pulse palpation and $_{SL}$ECG) were determined using a Wilcoxon signed-rank test, which is the test of choice to measure the differences between two dependent observations of non-normally distributed data (Coleman 2018).

2.7.2 Diagnostic outcome analysis

The diagnostic accuracy of the test is influenced greatly by the prevalence of the condition in question, therefore it is essential to define the measures of prevalence prior to estimating the accuracy of each index test (Mallett *et al.* 2012; Trevethan 2017). Following the example of several previous AF screening studies using KMD in primary care/community settings (Lowres *et al.* 2014; Chan & Choy 2016), this enquiry defined the total prevalence of AF as the proportion of all participants who are confirmed as 'Possible AF' by the cardiologist's interpretation of $_{SL}$ECG. The total prevalence of AF was expressed as a mean (95% confidence intervals (CI)), and divided into 'unknown' ('previously undiagnosed') and 'known' (or 'previously diagnosed') AF based on whether or not the AF diagnosis was documented in participant's medical records (during the PDAF study; **Chapters 3 and 5**), or whether or not the participant was aware of their condition (during the screening within the South Asian community; **Chapter 6**). The final yield of screening was defined as the proportion of all participants who are diagnosed with 'new' AF after a confirmatory $_{12L}$ECG (Lowres *et al.* 2014; Orchard *et al.* 2016).

All diagnostic accuracy measures for index tests (pulse palpation, KMD algorithm and CP's interpretation of $_{SL}$ECG) were estimated from 2 x 2 contingency tables using the cardiologist's interpretation of $_{SL}$ECG as a reference standard (**Figure 2.4**). The measures were expressed as percentages with respective 95% CI to indicate the reliability of each measure (Gushta & Rupp 2010). All diagnostic accuracy analyses were performed in SPSS (v25), however the 95% CI were computed using the Microsoft Excel 2016 and the template provided by Mackinnon (2000). The selection of diagnostic accuracy measures employed by all quantitative components of this enquiry was based on the most common outcome measures used by previous studies investigating the accuracy of pulse palpation and/or the KMD (Sudlow *et al.* 1998a; Somerville *et al.* 2000; Morgan & Mant 2002; Hobbs *et al.* 2005; Lau *et al.* 2013; Lowres *et al.* 2014; Orchard *et al.* 2016; Chan & Choy 2016), and by recent systematic reviews of AF detection methods (Taggar *et al.* 2016a; Welton *et al.* 2017). The key measures included:

- *Sensitivity*, defined as the test's ability to correctly identify individuals with AF, i.e. those with true positive diagnoses. This was estimated by dividing the number of true positive diagnoses by the sum of true positives and false negatives.
- *Specificity*, defined as the test's ability to correctly identify individuals without AF i.e. those with true negative diagnoses. This was estimated by dividing the number of true negative diagnoses by the sum of true negatives and false positives.
- *Accuracy (correct classification rate)*, defined as a composite of sensitivity and specificity. This was calculated by adding the true positives and true negatives and dividing them by the total number of individuals tested (Baratloo *et al.* 2015; Trevethan 2017).

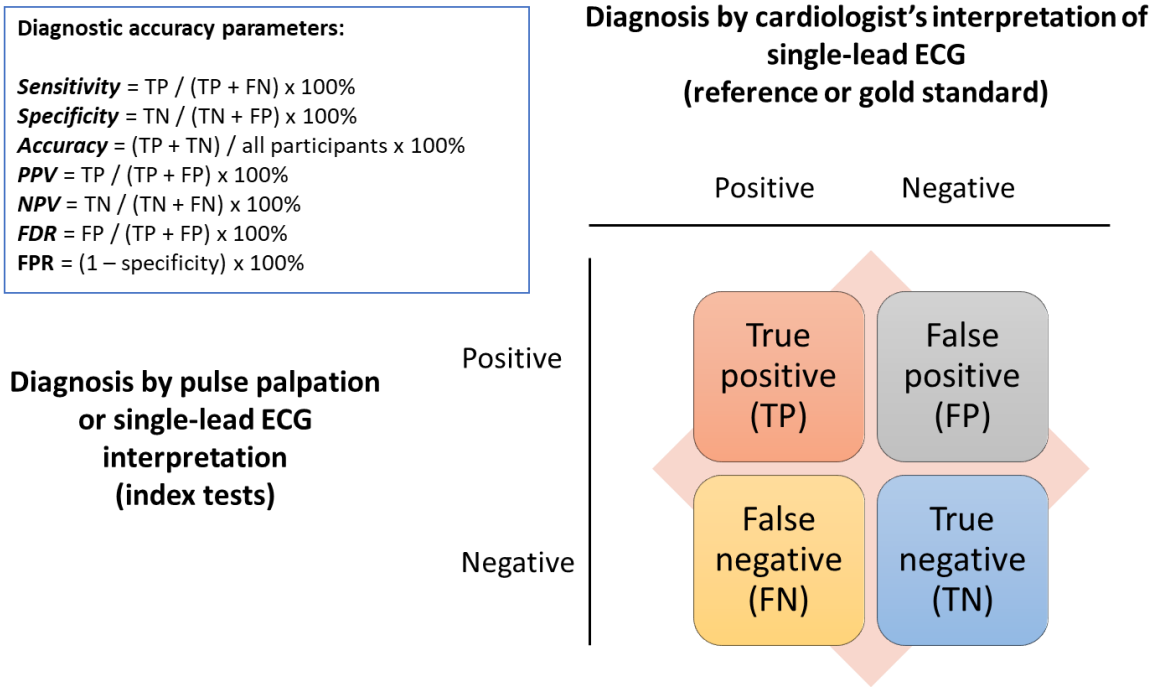


Figure 2.4 Diagnostic accuracy measures used during the quantitative studies of this enquiry

A 2 x 2 contingency table between the diagnoses derived through index tests and the reference standard is provided to explain the estimation of each diagnostic accuracy parameter. Abbreviations: ECG – electrocardiogram; FDR – false discovery rate; FPR – false positive rate; NPV – negative predictive value; PPV – positive predictive value.

In addition to key diagnostic accuracy measures defined above, the diagnostic studies of this enquiry also included the additional measures of PPV and the false discovery rate (FDR). The aim of this inclusion was to evaluate the index test's ability to correctly classify

those which it considers to be AF positive. As an add-on to sensitivity or specificity, PPV has been utilised by several AF screening studies (Sudlow *et al.* 1998a; Morgan & Mant 2002; Hobbs *et al.* 2005; Desteghe *et al.* 2017; Svennberg *et al.* 2017). This measure, also referred to as the % agreement with the cardiologist in this enquiry, indicates the proportion of individuals identified by the index test as positive who actually have the condition based on the reference standard (true positives divided by the sum of true positives and false positives) (Trevethan 2017). Note that the equivalent measure to PPV for index test-negative results is referred to as the NPV (Trevethan 2017). Similar to PPV, it is dependent on the prevalence of the disease, and for low-prevalence conditions, such as AF, often approaches 100% (Sudlow *et al.* 1998a; Morgan & Mant 2002; Svennberg *et al.* 2017). As such, the added value of NPV to the measures of sensitivity and specificity may be limited and it is not presented in this enquiry.

The concept of FDR is the opposite to PPV and indicates the proportion of those identified by the index test as positive who do not actually have the condition, i.e. are discovered falsely as presenting with AF (false positives divided by the sum of true positives and false positives) (Colquhoun 2014). Whilst rarely reported (Baek *et al.* 2015; Tarnutzer *et al.* 2017), this measure helps appreciate the substantial rate of false positive misclassification by the index test, which may have both clinical and economic consequences, and may be as high as 86% for a disease of 1% prevalence detected by a highly accurate test displaying 95% specificity (Colquhoun 2014). The FDR is not to be confused with the rate of false positives or false positive rate (FPR) which was also discussed in this enquiry and was estimated as the number of false positive diagnoses divided by sum of false positives and true negatives. Alternatively, it may be estimated as one minus the specificity of the test (Mallett *et al.* 2012).

Apart from descriptive diagnostic accuracy measures, the inter-rater agreement (Cohen's Kappa statistic) was computed during all quantitative studies to compare the level of concordance between each index test and the reference standard with regards to diagnostic classification of AF positive and AF negative diagnoses (expressed as a mean from 0 to 1 (95% CI)) (Mabmud 2010; Lowres *et al.* 2014). The inter-rater agreement was deemed to be excellent if it was > 0.80, substantial if 0.61-0.80, moderate if 0.41-0.60 and poor if ≤ 0.40 (Landis & Koch 1977; Fleiss *et al.* 2003). During the PDAF study, the diagnostic accuracy of each index test (for 'Normal SR', 'Possible AF' and 'Unclassified/Unreadable' diagnoses) was also compared to each other and the reference standard using a Cochran's Q test followed by post-hoc McNemar's Chi-square tests and a Bonferroni correction for multiple comparisons. The McNemar's test aims to ascertain the equality of two dichotomous proportions based on the same individuals (Morrison 2010), and thus enables

an inferential comparison of sensitivity and specificity between the two selected diagnostic modalities as previously described for other AF detection studies in primary care (Somerville *et al.* 2000; Quinn *et al.* 2018). The Cochran's Q test is an extension of the McNemar's test to enable an assessment of significant differences between two or more matched samples, for instance between the pulse palpation and cardiologist's or pharmacist's interpretation of $_{SL}$ECG (Huedo-Medina 2010).

2.7.3 Questionnaire data analysis

Responses to closed-ended questions of all participant, GP or CP feedback questionnaires obtained during the PDAF study in GP surgeries (**Chapter 3**) and the AF screening study within the South Asian community (**Chapter 6**) were analysed using SPSS (v25). All nominal and ordinal data obtained were analysed using descriptive statistics and were expressed as other categorical variables from the CRF analyses. The between-group differences in participant responses collected during AF screening within the South Asian communities of Kent and South Yorkshire were ascertained using the Pearson's Chi-square or Fisher's exact test as outlined in section **2.7.1** above (Freeman & Halton 1951; Kim 2017; McEwan 2017).

Any responses to open-ended (free-text) questions of the questionnaires were imported into NVivo (v12) and analysed using content-analysis, an objective, systematic approach commonly applied to the analysis of verbatim questionnaire data (Lavrakas 2008). Initially, the words and phrases extracted from each question were coded inductively based on their content. The emerging categories were then grouped and refined considering the frequency of their occurrence to produce a smaller set of meaningful categories. In light of the large number of responses, the analysis of open-ended feedback from study participants was also accompanied by the visual representation of categories using a word-cloud approach as described by Vasconcellos-Silva *et al.* (2013). The NVivo 'word frequency' function was used to construct a word-cloud of participant responses by including 1,000 most commonly used words from all open-ended questions. The words used more frequently appeared in larger font and closer to the centre of the word-cloud, thereby indicating the most significant content/categories in relation to the development and/or implementation of the intervention.

2.8 Economic analysis

2.8.1 Markov model and cost-effectiveness definitions

The economic analyses of interventions investigated by all three quantitative studies of this enquiry (**Chapters 3, 5 and 6**) were constructed using the methodology of the Markov cohort simulation (Sonnenberg & Beck 1993). This cost-effectiveness model is particularly useful for the assessment of decision problems which involve a continuous risk over time, for instance the risk of haemorrhage due to OAC or the risk of ischaemic stroke due to AF (Sonnenberg & Beck 1993). It has therefore been widely accepted as the economic model of choice for use by health services research (Komorowski & Raffa 2016; Di Tanna *et al.* 2019) and policy- or decision-makers, including NICE (NICE 2012a; NICE 2019b). The variations of this model have also been frequently utilised by individual studies (Maeda *et al.* 2004; Lowres *et al.* 2014; Aronsson *et al.* 2015; Moran *et al.* 2016; Jacobs *et al.* 2018; Oguz *et al.* 2019) or systematic reviews (Welton *et al.* 2017; Duarte *et al.* 2019) into the cost-effectiveness of various AF detection strategies.

The Markov model is based on the assumption that a cohort of individuals transition between the finite number of health states (referred to as 'Markov states') at equal intervals (referred to as 'Markov cycles') for a defined period of time (referred to as the 'time horizon') from several years to a lifetime (Sonnenberg & Beck 1993). As shown in the Markov state diagram developed for this enquiry (**Figure 2.5**), all patients with AF enter the model in the state 'Stable AF' and over time transition into either the states of 'Post-stroke' (if they suffered a stroke), 'Post-major bleed' (if they suffered a major bleed) or 'Death' (if they died). The likelihoods of transition between these states (expressed as 'p_transition state') are referred to as 'state-transition probabilities' (Sonnenberg & Beck 1993) and may be derived from either relevant population studies (Lowres *et al.* 2014), systematic reviews (Welton *et al.* 2017) or RCTs (Jacobs *et al.* 2018). Each transition state is allocated a cost and a utility value corresponding to the QOL, which typically ranges from zero for death to one for perfect health (Komorowski & Raffa 2016). These values may be obtained through commonly administered QOL questionnaires, such as the popular EQ-5D instruments (Komorowski & Raffa 2016). The costs and utility-related health gains at the start of the simulation are conventionally valued more than those occurring in the future, which are discounted by a defined annual % value (Sonnenberg & Beck 1993; NICE 2012b).

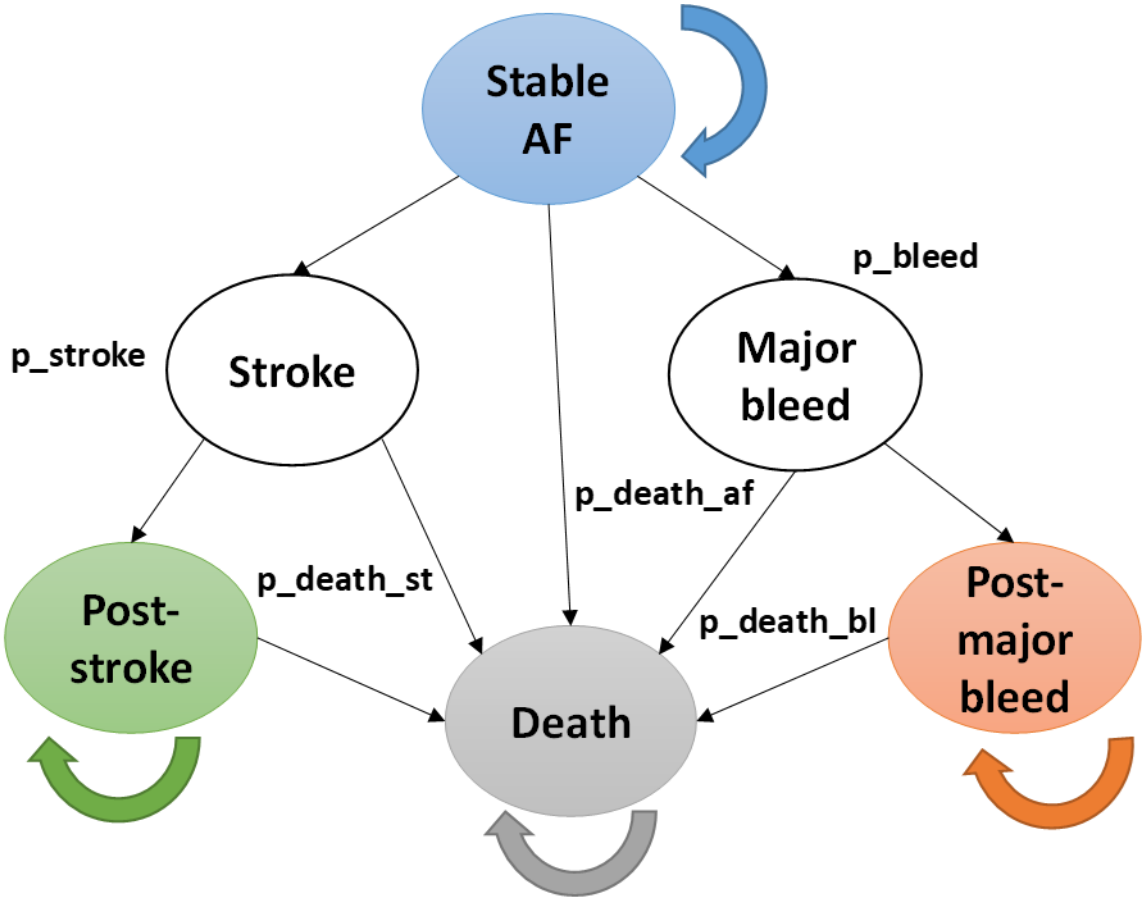


Figure 2.5 Markov-state diagram used in all cost-effectiveness evaluations of this enquiry

Adapted from: Edlin et al. (2015). The diagram displays the health states of 'Stable AF', 'Post-stroke', 'Post-major bleed' and 'Death'. It also displays the temporary states of 'Stroke' and 'Major bleed' which lead onto the 'Post-stroke' and 'Post-major bleed' states, respectively. Each transition from one health state to another is accompanied by the transition probability denoted by letter 'p'. For the purpose of this evaluation, it was assumed that once patients entered the health states of 'Post-stroke' or 'Post-major bleed' they might only transition into 'Death' and no other health states. N.b. 'stroke' includes all incidences of ischaemic stroke.

The result of the cohort simulation over the time horizon is the total cumulative cost per total cumulative utility. This is commonly referred to as the cost-effectiveness ratio (CER) or the cost-utility ratio (CUR), and is expressed as the cost per QALY, a one year of perfect health (Jakubiak-Lasocka & Jakubczyk 2014; Komorowski & Raffa 2016). The estimation of CER enables a cost-utility comparison between the alternative decisions or scenarios, such as the different AF screening strategies (Welton *et al.* 2017) or AF screening compared to no screening (Jacobs *et al.* 2018). Two separate Markov simulations relating to different

scenarios are performed as shown in **Figure 2.6** and produce two different CERs. The comparison of these parameters is referred to as the incremental CER (ICER) or incremental CUR (ICUR), and is expressed as the difference in total costs between the two scenarios (i.e. incremental cost) divided by the difference in total utility (i.e. total health gains in QALYs) (Komorowski & Raffa 2016). Note that the term ICER may also be alluded to when estimating the incremental costs per life-year gained, the "currency" of cost-effectiveness analysis, which does not consider the utility of the intervention (Jakubiak-Lasocka & Jakubczyk 2014). In practice however, the terms cost-utility and cost-effectiveness are often used interchangeably and the term ICER is referred to more commonly than ICUR (Lowres *et al.* 2014; Welton *et al.* 2017; Jacobs *et al.* 2018; NICE 2019b; Duarte *et al.* 2019). As such, whilst in principle a cost-utility evaluation, the output of the Markov model is referred to as a cost-effectiveness evaluation throughout this enquiry.

Apart from indicating the difference in cost-effectiveness between the two decisions or interventions, ICER may also be used by commissioners or decision-makers to determine whether a particular intervention provides "value for money" and is worth investing in (Komorowski & Raffa 2016). This is commonly expressed as the aforementioned WTP, or a threshold of incremental cost per QALY gained below which the ICER of the intervention may be considered sufficiently cost-effective for investment (Shiroiwa *et al.* 2010). In the UK, NICE appraises the cost-effectiveness of all interventions for use within the NHS, and although arbitrary, interventions below the WTP of £20,000/QALY gained are viewed as cost-effective (NICE 2012a; NICE 2019b). The WTP may also be used to derive another measure of cost-effectiveness referred to as the incremental net benefit (INB). This measure indicates whether or not the net monetary benefit of the intervention (due to QALYs gained) outweighs its extra cost, and is calculated as the incremental QALYs multiplied by the WTP minus the incremental costs (Hoch & Dewa 2008). Therefore, an intervention with an ICER < WTP will have a positive INB and will be considered cost-effective whereas an intervention with an ICER > WTP will have a negative INB and will not be viewed as cost-effective (Welton *et al.* 2017). The per-person INB may also be multiplied by the size of the population that would benefit from the intervention (e.g. those with newly detected AF aged ≥ 65 years) to enable the larger-scale net benefit comparison between the alternative scenarios (Welton *et al.* 2017).

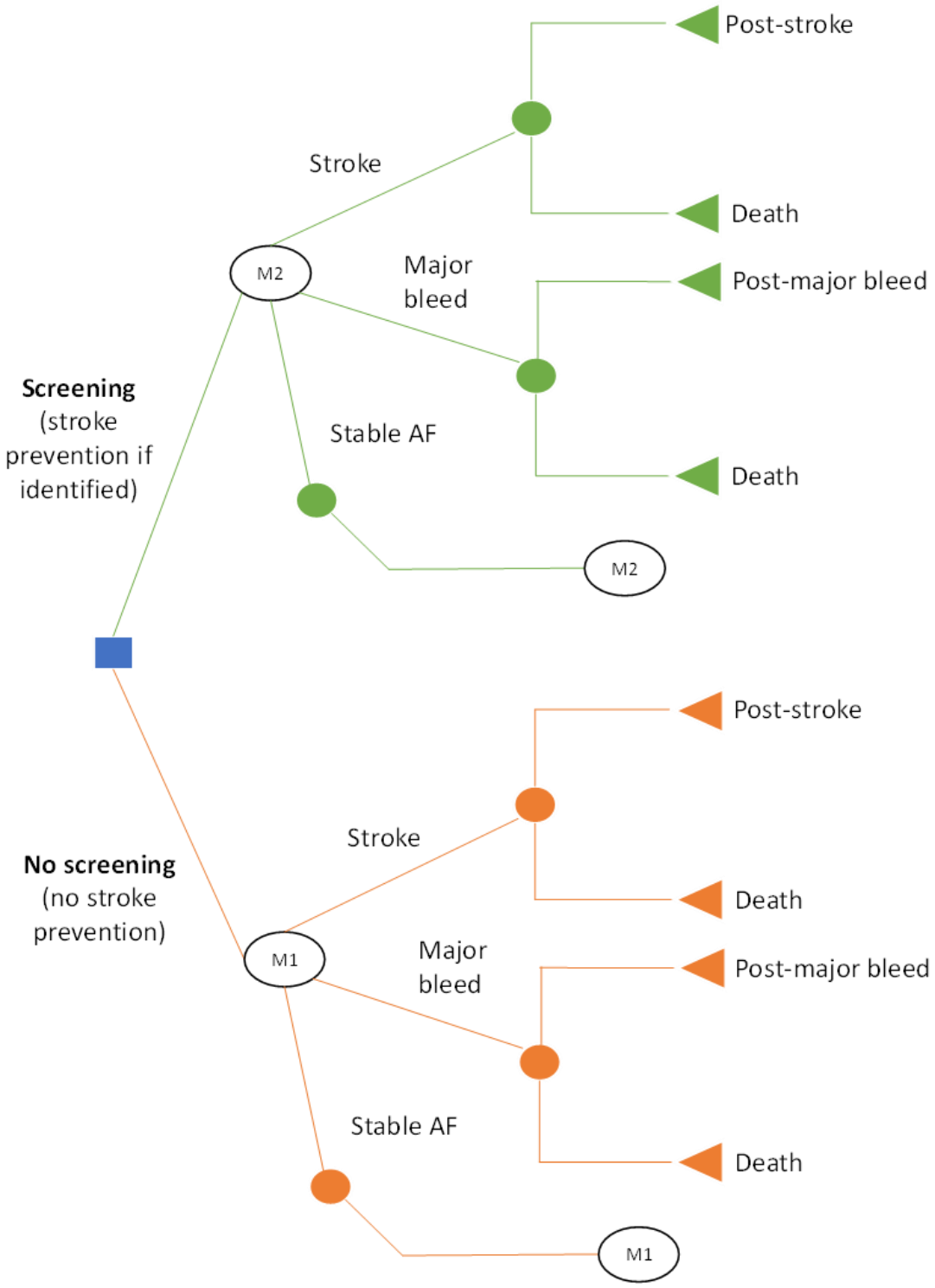


Figure 2.6 The decision tree used in the economic analyses of this enquiry

Adapted from: Jacobs et al. (2018). M1 and M2 refer to Markov Model 1 and Markov Model 2, respectively, i.e. Markov cohort simulations used to compare the incremental costs and health gains of the screening ('intervention') and no screening ('control') strategies.

2.8.2 Application of Markov model to economic analysis

The cost-effectiveness evaluation of the PDAF intervention in GP surgeries (**Chapter 3**) was built using the Markov model and the NICE costing report for AF (NICE 2014b; NICE 2014c; Veale *et al.* 2018). In order to enable a comparison, it was further refined using the parameters of economic models adapted from two previous studies evaluating the cost-effectiveness of $_{SL}$ECG screening for AF in ≥ 65s (Lowres *et al.* 2014; Jacobs *et al.* 2018). The original model developed for the PDAF intervention in GP surgeries was adapted to two other models involving the relevant target populations of care home residents and South Asian (British Indian) individuals as described below and in **Chapters 5 and 6**, respectively. The data input and analysis were carried out using Microsoft Excel 2016 and the health economics template adapted from Edlin *et al.* (2015).

As shown in **Figure 2.6**, the decision tree constructed for any of the three cost-effectiveness evaluations focused on the comparison between two hypothetical cohorts of individuals with AF, who were either invited to take part in a one-off screening, had an opportunity to be identified as having AF (if not already known) and were offered OAC (referred to as the 'intervention cohort' or the 'screening strategy'), and those who did not undergo screening and were therefore not offered stroke prevention (referred to as the 'control cohort' or the 'no screening strategy'). The two cohorts of patients were derived from the total population of England and Wales and were adjusted for target populations of each study defined in section **2.5.1** above (Office for National Statistics 2014; Office for National Statistics 2017a; Office for National Statistics 2017b; Office for National Statistics 2018c).

All individuals in each of the two cohorts started the simulation in the health state of 'Stable AF' and were followed up in conventional three-month cycles (Welton *et al.* 2017; Jacobs *et al.* 2018) for a time horizon of 10 years as described by Lowres *et al.* (2014). For the purpose of each evaluation, it was assumed that all participating individuals underwent the screening within a period of 12 months. The baseline transition probabilities between the health states were estimated using the data from landmark RCTs which evaluated the effectiveness and safety of OAC therapies (Petersen *et al.* 1989; Connolly *et al.* 1991; Mcbride 1991; Ezekowitz *et al.* 1992; EAFT Study Group 1993; Connolly *et al.* 2009; Granger *et al.* 2011; Patel *et al.* 2011). The baseline all-cause mortality rates were corrected for the rates observed in relevant target populations of each study (Office for National Statistics 2014; Office for National Statistics 2017a; Office for National Statistics 2017b; Bhopal *et al.* 2018). The all-cause mortality rates were also adjusted for increased mortality following an ischaemic stroke or a major bleed (factors of 3.7 and 1.5, respectively) (Jacobs *et al.* 2018; Eikelboom *et al.* 2006), whereas the probabilities of ischaemic stroke, stroke

mortality and major bleed were modified for care home residents or the British Indian individuals where appropriate (Wild & Mckeigue 1997; Gunarathne *et al.* 2009; Friberg *et al.* 2012; George *et al.* 2017). The utilities of health states were derived from the Dutch model by Jacobs *et al.* (2018) and varied from 0.84 for stable AF to 0.45 and 0.67 following ischaemic stroke and major bleed, respectively. As recommended by NICE, the future health gains and costs were discounted by 1.5% and 3.5%, respectively (NICE 2012b).

2.8.3 Model assumptions

The model-specific costs and parameters or assumptions are presented in individual chapters. However, several assumptions of the base-case scenario were applicable to all three models regardless of the target population:

- In the absence of direct evidence, participants with AF identified during the screening were assumed to display the same risk profile of ischaemic stroke and all-cause mortality as those with AF which is incidentally detected during routine care. This assumption has been commonly employed by previous cost-effectiveness models (Lowres *et al.* 2014; Aronsson *et al.* 2015; Jacobs *et al.* 2018) and is based on evidence that asymptomatic and symptomatic individuals with AF may experience a similar risk of mortality or major cardiovascular events (Flaker *et al.* 2005). This data is extrapolated to assume that the vast majority of patients with AF identified by published screening initiatives are asymptomatic (Duarte *et al.* 2019) whereas those identified during routine care would display symptoms (NICE 2014a).
- As suggested in the cost-effectiveness analysis by Aronsson *et al.* (2015), all three economic models also assumed that the risk of stroke or all-cause mortality in individuals with PAF was the same as in individuals with persistent or permanent AF. However, some evidence indicates that patients suffering from persistent or permanent AF may carry a greater risk of stroke/all-cause mortality compared to those suffering from PAF (Banerjee *et al.* 2013; Link *et al.* 2017), which may have led to an over-estimation of economic benefits.
- Similarly, as assumed by previous studies (Lowres *et al.* 2014; Aronsson *et al.* 2015; Jacobs *et al.* 2018), participants with AF identified during the screening were assumed to exhibit the same degree of response to OAC as those identified during routine care. The evidence in support of this assumption was provided by Martinez *et al.* (2014) who demonstrated that OAC might significantly reduce the risk of stroke and all-cause mortality in patients with asymptomatic, incidentally-detected AF compared to no therapy.

- The rates of clinical events and mortality were assumed to be constant over time as in the study by Jacobs *et al.* (2018).
- The participation in screening rate was assumed to be 50% as proposed by Lowres *et al.* (2014). Patients with undiagnosed AF who did not participate in the screening (50% of all undiagnosed AF cases) and those who participated but were not identified by index tests as having AF (false negatives) were assumed to display the same risk of stroke and all-cause mortality as patients with AF who are not on OAC therapy.
- The prevalence of total and 'unknown' AF for each economic model were derived through cardiologist's interpretation of $_{SL}$ECG recorded using KMD as reported by previous studies (Lowres *et al.* 2014; Chan & Choy 2016). This ensured that all participants who may have presented with AF at the time of screening (but not at the time of the confirmatory $_{12L}$ECG, e.g. those with PAF) were considered in accordance with ESC guidance, which indicates that a 30-second ECG recording of AF is diagnostic (Kirchhof *et al.* 2016). The prevalence of 'new', screening-detected AF included those with 'unknown' AF who were identified correctly based on the sensitivity of each index test.
- The sensitivity and specificity of all index tests for the detection of AF with reference to cardiologist's interpretation of $_{SL}$ECG were adjusted for individual economic models based on the data from each component study.
- The rate of 'Unclassified'/'Unreadable' diagnoses was assumed to be that determined by the interpretation of $_{SL}$ECG using the KMD algorithm. During the study within the South Asian community, this included the rate of 'Sinus Tachycardia'.
- The proportion of participants with 'new' AF eligible for OAC was determined from the data obtained during each study, and all participants with a CHA_2DS_2-VASc score of ≥ 2 for females or ≥ 1 for males qualified (NICE 2014a).
- The proportions of patients initiated on DOAC and VKA therapies were 56% and 44%, respectively as indicated by the percentages of patients receiving each therapy during the PDAF study in GP surgeries.
- The level of adherence to OAC therapy was assumed to be 55% to enable a comparison with the cost-effectiveness analysis by Lowres *et al.* (2014). The level of adherence to OAC therapy and its efficacy were assumed to be constant over time (Jacobs *et al.* 2018). Patients who did not adhere to OAC were assumed to display the same risk of stroke, all-cause mortality and major bleeding as those not receiving the OAC therapy.

2.8.4 Model costs

The costs of OAC therapy and health states, including ischaemic stroke and major bleed, were extracted from the NICE costing report and template for AF (NICE 2014b; NICE 2014c). The costs of relevant medical interventions were obtained from the NHS England's National Tariff Payment System 2017/2018 and 2018/2019 (NHS Improvement 2017) and from the systematic review and cost-effectiveness analysis by Welton *et al.* (2017). All costs were inflation-corrected for prices in 2019 (**Table 2.5**). The three-monthly cost of each AF screening strategy included the following:

- The cost of AF screening which was a composite of CP time (7-11 minute appointments depending on the study) at the Agenda for Change (AFC) Band 7 hourly rate assuming 4-5 years of experience (formerly referred to as Point 30) (NHS Employers 2019), and for KMD screening strategies, the acquisition cost of KMDs (166-6,000 units depending on the study) (The AHSN Network 2019a; AliveCor 2019c).
- The cost of a 'new' AF diagnosis, which was based on the prevalence of 'new', screening-detected AF in a respective target population. This parameter took into account the cost of $_{12L}$ECG procedures and associated GP interpretations following the initial referral as well as the cost of GP and cardiologist's appointments for 'new' AF diagnoses. It also considered the hypothetical costs of extra $_{12L}$ECG and GP interpretations which would have been incurred due to false positive AF and 'Unclassified/Unreadable' diagnoses resulting from the index test. Based on the PDAF data in GP surgeries (**Chapter 3**), all economic models assumed that 76% of those with 'Unclassified/Unreadable' diagnoses would be followed up with a $_{12L}$ECG and a GP interpretation.
- The cost of OAC (including appropriate monitoring for warfarin) as indicated in the costing report by NICE (2014b).

2.8.5 Probabilistic sensitivity analysis

In order to test the reliability of the economic model and to compare the selected deviations from the base case, each cost-effectiveness evaluation was subjected to a probabilistic sensitivity analysis (PSA) (Sonnenberg & Beck 1993). The PSA employed a Monte Carlo simulation of the Markov model, which has been commonly used for this purpose by cost-effectiveness studies into AF detection strategies (Lowres *et al.* 2014; Aronsson *et al.* 2015; Jacobs *et al.* 2018).

Table 2.5 Basic costs used in the design of cost-effectiveness evaluations

Abbreviations: AF – atrial fibrillation; ECG – electrocardiogram; GP – general practitioner; NICE – National Institute for Health and Care Excellence.

Unit	Cost/Unit (£)	Reference
Kardia Mobile® device	99.00	AliveCor (2019c)
AF screen by clinical pharmacist (Agenda for Change Band 7; 7-11 minutes)	2.22 to 3.49	NHS Employers (2019)
12-lead ECG and GP review of ECG	39.95	NICE (2015)
GP appointment for new diagnosis (10 min)	22.43	Welton *et al.* (2017)
Cardiologist appointment for new diagnosis (10 min)	23.82	Welton *et al.* (2017)
Warfarin annual acquisition	45.89	NICE (2014b)
Rivaroxaban annual acquisition	851.27	
Apixaban annual acquisition	890.36	
Anticoagulation clinic for warfarin (annual)	268.25	
Ischaemic stroke	13,580.30	
Major bleed	1,302.92	

The Monte Carlo method relies on the generation of random numbers from a selected probability distribution or distributions (Sonnenberg & Beck 1993). These numbers are then applied to transition probabilities, utilities and costs of the Markov model generating a large number of random simulations, which helps ascertain the 95% CIs of the cost-effectiveness measures (Sonnenberg & Beck 1993; Komorowski & Raffa 2016). The Monte Carlo simulation may also be used to test the sensitivity of the Markov's model to variations in certain parameters, such as the level of adherence to OAC therapy (Lowres *et al.* 2014).

During the PSAs of the three cost-effectiveness evaluations, Monte Carlo simulation was used to generate 100,000 simulations of the Markov model as in the analysis by Lowres *et al.* (2014). Transition probabilities and utilities were assumed to follow a beta distribution whereas the costs were assumed to display lognormal distribution as described by Edlin *et al.* (2015). The costs were varied between 50% and 150% of the base case as in the model by Jacobs *et al.* (2018) whilst the level of adherence to OAC therapy ranged from 40% to 80% as tested by Lowres *et al.* (2014). Specific deviations from the base case are discussed in individual chapters. The key deviations investigated by all three economic models included:

- Proportions of individuals with AF receiving DOAC and VKA therapies of 29% and 71%, respectively as indicated by NICE (2014c)
- Screening participation rate of 30% or 80%
- Rate of 'Unclassified'/'Unreadable' diagnoses divided in half.

The ICERs derived from each PSA were expressed as a mean (95% CI). The mean ICERs and INBs of each base case were presented and discussed alongside. The mean INBs were estimated per patient with AF entering the model, and for all patients with new, screening-detected AF in the target population. Following the previous examples (Welton *et al.* 2017; Jacobs *et al.* 2018), the cost-effectiveness of screening strategies was also displayed graphically via the 100,000-simulation scatterplots on the incremental cost-effectiveness planes, which indicated the proportion (%) of simulations under the WTP threshold of £20,000/QALY gained.

2.9 Coding and qualitative data analysis

The coding and analysis of qualitative data collected during the PDAF focus groups (**Chapter 4**) and semi-structured interviews with GPs (**Chapter 7**) were conducted using NVivo (v12) and a structured TDF approach adapted from Atkins *et al.* (2017), which is critiqued in section **2.4.2** above (**Figure 2.7)**. The transcripts were coded and analysed by VS and were independently verified by SC to ensure the credibility and confirmability of findings (Lincoln & Guba 1985b; Forero *et al.* 2018; Nowell *et al.* 2017). In order to maximise the credibility and confirmability, the key themes and subthemes derived at the end of the analysis were then subjected to further analyst and theory triangulation through peer debriefing, which involved an independent peer-review by additional three researchers of varying qualitative research experience and theoretical perspectives (Lincoln & Guba 1985b; Patton 1999; Nowell *et al.* 2017; Forero *et al.* 2018). One of them was an academic pharmacist with extensive experience of qualitative research who provided a specialist opinion (SB), and two were electrophysiologists with a quantitative research background who offered a non-specialist perspective (EV and AM). Field notes taken by VS or SC were consulted after the preliminary analysis to ensure the credibility of findings through the process of referential adequacy (Lincoln & Guba 1985b; Forero *et al.* 2018).

At the beginning of the analysis, all transcripts of focus groups or semi-structured interviews were read and re-read noting down initial ideas. Afterwards, the transcripts were deductively coded using TDF domains and component constructs as the parent and child nodes (Atkins *et al.* 2017). The coded data were subsequently refined and divided into facilitators and

barriers within each TDF domain. During the ongoing analysis, data coded into different TDF domains were compared removing any duplications as appropriate.

The TDF domains most likely to influence the intervention or service development and implementation were then selected using the criteria adapted from a TDF-based qualitative study by Islam *et al.* (2012):

- relatively high frequency of specific beliefs
- presence of conflicting beliefs, and
- evidence of strong beliefs that may impact on the behaviour.

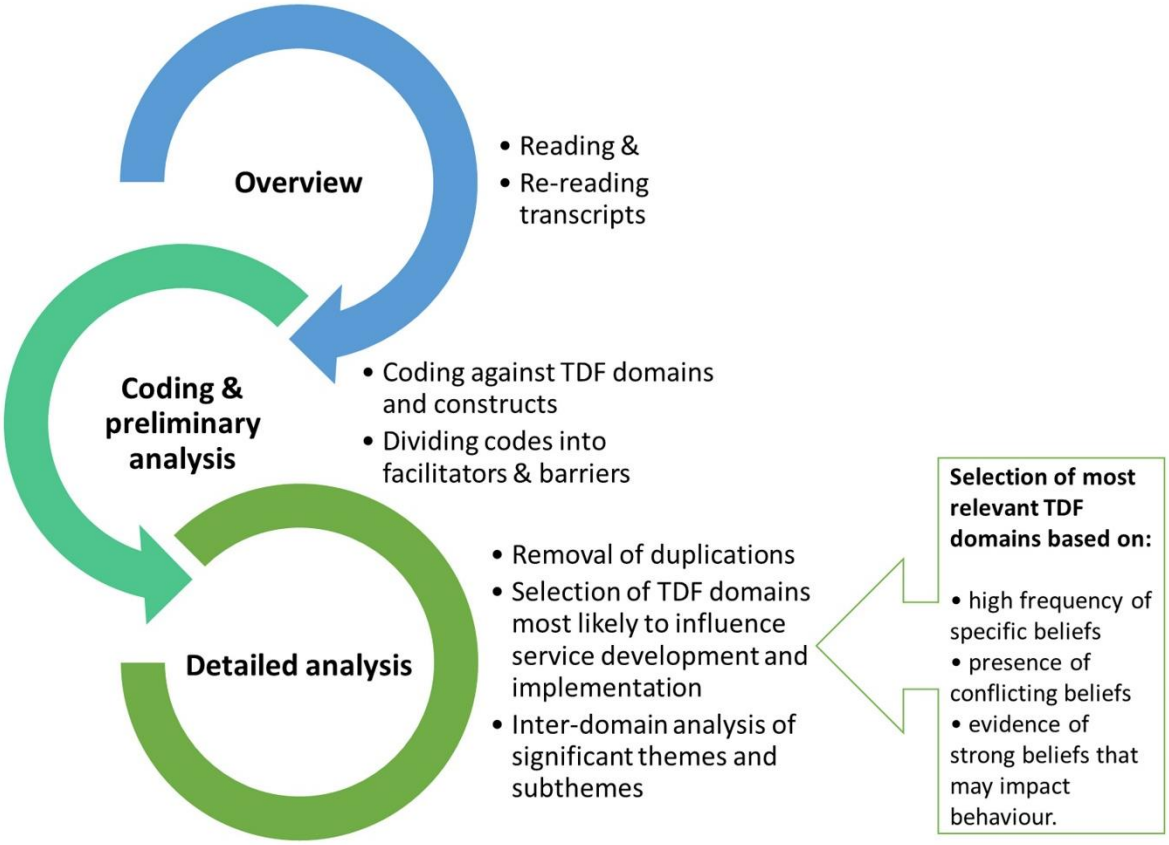


Figure 2.7 Three-step approach to qualitative data analysis employed by this enquiry
Based on the Theoretical Domains Framework (TDF) and analytical strategy adapted from: Islam et al. (2012); Atkins et al. (2017); Savickas et al. (2020c).

The major themes and subthemes derived from these TDF domains were selected for the final inter-domain analysis of key facilitators and barriers to the intervention or service development and implementation. The transcript of each focus group or semi-structured interview was coded and analysed separately. The key facilitators and barriers derived from

each interview were then compared amongst all participants of semi-structured interviews or within each stakeholder group and overall across all stakeholders participating in focus group interviews. This process of source (stakeholder) and theory (perspective) triangulation helps to uphold the credibility and confirmability of findings by highlighting the key shared qualitative themes amongst multiple participants or groups of stakeholders who may appraise the phenomenon from different angles (Patton 1999; Forero *et al.* 2018). Deviant case analysis was used to ensure that perspectives which diverged from dominant trends were not overlooked (Lincoln & Guba 1985b; Mills *et al.* 2012).

Whilst the transferability of qualitative data derived through a convenience sample to other contexts is somewhat limited (Saumure & Given 2008a; Waterfield 2018), during this enquiry it was enhanced by the process of *'thick description'* (Lincoln & Guba 1985a). The structured TDF approach to data analysis was helpful in this respect by describing the phenomenon in great detail and from several different dimensions, therefore potentially facilitating its transferability to other settings beyond the study sample (Nowell *et al.* 2017; Lincoln & Guba 1985a). The data saturation reached during the semi-structured interviews with GPs confirmed the completeness of this multidimensional description (Forero *et al.* 2018).

2.10 Ethical considerations

All component studies of this enquiry were conducted in accordance with recommendations for physicians involved in research on human participants adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions. The PDAF study in general practice surgeries and its extension in care homes (**Chapters 3-5**) received an approval of the Health Research Authority (HRA) and the London-Riverside Research Ethics Committee (REC) as appropriate for research carried out within the NHS setting (Project ID: 232663) (HRA 2020a). The other studies were not conducted within the NHS and were therefore subjected to an approval by the MSOP REC (study within the South Asian community (**Chapter 6**), Project ID: 310719; qualitative study with GPs (**Chapter 7**; Project ID: 090119). Prior to their enrolment onto a respective study, written informed consent was obtained from all study participants in line with guidance provided by the HRA (HRA 2019; HRA 2020b), and processes described in each chapter below.

All data collected during the study were managed according to the requirements of the Data Protection Act 2018 and the European Union General Data Protection Regulation, and were retained for a period of five years after the end of the recruitment process (GOV.UK 2018a;

University of Kent 2018). Password-protected electronic databases and physical expression of interest forms, which contained personal identifiable information of participants attending qualitative interviews (**Chapters 4 and 7**), were an exception and were permanently deleted one month after the respective interviews. All CRFs and interview records were pseudonymised by assigning participants a unique participant identification number (UPIN), and by replacing the names of other individuals, organisations or locations with pseudo-names as appropriate. The stakeholder questionnaires were fully anonymous. Most physical data were stored in individual sections of the designated, locked cabinet at MSOP. The copies of participant consent forms and letters of provisional diagnoses issued during the PDAF study contained personal identifiable information and were stored in a locked, designated cabinet within each participating surgery. The consent forms for participation in the PDAF study focus group interviews were stored in the designated locked cabinet at MSOP. Similarly, physical copies of consent forms and letters of provisional diagnoses collected during the other studies were separated from the remaining physical data and stored in designated locked cabinets at MSOP. The relevant cabinets were only accessible to VS and the PIs of respective studies. The electronic data, including audio recordings and databases, were stored on a password-protected University of Kent network and were only accessible to members of the PDAF research team.

Chapter 3: Pharmacists Detecting Atrial Fibrillation in General Practice Surgeries (Quantitative Evaluation)

3.1 Introduction

The universal medical coverage provided by general practice makes this primary care setting a viable option for structured AF screening programmes (NHS Digital 2009; NHS Digital 2020). As outlined in **Chapter 1**, however the implementation of such initiatives may be hindered by the growing imbalance between the service demand and supply of GPS (The King's Fund 2019a; NHS Digital 2019b; Buchan *et al.* 2019). Centralised effort has been made to encourage AF detection by primary care HCPs outside of GP surgeries, for instance the community pharmacists (Public Health England 2019c; Wessex AHSN 2019; NHS England 2020d). The concept of community pharmacy-based opportunistic AF detection was also explored by several research groups, demonstrating the capability of pharmacists to deliver accurate and (cost)-effective AF screening using pulse palpation, $_{SL}$ECG devices or mBPMs (Lowres *et al.* 2014; Sandhu *et al.* 2016; Twigg *et al.* 2016; Bacchini *et al.* 2019; Antoniou *et al.* 2019). Despite the promising results, numerous sources highlighted multiple barriers that may compromise the sustainability of AF screening services in community pharmacies, including the lack of structured remuneration, inadequate follow-up and privacy issues (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020).

The CPGP pilot offered a possible solution to both staffing problems faced by general practice and the infrastructure deficiencies encountered in community pharmacies (Snow-Miller 2015b; NHS England 2017b). Coincidentally, the evolution of CP roles in general practice matched the timeline of the AHSN's AF initiative, placing CPs in an excellent position to conduct opportunistic AF screening and to fast-track the management of patients with 'new' AF (Wessex AHSN 2019). An isolated case report included in the AHSN evaluation reflected on a CP-led opportunistic AF detection during the general practice medication reviews, albeit without a formal evaluation of screening outcomes (Wessex AHSN 2019). Whilst targeted AF screening of patients with comorbidities, such as diabetes or hypertension, during routine reviews may help detect the co-existence of asymptomatic AF (Benjamin *et al.* 1994; Staerk *et al.* 2018; Watanabe *et al.* 2009), they would likely capture only a fraction of the ≥ 65-year-old population and may not offer the most cost-effective screening strategy (Hobbs *et al.* 2005; Welton *et al.* 2017). As shown by several research studies discussed in section **1.2.3** (Rhys *et al.* 2013; Orchard *et al.* 2016; Kaasenbrood *et al.* 2016; Jacobs *et al.* 2018), due to the matching age criteria, seasonal

influenza vaccinations clinics of ≥ 65s may offer a feasible and cost-effective alternative for opportunistic AF detection (Kirchhof *et al.* 2016; Public Health England 2020a).

This chapter presents the quantitative findings of the PDAF study in GP surgeries, which made use of the evolving roles of CPs in general practice to evaluate the feasibility of pharmacist-led opportunistic/population-based AF detection programme targeting those aged ≥ 65 during the influenza vaccination season (Veale *et al.* 2018; Savickas *et al.* 2018; Savickas *et al.* 2020b). It builds on the evidence of community pharmacy- and general practice-based AF detection programmes presented above, and hypothesises that trained CPs working in general practice are sufficiently qualified and appropriately placed to accurately identify patients with AF using either pulse palpation or $_{SL}$ECG devices whilst producing economic benefits for the NHS. In order to address this hypothesis, we outline the evidence of feasibility in relation to the recruitment of a relevant study sample, diagnostic accuracy, multi-stakeholder feedback and economic impact related to the PDAF intervention. As such, this chapter maps onto both the feasibility/piloting and evaluation elements of the MRC (2006) guidance for developing and evaluating complex interventions' described in section **2.2.**

3.2 Aim and objectives

Aim:

To assess the feasibility, accuracy and economic impact of CP-led AF screening in GP surgeries using either pulse palpation or $_{SL}$ECG during the influenza vaccination season.

Objectives:

1. To determine the recruitment efficiency of a single time point population screening strategy of AF, which selectively targets individuals ≥ 65 eligible for seasonal influenza vaccinations.
2. To measure the total prevalence of AF in the study sample as determined by the study cardiologist, including the prevalence of 'known' and 'unknown' AF cases, and the proportion of each that may qualify for OAC therapy.
3. To measure the prevalence of 'Unclassified' and 'Unreadable' provisional diagnoses in the study sample ascertained by CPs using pulse palpation or the $_{SL}$ECG device compared to the study cardiologist.
4. To determine the differences in prevalence of non-AF comorbidities amongst those participants with 'Possible AF' and those with 'Normal SR' diagnoses.
5. To determine the quality of $_{SL}$ECG recordings produced by CPs.

6. To determine the accuracy of AF screening by trained CPs compared to the study cardiologist.
7. To compare the accuracy of AF screening using pulse palpation with either the $_{SL}$ECG interpretation by CPs or the automated algorithm.
8. To ascertain the proportion of screened individuals who were referred to the GP and were followed-up, including the yield of 'new' AF and non-AF diagnoses after an appropriate follow-up action.
9. To determine the feasibility of AF screening and the acceptability of the intervention proposed by obtaining the feedback from participating patients, CPs and GPs.
10. To estimate the financial impact of the AF screening strategy proposed for the healthcare system.

3.3 Methods

3.3.1 Study design

This was a multi-site, prospective, cross-sectional diagnostic accuracy study (Thiese 2014), which evaluated a systematic population screening strategy of individuals aged ≥ 65 eligible for seasonal influenza vaccinations at participating GP surgeries (Welton *et al.* 2017). Systematic opportunistic screening for AF was also offered to eligible individuals aged ≥ 65 on the day of their seasonal influenza vaccination clinic (Welton *et al.* 2017). Participants with provisional AF or inconclusive diagnoses were followed-up to confirm the status of their diagnosis and any further actions undertaken by the GP. The screening was conducted over two influenza vaccination seasons (2017-2018 and repeated in 2018-2019).

The index tests selected for the study were appraised in section **2.6.1**, and included pulse palpation, $_{SL}$ECG interpretation by the automated algorithm of the KMD and $_{SL}$ECG interpretation by the CP. The accuracy of index tests was compared against the reference standard which was defined as the cardiologist's interpretation of $_{SL}$ECG.

3.3.2 Study setting and sites

The study was conducted in a general practice setting. The selection of participating GP practices was determined by their geographical proximity relative to MSOP and their level of interest and involvement in clinical research. A total of four GP practices in Kent, UK took part in this initiative. All surgeries were based in the area of Canterbury and Coastal CCG, with two of the surgeries located in Faversham and one each in Whitstable and Canterbury.

3.3.3 Selection and training of CPs

Prior to agreeing to take part, each prospective CP received the detailed information about the study from the PDAF research team in a form of the study protocol and were given an opportunity to ask any questions they may have. Researchers from the PDAF team then obtained a written informed consent from all selected individuals (**Appendix 11**). A total of seven CPs were recruited to deliver AF screening using a convenience sampling method (Martínez-Mesa *et al.* 2016). Five pharmacists were selected from the pool of CPs at the Kent Community Health NHS Foundation Trust by the gatekeeper of the organisation. Another CP was invited to participate through direct contact between the University of Kent and a local GP surgery. The last CP (VS) was recruited as a PhD researcher by the PDAF research team at MSOP. The recruited CPs had between five and 14 years of professional experience. Five worked at the AFC Band 7 and two – at Band 8 pay grades (NHS Employers 2019).

In preparation for the study, each CP underwent a structured theory-practice training using a similar approach to those described for community pharmacist-led AF screening interventions by Lowres *et al.* (2014) or Twigg *et al.* (2016). The aim of the training was to expand CPs' knowledge of AF, to familiarise them with study documentation and to enable them to deliver AF screening using either pulse palpation or KMD. The first part of the training involved self-directed learning about the fundamentals of AF and the interpretation of ECG using the lecture notes prepared by the study cardiologist. This was followed by the minimum of one-hour hospital-based training with the study cardiologist to be able to perform and interpret the findings of pulse palpation, and to be able to record and read $_{SL}$ECG using the KMD. The final step of the training involved the participation in a two-hour practice clinic which consolidated the previous training and helped CPs become more efficient in using the relevant study documentation. Apart from core training, all CPs were asked to complete two one-hour-long electronic quizzes consisting of 25 de-identified $_{SL}$ECG traces, which were followed by bespoke feedback from the study cardiologist. CPs were also offered immediate feedback by the cardiologist throughout the study. Those CPs who required additional support were given an opportunity to attend two optional drop-in training sessions with the cardiologist which focused on the interpretation of more complex $_{SL}$ECG traces.

3.3.4 Outcome measures

The diagnostic accuracy measures used for both primary and secondary outcome measures included: sensitivity, specificity, accuracy, PPV, FDR and FPR. The complete definitions of each measure are provided in section **2.7.2**.

Primary outcomes

1. The diagnostic accuracy of CP-led AF screening using pulse palpation compared to the reference standard of cardiologist's interpretation of $_{SL}$ECG.
2. The diagnostic accuracy of CP-led AF screening using the KMD compared to the reference standard. The diagnostic accuracy of $_{SL}$ECG interpretation by CPs and the automated KMD algorithm were both estimated as part of this outcome measure.

Secondary outcomes

1. The time required to achieve a desired sample size (months).
2. The total prevalence (%) of AF in the study sample, including the prevalence of 'known' and 'unknown' AF as determined by the reference standard.
3. The proportion (%) of individuals with 'known' and 'unknown' AF who may qualify for OAC therapy (defined as males with a CHA_2DS_2-VASc score of ≥ 1 or females with a score of ≥ 2 (NICE 2014a)).
4. The prevalence (%) of 'Unclassified' and 'Unreadable' diagnoses ascertained through pulse palpation or $_{SL}$ECG interpretation by CPs or the KMD algorithm compared to the reference standard.
5. Statistically significant differences in the prevalence of non-AF comorbidities amongst those participants with reference standard-determined 'Possible AF' and a randomly selected sample of participants with 'Normal SR' diagnoses.
6. The comparative diagnostic accuracy of:
    a. Pulse palpation by CPs and either the $_{SL}$ECG interpretation by CPs or the KMD algorithm
    b. $_{SL}$ECG interpretation by CPs and the KMD algorithm.
7. The inter-rater agreement (Cohen's kappa) between the:
    a. Pulse palpation by CPs and the reference standard
    b. $_{SL}$ECG interpretation by CPs or the KMD algorithm and the reference standard
    c. Pulse palpation by CPs and either the $_{SL}$ECG interpretation by CPs or the KMD algorithm.
    d. $_{SL}$ECG interpretation by CPs and the KMD algorithm

8. The quality of $_{SL}$ECG recordings produced by CPs using KMD, defined as proportions (%) of $_{SL}$ECG recordings classified by CPs as 'Excellent', 'Acceptable', 'Poor' or 'Unreadable'.
9. The proportion (%) of screened individuals who were referred to the GP and were followed-up, including the yield of 'new' AF and non-AF diagnoses after the confirmation by $_{12L}$ECG.
10. The feasibility and acceptability of the AF screening strategy proposed, ascertained through multi-stakeholder feedback questionnaires for study participants, CPs and GPs of participating practices.
11. The cost-effectiveness of the AF screening strategy proposed with either pulse palpation or $_{SL}$ECG compared to the no-screening scenario. The cost-effectiveness of the intervention compared to no-screening was defined as an ICER < WTP of £20,000/QALY gained and a positive INB (NICE 2012a; Welton *et al.* 2017).

3.3.5 Sample size calculation

The sample size for this study was estimated from the minimum number of AF cases required for a statistically accurate comparison of diagnostic accuracy between the index tests and the reference standard (the primary outcome measures). The total prevalence of AF amongst the individuals aged ≥ 65 years in UK primary care ranges from approximately 5% identified by earlier studies (Sudlow *et al.* 1998b; Majeed *et al.* 2001) to as much as 10% according to the more recent estimates (Ball *et al.* 2013; Public Health England 2017a). Assuming the lowest reported prevalence of 5%, a sample size of 600 participants would produce an expected 30 cases of AF with a 95% confidence interval (CI) of between 20 and 40 cases. Where the statistical power is assumed to be 80% and the type I error rate is 5%, even the lower end of this range (20 cases) would allow an accurate comparison of diagnostic accuracy between the index tests and the reference standard using the McNemar's test for paired categorical data (Connor 1987).

3.3.6 Eligibility criteria

Inclusion criteria

- Age ≥ 65 years
- Eligible for seasonal influenza vaccination
- Registered at one of participating GP practices.

Exclusion criteria

- Age < 65 years

- Patients fitted with a pacemaker or defibrillator
- A lack of mental capacity to provide written informed consent with reference to criteria outlined in the Mental Capacity Act 2005 (The National Archives 2005)
- Severe co-existing medical condition which a researcher considers to be the reason to exclude the patient from the study (e.g. terminal illness with life expectancy under 1 month).

3.3.7 Recruitment and informed consent

Study participants were recruited using a convenience sampling approach, which included consecutively enrolling all eligible individuals (Martínez-Mesa *et al.* 2016). Prospective participants were recruited during two influenza vaccination seasons, between November 2017 and February 2018 and then again between October and December 2018, using three main strategies: self-referral by responding to study advertising, an invitation at the time of booking for the vaccination, or opportunistic recruitment on the day of the clinic (**Figure 3.1**). The study was advertised via promotional posters/leaflets displayed at each participating surgery (**Appendices 12 and 13**), the MSOP website (**Appendix 14**) and text messages sent to individuals aged ≥ 65 by the research co-ordinator at one of the surgeries (**Appendix 15**). Individuals aged ≥ 65 who were booking to attend their influenza vaccination clinic at the same surgery were invited to take part by the administrative team face-to-face or via the telephone. On the day of the influenza vaccination clinic, attending individuals were approached and offered to take part by the research team (including CPs) either before or after their vaccination. In a small number of cases, eligible individuals attending other (non-influenza vaccination) appointments at their surgery, were invited to participate by the research team before or after their appointment.

Prior to their enrolment onto the study, GPS or the research team confirmed the individual's eligibility (**Appendix 16**) and provided them with a participant information leaflet (PIL; **Appendix 17**). The PIL contained information about the purpose of the study, the eligibility criteria, the AF screening process, the follow-up, data processing and management, the process of withdrawal from the study, the funding information and relevant contact details. The research team also provided each prospective participant with a brief explanation of the study, the screening procedure and the management of data in accordance with the PIL. Each prospective participant was given as much time as they needed to decide whether or not to take part, and were offered an opportunity to ask the research team any questions they may have.

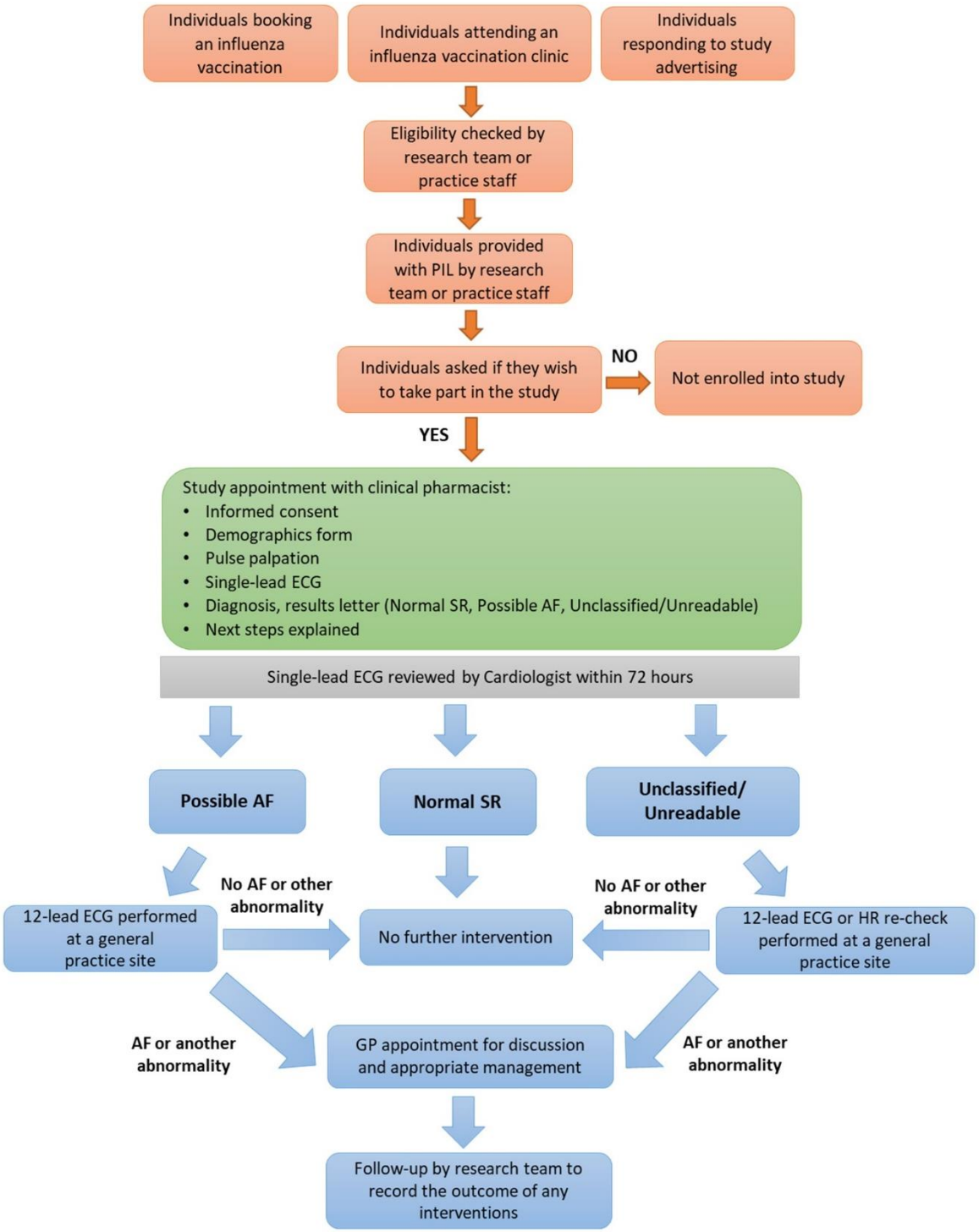


Figure 3.1 The flowchart of the Pharmacists Detecting Atrial Fibrillation study in GP surgeries

The figure includes the details of recruitment, informed consent, screening procedure and the post-appointment processes. Abbreviations: AF – atrial fibrillation; ECG – electrocardiogram; GP – general practitioner; HR – heart rate; PIL – participant information leaflet; SR – sinus rhythm.

Those interested could choose to undergo the screening the same day as their other appointment or to book an appointment to attend the screening at a more convenient time. A written informed consent to take part was obtained from each participant immediately before the screening procedure by the research team, with one copy of the consent form (**Appendix 18**) retained by researchers and one copy given to the participant.

3.3.8 Screening protocol and follow-up

After obtaining consent, the research team asked participants to complete a basic demographic form (**Appendix 19**) and assisted them as necessary. Where participants could not remember their height or weight, the most recent estimates were obtained from their medical record within the practice if available. The CP then performed a radial pulse palpation over 60 seconds noting down the HR in bpm and the regularity of the pulse as 'Normal SR' (regular pulse), 'Possible AF' (suspected AF or irregularly irregular pulse), 'Unclassified' (inconclusive or non-AF abnormality, e.g. ectopic beats) or 'Unreadable' (impalpable) in the pulse and ECG recording form (**Appendix 20**) as described in section **2.6.1**. Where radial pulse was impalpable or unclear, the CP proceeded with the palpation of ulnar pulse recording the same clinical information.

Afterwards, the CP used a KMD device to record a 30-second $_{SL}$ECG trace. All participants were advised to remain silent during the recording whereas participants wearing hearing aids were also asked to temporarily switch them off to minimise the impact of noise on the quality of the recording. Only one $_{SL}$ECG recording was performed unless the trace was of poor quality or unreadable, in which case a second ECG was recorded accordingly. The information of the last recording was used for data analysis.

Once the $_{SL}$ECG recording was complete, CPs made a note of the provisional diagnosis by the automated KMD algorithm as either 'Normal SR', 'Possible AF', 'Unclassified' or 'Unreadable' explaining the meaning of the appropriate diagnosis to the participant. They then manually interpreted the trace for the presence of AF (**Figure 3.2**), explaining to the participant what they could see in a patient-friendly language whilst noting down whether or not:

- The recording contained consistent and distinct P waves, and
- The P waves were always followed by QRS complexes, and
- The intervals between QRS complexes (R-R intervals) were consistently regular. (Fuster *et al.* 2006; Bunce & Ray 2017).

Note that the presence of AF may also be associated with f waves, which indicate that electrical stimuli are originating from sites other than the SA node and that the heart is 'fibrillating' (Fuster *et al.* 2006; Bunce & Ray 2017). For the purpose of this study, the absence of distinct p waves was considered to be inclusive of the f waves. More information about the individual components of the ECG cycle is provided in section **1.1.1**.

The CPs were also asked to rate the quality of the $_{SL}$ECG trace from 'Excellent' (atrial activity clearly visible or absent) to 'Acceptable' (atrial activity not reliably seen but rhythm interpretation possible on the basis of the R-R interval), 'Poor' (excessive noise, difficult to interpret) or 'Unreadable' (where the quality of the trace was too poor to interpret). Depending on their interpretation of $_{SL}$ECG, CPs then indicated their own provisional diagnosis as either 'Normal SR' (where they did not identify any obvious abnormalities), 'Possible AF' (where they suspected AF), 'Unclassified' (where they suspected a non-AF abnormality) or 'Unreadable'. CPs were not expected to identify any non-AF abnormalities, however they were able to provide additional comments where they had a suspicion of a particular pattern (e.g. a BBB) or where they identified any factors which may have influenced the quality of the ECG recording.

After $_{SL}$ECG interpretations by the KMD and the CP were obtained, CPs used their professional judgement to record the final provisional diagnosis and provide each participant with an appropriate letter of results (**Appendices 21, 22 and 23**), explaining the details of any follow-up steps which may be required. They also reassured the patient that the provisional diagnosis would be verified by the study cardiologist. Participants with 'Normal SR' diagnoses were advised that no further action was required unless the cardiologist determined otherwise, in which case they would be contacted by their GP practice. Those with 'Possible AF', 'Unclassified' or 'Unreadable' diagnoses were advised that they would be contacted by their GP practice within two weeks once the cardiologist reviewed their ECG to determine whether or not any follow-up action, such as a $_{12L}$ECG, was required. Participants with a 'Possible AF' diagnosis were also given further information about AF in a form of the British Heart Foundation's (BHF) booklet (BHF 2014). Lastly, all participants were asked to complete a short feedback questionnaire (**Appendix 24**) and, if interested, were given a pre-paid envelope containing information about the optional focus group interviews, which are discussed in more detail in **Chapter 4**.

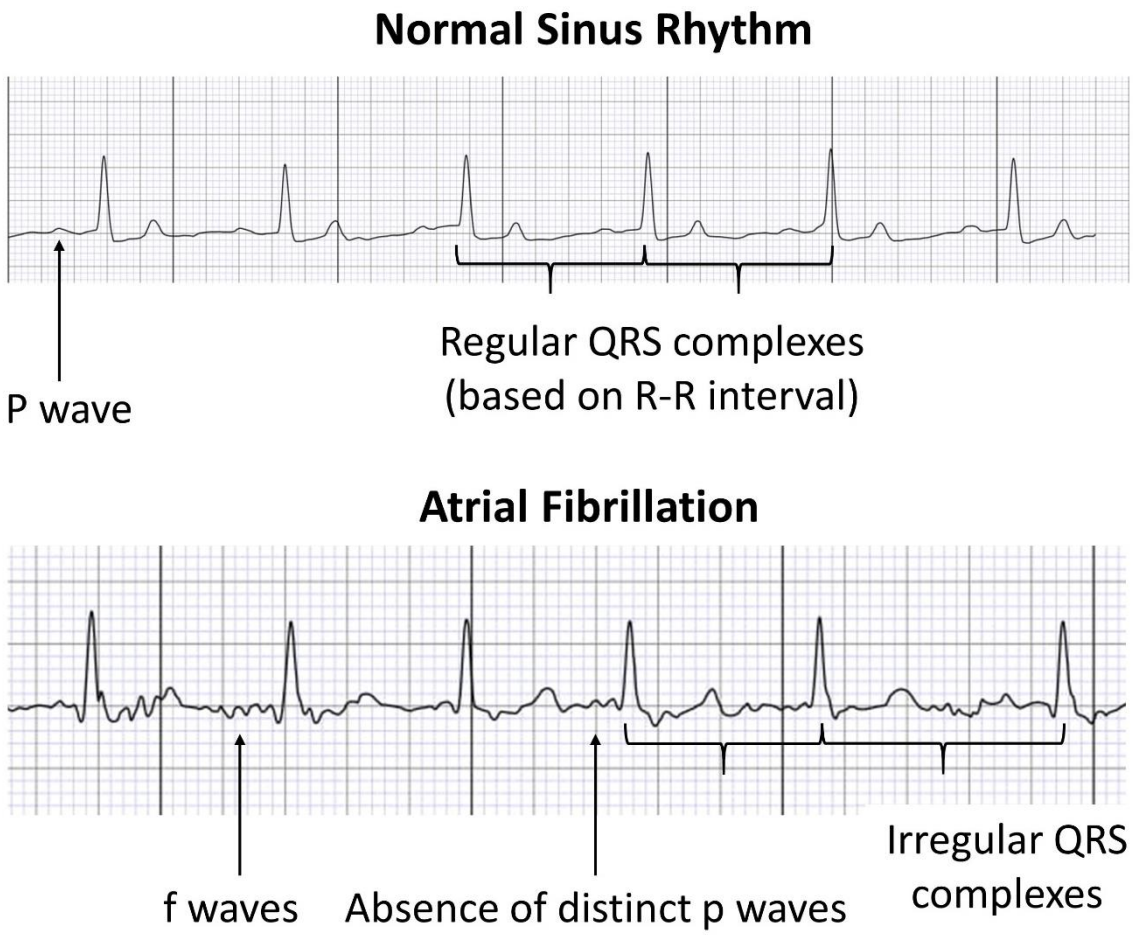


Figure 3.2 The key elements of $_{SL}$ECG traces indicating either normal sinus rhythm or atrial fibrillation

Abnormalities indicating atrial fibrillation were used to guide clinical pharmacists when interpreting $_{SL}$ECG recordings produced by the Kardia Mobile® device. Abbreviations: $_{SL}$ECG – single-lead electrocardiogram.

All $_{SL}$ECG traces were pseudonymised and securely emailed by the CP to the study cardiologist who over-read them within 72 hours to confirm or reject the provisional diagnosis and to recommend an appropriate action, for instance a $_{12L}$ECG or a HR re-check. The GP practice was then informed accordingly to make arrangements for any follow-up actions as per in-house procedures. After the appropriate action by the surgery, the research team followed-up all participants with 'Possible AF', 'Unclassified' and 'Unreadable' diagnoses by collating their enhanced demographic data and any screening-related outcomes or interventions (e.g. a new diagnosis of AF or initiation of OAC therapy; **Appendix 25**). The records of participants with 'Normal SR' diagnoses were only reviewed if they required a follow-up action (e.g. where the participant reported a previous history of

AF) or where they were randomly selected amongst the sub-group of 100 participants with 'Normal SR' for demographic comparison.

3.3.9 Stakeholder feedback questionnaires

The 17-item participant feedback questionnaire (**Appendix 24**) was offered to all study participants and aimed to ascertain their knowledge about AF, their experience during the test and their views about the future screening. It included 16 closed-ended questions, which consisted of a mixture of three or four-point Likert scale questions (from 'Very important', 'Very good' or 'Very satisfied' to 'Not important', 'Very Poor' or 'Very dissatisfied') and several 'Yes' or 'No' answer questions. Participants were also able to provide free-text responses to three of these questions in relation to positive/negative aspects of the service and any future screening initiatives by CPs. The open-ended question item at the end of the questionnaire appealed to study participants for any potential improvements to the AF screening strategy proposed.

All CPs involved in the study were asked to complete a 14-item study feedback questionnaire (**Appendix 26**), which aimed to determine any improvement in their knowledge of AF following the study, their satisfaction with various aspects of study experience (e.g. support from the research team) and their perceptions about the role of CPs in the detection of AF. The questionnaire consisted of 11 five-point Likert scale-based questions (from 'Very good', 'Very important' or 'Very satisfied' to 'Very Poor', 'Not very important' or 'Very dissatisfied'), three open-ended questions to explore the positive/negative aspects of the service or role of CPs in AF detection, and a short, anonymous demographic form. In addition, all CPs were given an opportunity to evaluate the training received in preparation for AF screening (**Appendix 27**). This questionnaire covered the specific aspects of training, such as the clinical assessment using pulse palpation or the training in using the study protocol, and consisted of eight five-point Likert scale questions (from 'Excellent' to 'Very Poor'). CPs were also able to add free-text comments to justify each of their answers.

The feedback from GPs working in participating practices was sought via a 14-item questionnaire (**Appendix 28**), which aimed to find out more about the routine process of AF diagnosis at their surgery, their individual experience of the service delivered during the study and their views about AF screening. The questionnaire included 12 closed-ended questions, which consisted of a mixture of 'Yes/'No'/'Possibly' and three or four-point Likert scale-based questions (from 'Very important', 'Excellent' or 'Very well' to 'Not important', 'Poor' or 'Not well'). Participants were able to add free-text comments under six of these

questions, relating to the performance/interpretation of $_{12L}$ECG, the positive/negative aspects of the service and the utilisation of CPs to deliver AF screening in the future. They were also asked to provide any additional comments on how the proposed service could be improved and to rate the likelihood that the AF screening proposed would become a national screening programme from 1 – not at all to 10 – extremely likely.

All stakeholder questionnaires were anonymous and were developed and validated as described in section **2.6.1**. The CPs and GPs handed in their completed questionnaires to the gatekeeper of their organisation who forwarded them to the research team without affecting the anonymity of the respondent.

3.3.10 Quantitative data analysis

The quantitative data analysis followed the fundamental assumptions and statistical considerations presented in section **2.7**. Responses to open-ended questions of stakeholder feedback questionnaires were analysed using a content analysis (Lavrakas 2008), accompanied by the word-cloud approach for participant feedback questionnaires (Vasconcellos-Silva *et al.* 2013) as described in section **2.7.3**.

3.3.11 Economic analysis

The economic model was constructed as a Markov cohort simulation and focused on a cost-effectiveness comparison between two hypothetical cohorts of patients with AF aged ≥ 65 years, derived from the total population of England and Wales (a population of 10,517,461) (Office for National Statistics 2017a; Office for National Statistics 2017b). One group of patients were offered to participate in a single time point AF screening, had a chance to be detected as AF positive (if not already known) and may have been initiated on OAC therapy (the 'intervention cohort' or the 'screening strategy'). The other group did not undergo screening, were not identified as AF positive and hence were not offered OAC (the 'control cohort' or the 'no-screening strategy'). The model also compared the cost-effectiveness of AF screening using the KMD with that using the conventional pulse palpation. The detailed rationale for this method and the breakdown of key model assumptions is provided in section **2.8**.

Both cohorts entered the model in the state of 'Stable AF' and were allowed to transition to either the states of 'Post-stroke', 'Post-major bleed' or 'Death' every 3 months for a total of 10 years. The baseline transition probabilities between the health states were obtained from major OAC trials and are presented in **Appendix 29**. The baseline all-cause mortality rate was adjusted for mortality rate observed in individuals aged ≥ 65 years in England and

Wales, and corrected for increased mortality following an ischaemic stroke or major bleed (Jacobs *et al.* 2018; Eikelboom *et al.* 2006). In addition to general model assumptions described in section **2.8.3**, and with reference to study findings discussed below, the base-case economic analysis assumed the following:

- The prevalence of total and 'unknown' AF of 4.3% and 1.3%, respectively as determined by the cardiologist's interpretation of $_{SL}$ECG (reference standard).
- The rate of 'Unclassified'/'Unreadable' diagnoses of 13.4% as determined by $_{SL}$ECG interpretation using the KMD algorithm.
- The sensitivity and specificity of the KMD algorithm with regards to the reference standard of 92.3% and 97.4%, respectively.
- That all participants with 'new' AF were eligible for OAC therapy (a CHA_2DS_2-VASc score of ≥ 2 for females, or ≥ 1 for males).

The general costs of the base-case model were as outlined in section **2.8.4** and **Appendix 29**, and included the purchasing cost of KMDs, CP time (11 minutes/appointment based on PDAF data) (NHS Employers 2019), relevant medical interventions ($_{12L}$ECG/GP interpretation and GP/cardiologist appointments for 'new' AF) (NHS Improvement 2017; Welton *et al.* 2017), the cost of OAC therapy, ischaemic strokes/major bleeds (NICE 2014b) and false positive (AF/'Unclassified'/'Unreadable') diagnoses when using the KMD. The purchasing cost of KMD included 6,000 devices with reference to the estimates from the AHSN initiative in England (The AHSN Network 2019a; AliveCor 2019c). This cost was excluded from the AF screening strategy using pulse palpation.

The PSA employed a Monte Carlo simulation of the Markov model generating 100,000 simulations to test deviations from the base case listed in section **2.8.5**. The scenario of AF screening using pulse palpation assumed the respective sensitivity (76.9%), specificity (92.2%) and rate of 'Unclassified'/'Unreadable' diagnoses (2.2%) observed when using this method during the PDAF study. The mean INBs for both AF screening scenarios were calculated per patient with AF and per all patients with 'new' AF detected using each method across England and Wales (Office for National Statistics 2018c).

3.4 Results

3.4.1 Study participants

The desired sample size of 600 participants was achieved over a period of seven months, spread across two influenza vaccination seasons. A total of 615 eligible individuals were recruited for CP-led AF screening at four participating GP practices in Kent. As shown in **Figure 3.3**, 11 of them (1.8%) were subsequently excluded from the study, either because they underwent the same AF screening during the previous influenza vaccination season (1.1%, 7/615), were not registered at any of the participating surgeries (0.5%, 3/615) or retracted their consent to take part (0.2%, 1/615). As such, a total of 604 participants entered the study and were included in data analysis. Nearly three quarters of all participants (74.2%, 448/604) were recruited at one of the surgeries.

The median age of all participants was 73 [69; 78] years and the majority of them (57.3%, 346/604) were female (**Table 3.1**). About 97% of individuals (96.9%, 585/604) considered themselves to be White British, followed by the minority of those who either declared another White (2.3%, 14/604) or non-White (0.8%, 5/604) ethnicity. Less than one in 10 were smokers (8.9%, 54/604), however over 60% (62.9%, 380/604) consumed at least one unit of alcohol each week with a median of 6 [2; 14] units. The average BMI across the study sample was 26.1 [23.5; 29.3] kg/m^2. Approximately 85% of all study participants had only one $_{SL}$ECG recording (84.8%, 512/604).

Two or more $_{SL}$ECGs were performed in 15.2% (92/604) of participants where the first recording was deemed by the CP to be ‘Unreadable’ or of poor quality, resulting in a median appointment time of 11 [10; 15] minutes across the study sample.

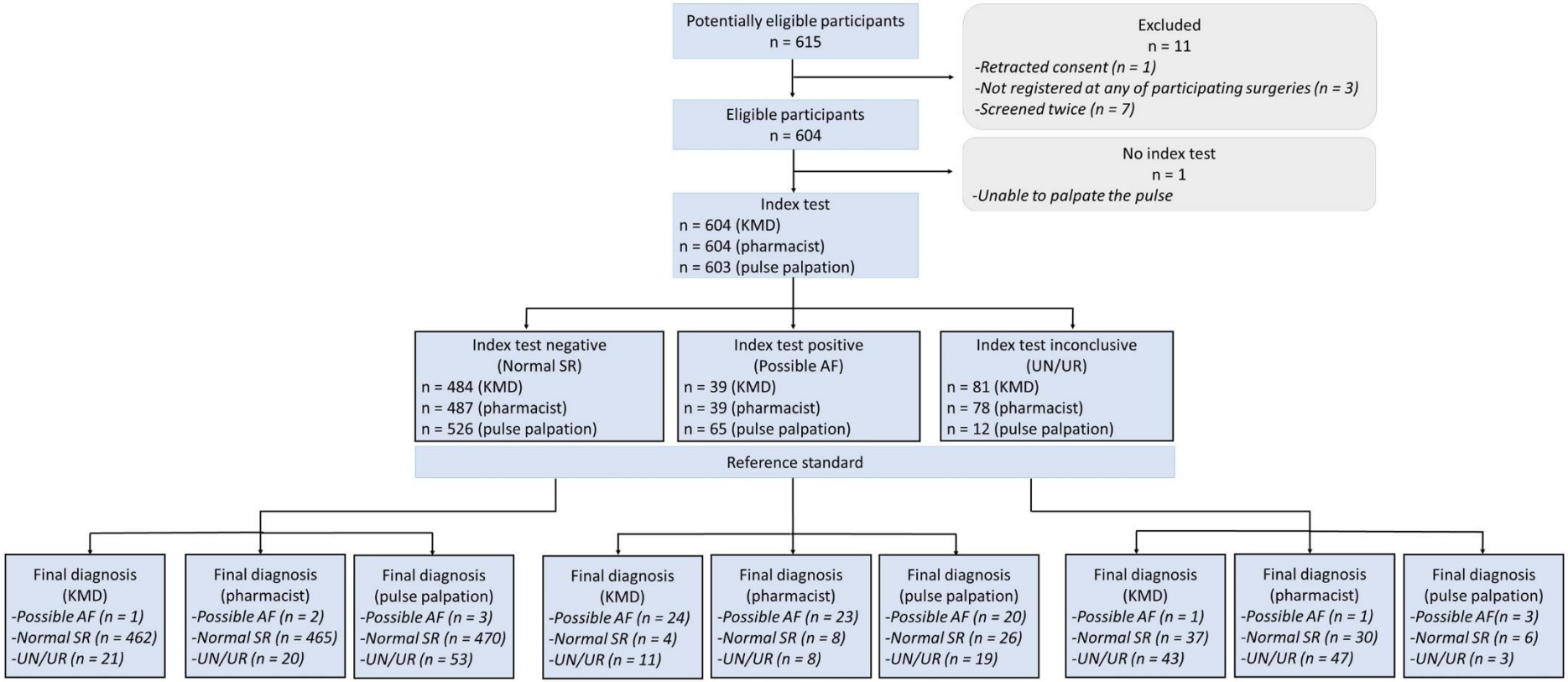


Figure 3.3 STARD flow diagram for the PDAF study in general practice surgeries

The figure was adapted from Cohen et al. (2016), and displays the inclusion/exclusion of study participants and the diagnostic classification by each index test (KMD interpretation of $_{SL}$ECG, pharmacist's interpretation of $_{SL}$ECG or pulse palpation) and the reference standard. Abbreviations: AF – atrial fibrillation; KMD – Kardia Mobile® device; PDAF – Pharmacists Detecting Atrial Fibrillation; $_{SL}$ECG – single-lead electrocardiogram; SR – sinus rhythm; STARD - Standards for Reporting Diagnostic Accuracy Studies; UN – Unclassified; UR – Unreadable.

Table 3.1 Demographic characteristics of participants screened in GP surgeries

*Continuous variables are expressed as a median [interquartile range]. Categorical variables are expressed as a number of participants (% total of the group). *White European, Flemish, Italian, Scottish and South African (n = 1 each), and White Non-specified or Other (n = 2). **Kazakh, American, Australian, Hungarian and Norwegian (n = 1 each). Abbreviations: BMI – body mass index; bpm – beats per minute; GP – general practitioner.*

Characteristics	N = 604
Age, years	73 [69; 78]
Male	258 (42.7%)
Ethnicity	
White British	585 (96.9%)
White Irish	3 (0.5%)
White American	2 (0.3%)
White Dutch	2 (0.3%)
*White Other**	7 (1.2%)
*Other***	5 (0.8%)
Current alcohol drinker	380 (62.9%)
Alcohol, units/week	6.0 [2.0; 14.0] (n = 372)
Current smoker	54 (8.9%)
Height, cm	167.0 [160.0; 174.0] (n = 596)
Weight, kg	73.0 [64.0; 83.0] (n = 588)
BMI, kg/m^2	26.1 [23.5; 29.3] (n = 585)
Heart rate device, bpm	72 [65; 81]

3.4.2 Screening outcomes

Participants with 'Possible AF'

The study cardiologist was able to interpret $_{SL}$ECG recordings pertaining to 99% of all participants, with only 1% (6/604) of traces deemed 'Unreadable' (**Figure 3.4**). Twenty-six participants (4.3%, 26/604) displayed a 'Possible AF' diagnosis resulting in a total AF prevalence of 4.3% (95% CI, 2.8-6.2%). Of these, 16/604 (2.6%) participants reported no previous history of AF at the time of screening and were referred to their GP for a $_{12L}$ECG. Six participants (1.0%, 6/604) did not require any further follow-up action because they were aware of their AF diagnosis and received OAC accordingly. Another patient with 'known' AF (0.2%, 1/604) had a HR of 145 bpm at the time of screening and were referred back to the GP to review their rate-control (beta blocker) therapy as appropriate. Three participants with 'Possible AF' (0.5%, 3/604) were unsure if they had AF or received treatment for it at the time of screening and required a further confirmation by review of their GP records. Following the review of medical records, all three were confirmed to have a 'known' and

anticoagulated AF. Eight of the 16 patients with suspected AF, who were referred for $_{12L}$ECG (1.3%, 8/604), were also found to have AF and were taking OAC therapy, resulting in a total of 18/604 participants with 'known' AF at the time of screening, or a 'known' AF prevalence of 3.0%. The remaining 8/604 participants who were referred for $_{12L}$ECG had no recorded history of AF and formed the 1.3% prevalence of 'unknown' AF. All 18 participants with 'known' AF had a CHA_2DS_2VASc score ≥ 2 and were receiving either a DOAC (55.6%, 10/18) or warfarin (44%, 8/18). Similarly, all patients with an 'unknown' AF qualified for OAC, with a CHA_2DS_2VASc score of ≥ 2 for seven participants and a score of 1 for one male aged 74.

In order to compare the enhanced demographic characteristics of those with cardiologist-confirmed 'Possible AF' and those who did not have a history of AF, the research team reviewed the GP records of a random sub-group of 100 participants with 'Normal SR' diagnoses (**Table 3.2**). Seven of these 'Normal SR' cases (1.2%, 7/604) were subsequently excluded from the analysis because they had a record of a previous or current AF despite testing negative during the screening. Five had a current record of PAF (0.8%, 5/604), and one each (0.2%, 1/604) either a current record of AF with an unspecified pattern or a past medical history of AF. Compared to the rest of the 'Normal SR' sub-group (n = 93), those with 'Possible AF' (n = 26) were more likely to be male (57.7%, 15/26 vs. 38.7%, 36/93), were significantly older (82 [73; 85] years vs. 72 [69; 76] years; Mann-Whitney U test, $p < 0.001$), had a higher median BMI (28.5 [24.2; 33.5] kg/m^2 vs. 25.7 [23.1; 28.0] kg/m^2; Mann-Whitney U test, $p = 0.01$) and displayed a greater CHA_2DS_2VASc score (3.0 [3.0; 4.3] vs. 3.0 [2.0; 3.0]; Mann-Whitney U test, $p = 0.002$). Participants with 'Possible AF' were also significantly more likely to suffer from several comorbidities, including hypertension, renal disease, diabetes mellitus and heart failure. The average number of non-AF comorbidities per participant with 'Possible AF' was 2.0 [1.0; 3.0] compared to 1.0 [0.0; 2.0] amongst those with 'Normal SR' diagnoses (Mann-Whitney U test, $p < 0.001$).

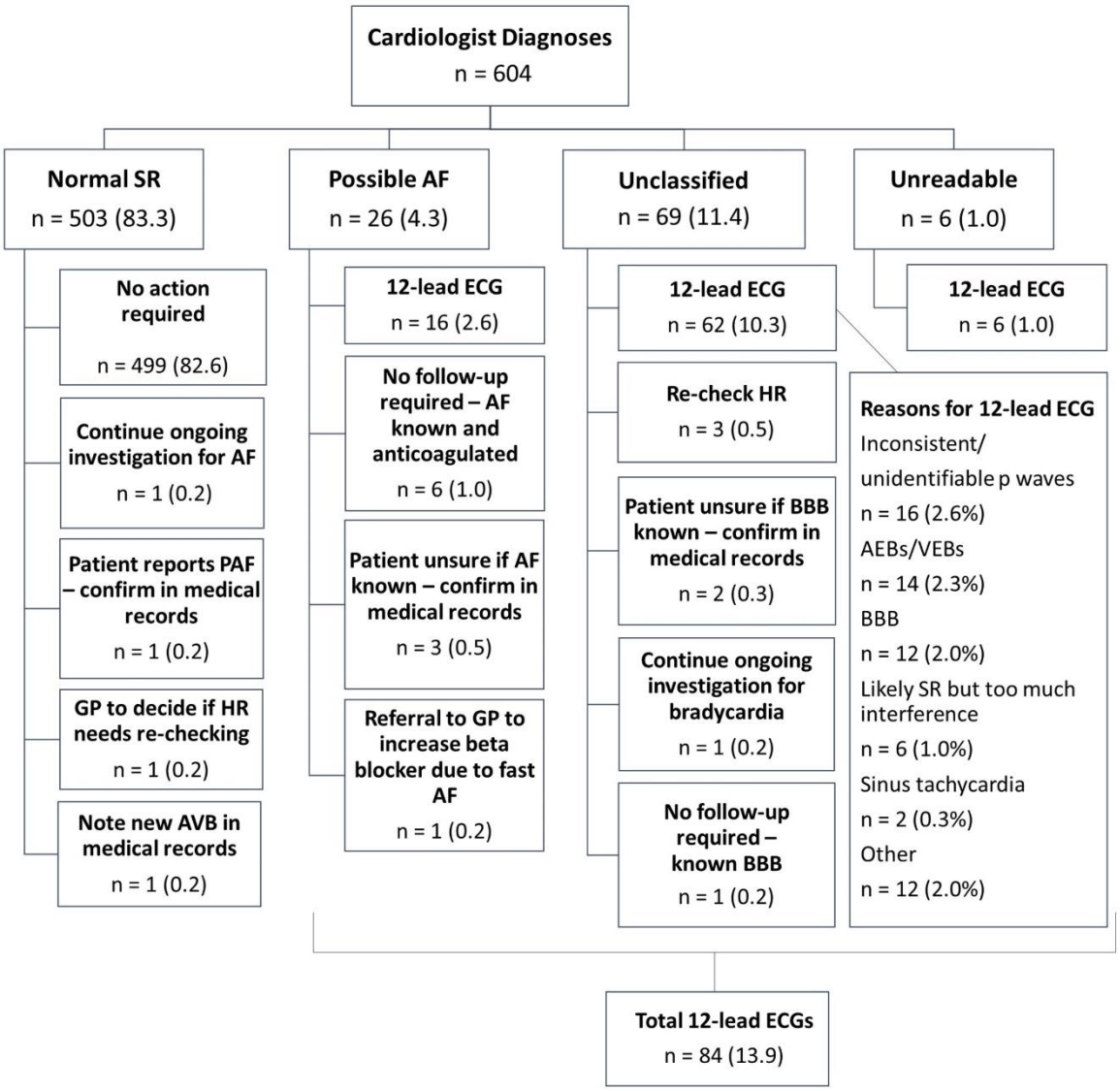


Figure 3.4 Cardiologist's diagnoses and recommended follow-up actions based on the interpretation of single-lead ECG recordings

All variables are expressed as a number of participants (% total). Abbreviations: AEB – atrial ectopic beat; AF – atrial fibrillation; AVB – atrioventricular block; BBB – bundle branch block; ECG – electrocardiogram; GP – general practitioner; HR – heart rate; PAF – paroxysmal AF; SR – sinus rhythm; VEB – ventricular ectopic beat.

Table 3.2 Demographic comparison of cardiologist-confirmed 'Possible AF' cases and a random sample of participants with 'Normal SR' diagnoses

Continuous variables are expressed as a median [interquartile range]. Categorical variables are expressed as a number of participants (% total of the group). Between-group differences were determined using a Mann-Whitney U test for numerical variables and a Pearson's Chi-square or Fisher's exact test as appropriate for categorical variables. Abbreviations: AF – atrial fibrillation; BMI – body mass index; COPD – chronic obstructive pulmonary disease.

Characteristics	Participants with cardiologist-confirmed Possible AF (n = 26)	Random Sample with cardiologist-confirmed Normal SR (n = 93)	P value (2-sided)
Age, years	82 [73; 85]	72 [69; 76]	< 0.001
Male	15 (57.7)	36 (38.7)	0.116
Current alcohol drinker	16 (61.5)	72 (77.4)	0.103
Alcohol, units/week	10.0 [2.0; 14.0] (n = 16)	5.5 [2.0; 14.0] (n = 70)	0.482
Current smoker	3 (11.5)	6 (6.5)	0.408
Height, cm	167.5 [162.5; 177.5]	170.0 [162.5; 175.0] (n = 91)	0.634
Weight, kg	78.3 [69.7; 97.0]	73.0 [65.1; 81.9] (n = 90)	0.055
BMI, kg/m^2	28.5 [24.2; 33.5]	25.7 [23.1; 28.0] (n = 89)	0.010
CHA_2DS_2VASc score	3.0 [3.0; 4.3]	3.0 [2.0; 3.0]	0.002
Hypertension	18 (69.2)	38 (40.9)	0.010
Renal disease	11 (42.3)	16 (17.2)	0.007
Diabetes mellitus	8 (30.8)	12 (12.9)	0.041
Thyroid disease	4 (15.4)	8 (8.6)	0.293
Transient ischaemic attack	3 (11.5)	3 (3.2)	0.117
Ischaemic heart disease	3 (11.5)	7 (7.5)	0.454
Heart failure	2 (7.7)	0 (0.0)	0.046
Intracranial bleed	1 (3.8)	1 (1.1)	0.391
Peripheral vascular disease	0 (0.0)	4 (4.3)	0.575
COPD	2 (8.0)	8 (8.6)	1.000

Participants with non-AF diagnoses

According to the interpreting cardiologist, more than 80% of study participants (83.3%, 503/604) displayed a 'Normal SR' at the time of AF screening. Of these, the majority (82.6%, 499/604) required no further action. One participant (0.2%, 1/604), who tested positive for 'Possible AF' by all index tests and was already undergoing a GP investigation for AF prior to screening, was thought by the cardiologist to display a 'Normal SR' with VEBs. This

participant was advised to continue their ongoing investigation. Another participant tested negative for 'Possible AF' by all tests, however self-reported a history of PAF and was on OAC therapy, which was confirmed upon the review of their GP medical records. One individual with 'Normal SR' presented with mild sinus tachycardia (HR 110 bpm), the investigation of which was left at the discretion of their GP. The $_{SL}$ECG of the last participant with 'Normal SR' showed the signs the first-degree AVB, which did not warrant any further action apart from being noted in their medical record.

Besides the six 'Unreadable' diagnoses all of whom required a $_{12L}$ECG follow-up (1.0%, n – 6/604), the study cardiologist identified another 69/604 participants (11.4%) whose $_{SL}$ECG was either of poor quality or displayed a suspected non-AF abnormality requiring a further investigation. Out of the 69 participants with 'Unclassified' diagnoses, 62 (10.3%, 62/604) were referred to their GP for a confirmatory $_{12L}$ECG, often because their $_{SL}$ECG displayed inconsistent or unidentifiable p waves (2.6%, 16/604), frequent VEBs/AEBs (2.3%, 14/604) or a left or right BBB (2.0%, 12/604). Three participants who displayed sinus tachycardia (0.5%, 3/604) were referred for a HR re-check. Another 2/604 participants with a suspected BBB (0.3%) were unsure about their diagnosis at the time of screening and were confirmed as 'known' BBB after the review of their GP records. One participant with a cardiologist-suspected sinus bradycardia was already undergoing a GP investigation for this condition and was advised to continue whereas a different patient self-reported a history of BBB and required no further action.

3.4.3 Diagnostic accuracy

$_{SL}$ECG interpretation by the KMD algorithm

The KMD algorithm classified 484/604 (80.1%) participants as displaying 'Normal SR', 39/604 (6.5%) – as 'Possible AF', 75/604 (12.4%) – as 'Unclassified' and 6/604 (1.0%) – as 'Unreadable' (*N.b.* all 'Unreadable' diagnoses matched those by the cardiologist; **Figure 3.5**). Compared to reference standard, the KMD algorithm correctly identified 24 out of 26 cases of 'Possible AF' but misdiagnosed 15 participants without AF as 'Possible AF'. This produced a sensitivity of 92.3% with an FPR of 2.6% and a moderate FDR of 38.5% (**Table 3.3**). The overall accuracy of the KMD algorithm was high at 97.2% whilst the Cohen's Kappa between the KMD algorithm and the interpreting cardiologist remained substantial at 0.72.

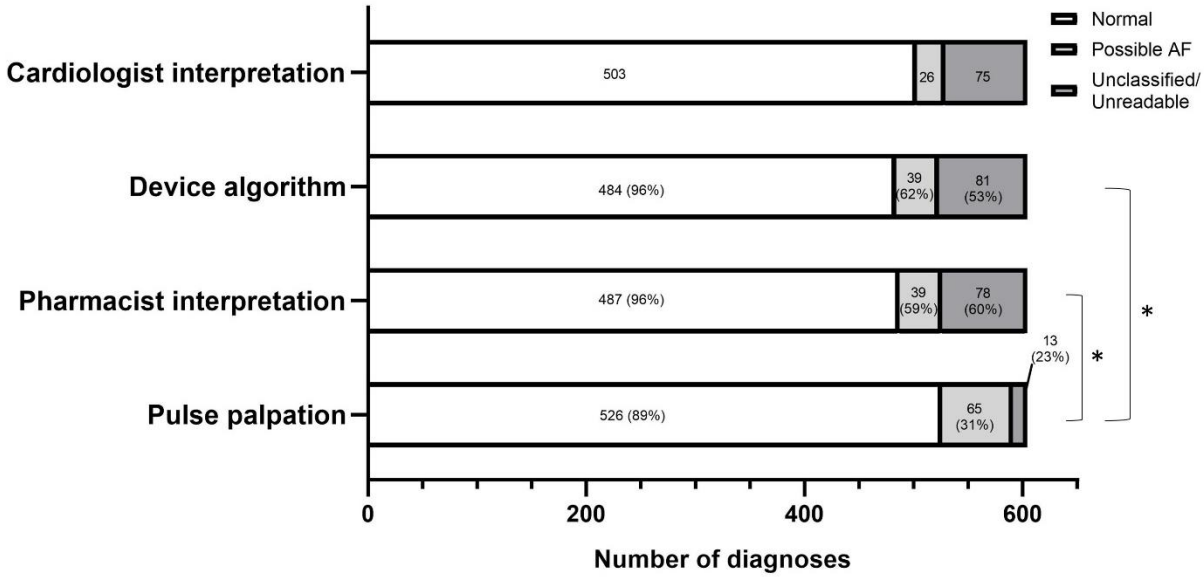


Figure 3.5 Diagnostic breakdown by index tests compared to the reference standard when conducting AF screening in GP surgeries

*Adapted from: Savickas et al. (2020b). Pulse palpation, KMD algorithm and clinical pharmacist's interpretation of $_{SL}$ECG (index tests) are compared to the cardiologist's interpretation of the $_{SL}$ECG (reference standard). All data are expressed as the number of cases in each diagnostic category (% mean positive predictive value). *p = 0.001 for between-measurement differences derived from 2 x 2 contingency tables using a Cochran's Q test followed by post-hoc McNemar's tests and a Bonferroni correction for multiple comparisons. Abbreviations: AF – atrial fibrillation; GP – general practitioner; KMD – Kardia Mobile® device; $_{SL}$ECG – single-lead electrocardiogram.*

According to the cardiologist, one of the two individuals who were falsely classified by the KMD as 'Normal SR' displayed the signs of PAF on their $_{SL}$ECG. The other patient showed a 'Possible AF' but was misdiagnosed by the KMD algorithm as 'Unclassified'. Four participants with false positive AF diagnoses by the KMD algorithm were thought to display a 'Normal SR' (0.7%, 4/604; *N.b.* one had AEBs/VEBs) whereas the others were 'Unclassified' (1.8%, 11/604) due to the presence of AEBs/VEBs (1.0%, 6/604), too much interference (0.3%, 2/604), inconsistent/unidentifiable p waves (0.2%, 1/604), irregular baseline (0.2%, 1/604) or a possible BBB (0.2%, 1/604).

Table 3.3 Diagnostic accuracy of index tests for the detection of AF compared to the reference standard

The accuracy of $_{SL}$ECG interpretation by the KMD algorithm or clinical pharmacist, and pulse palpation (index tests) when compared to the cardiologist's interpretation of $_{SL}$ECG (reference standard). All measures are expressed as a mean (95% confidence intervals). Abbreviations: AF – atrial fibrillation; FDR – false discovery rate; FPR – false positive rate; KMD – Kardia Mobile® device; PPV – positive predictive value, $_{SL}$ECG – single-lead electrocardiogram.

Diagnostic Accuracy Measures	**Index Tests**		
	KMD algorithm	*Pharmacist interpretation*	*Pulse palpation*
Sensitivity	92.3 (74.9 -99.1)	88.5 (69.9-97.6)	76.9 (56.4-91.0)
Specificity	97.4 (95.8-98.5)	97.2 (95.5-98.4)	92.2 (89.7-94.3)
Accuracy	97.2 (95.5-98.4)	96.9 (95.1-98.1)	91.6 (89.1-93.7)
FPR	2.6 (1.5-4.2)	2.8 (1.6-4.5)	7.8 (5.7-10.3)
PPV	61.5 (44.6-76.6)	59.0 (42.1-74.4)	30.8 (19.9-43.5)
FDR	38.5 (23.4-55.4)	41.0 (25.6-57.9)	69.2 (56.6-80.1)
Cohen's Kappa	0.72 (0.60-0.85)	0.69 (0.56-0.82)	0.40 (0.27-0.53)

Other than false positive AF diagnoses, the KMD algorithm also issued 37 false positive 'Unclassified' diagnoses to participants who were deemed by the cardiologist to exhibit a 'Normal SR' (6.1%, 37/604). Where indicated by the cardiologist, the key reasons underlying such false positive diagnoses included AEBs/VEBs (1.7%, 10/604) and mild sinus tachycardia (0.3%, 2/604). Together with four cases of false positive AF, these false diagnoses by the KMD algorithm would have resulted in 41 unnecessary referrals for $_{12L}$ECG (6.8%, 41/604).

$_{SL}$ECG interpretation by CPs

After the $_{SL}$ECG interpretation by the KMD algorithm, each CP was asked to manually interpret the trace noting down their own provisional diagnosis. The interpreting CPs classified the $_{SL}$ECGs of 487/604 (80.6%) participants as 'Normal SR', 39/604 (6.5%) – as 'Possible AF', 71/604 (11.8%) – as 'Unclassified' and 7/604 (1.2%) – as 'Unreadable' (*N.b.* all except one 'Unreadable' diagnoses matched those by the cardiologist or KMD). With reference to the cardiologist's interpretation of $_{SL}$ECG, CPs identified 23 out of 26 participants with true positive 'Possible AF', however also issued 16 false positive AF diagnoses. This resulted in diagnostic accuracy measures comparable to those of the KMD algorithm (**Table 3.3**), and a substantial inter-rater agreement with the cardiologist of 0.69.

There were no statistically significant differences between the diagnostic accuracy of the KMD algorithm and $_{SL}$ECG interpretation by CPs (McNemar's test; $p > 0.05$), giving rise to an excellent inter-rater agreement of 0.89 (95% CI, 0.82-0.97). A total of 35 'Possible AF' diagnoses identified by CPs (5.8%, 35/604) matched the ones derived through the KMD algorithm, including all 23 true positives and 12 out of 16 false positives. Compared to the KMD algorithm, CPs classified an additional four participants with 'Normal SR' as 'Possible AF' (0.7%, 4/604; *N.b.* three of these showed AEBs/VEBs). Two of the three false negative AF diagnoses by CPs matched the ones issued by the KMD whereas the third participant was given a false 'Unclassified' diagnosis.

Similar to the KMD algorithm, $_{SL}$ECG interpretation by CPs produced an additional 30 false positive 'Unclassified' diagnoses in participants with a 'Normal SR' (5.0%, 30/604). Where indicated by the cardiologist, this may have occurred due to AEBs/VEBs (1.2%, 7/604), mild sinus tachycardia (0.2%, 1/604) or the first-degree AVB with VEBs (0.2%, 1/604). In total, $_{SL}$ECG interpretation by CPs would have resulted in 38 unnecessary referrals for a $_{12L}$ECG (6.3%, 38/604), three fewer than observed with the KMD algorithm above.

Apart from their diagnostic interpretation, CPs were asked to rate the quality of each KMD recording. Over 90% of participants displayed $_{SL}$ECG recordings corresponding to either 'Excellent' (60.1%, 363/604) or 'Acceptable' (32.9%, 199/604) quality. Considerably fewer participants had a 'Poor' quality trace (5.3%, 32/604) and only 10/604 (1.7%) were deemed to be 'Unreadable'. Five of these 'Unreadable' quality traces matched the 'Unreadable' diagnoses by interpreting CPs, whereas the remaining five related to four 'Unclassified' and one 'Normal SR' diagnoses. The other two participants with CP-interpreted 'Unreadable' diagnoses had 'Poor' quality $_{SL}$ECG.

Pulse palpation by CPs

By relying on pulse palpation, CPs categorised 526/604 (87.1%) participants as 'Normal SR', 65/604 (10.8%) – as 'Possible AF', 12/604 (2.0%) – as 'Unclassified' and 1/604 (0.2%) – as 'Unreadable' (i.e. impalpable). Although statistically different, the average HR derived through pulse palpation was clinically comparable to that obtained through KMD: 70 [62; 78] and 72 [65; 81] bpm, respectively (Wilcoxon signed-rank test, $p < 0.001$). Compared to the cardiologist's interpretation of $_{SL}$ECG, pulse palpation identified 20 out of 26 true positive cases of 'Possible AF' but produced as many as 45 false positive AF diagnoses, resulting in a modest sensitivity of 76.9%, an FPR of 7.8% and a high FDR of 69.2%. Whilst this significant rate of false diagnoses was not apparent from the overall diagnostic accuracy (91.6%), it was reflected in the poor inter-rater agreement with the study cardiologist (0.40).

The diagnostic classification of AF positive and AF negative cases differed significantly between the cardiologist's interpretation of $_{SL}$ECG and any of the three index tests (McNemar's test, p = 0.012 for KMD algorithm, p = 0.024 for CP interpretation and p < 0.001 for pulse palpation). However, apart from displaying a poor diagnostic agreement with reference standard, the diagnostic accuracy of pulse palpation was also significantly different compared to either of the other two index tests (McNemar's test, p = 0.001 and Cohen's Kappa of 0.52 (95% CI, 0.40-0.64) for both comparisons). As such, only twenty-nine out of the 65 'Possible AF' diagnoses identified by pulse palpation (4.8%, 29/604) matched the 'Possible AF' diagnoses of either the KMD algorithm or the CP interpretation of $_{SL}$ECG: 19 of 20 true positives and 10 out of 45 false positives each. Twenty-six of the false positive AF diagnoses by pulse palpation were ruled out by the cardiologist as 'Normal SR' (4.3%, 26/604; *N.b.* nine displayed AEBs/VEBs). The rest were 'Unclassified' (3.1%, 19/604) due to the occurrence of AEBs/VEBs (1.8%, 11/604), inconsistent/unidentifiable p waves (0.5%, 3/604), mild sinus tachycardia or bradycardia (0.3%, 2/604), irregular baseline (0.2%, 1/604), too much interference (0.2%, 1/604) or a BBB (0.2%, 1/604). Only one of the six false negative AF cases who were issued a 'Normal SR' diagnosis by pulse palpation (0.2%, 1/604) matched with either the KMD algorithm or the CP interpretation of $_{SL}$ECG (the participant with PAF). The other five false negative cases were inappropriately classified as either 'Normal SR' (0.3%, 2/604) or 'Unclassified' (0.5%, 3/604).

Compared to the other two index tests, a relatively small proportion of participants with cardiologist-determined 'Normal SR' were issued a false positive 'Unclassified' diagnosis following pulse palpation (1.2%, 7/604). Therefore, at 33/604 (5.5%) participants, the total number of unnecessary referrals for $_{12L}$ECG as a result of pulse palpation was lower than either that encountered with the KMD algorithm or the CP interpretation of $_{SL}$ECG.

3.4.4 Follow-up outcomes

After the initial screening and cardiologist's interpretation of $_{SL}$ECG, a total of 87/604 (14.4%) participants with 'Possible AF' or 'Unclassified'/'Unreadable' diagnoses were referred to their GP for either a $_{12L}$ECG (13.9%, 84/604) or a HR re-check (0.5%, 3/604). The $_{12L}$ECG was performed in 63 out of 84 participants referred for the procedure (75.0%), and in all 3 participants referred for a HR re-check (75.9%, 66/87), with a median time between the screening and $_{12L}$ECG of 16.0 [11.0; 24.0] days (**Figure 3.6**). A total of 16/84 participants (19.0%) did not require a $_{12L}$ECG because they either: had a 'known' AF (10.7%, 9/84; *N.b.* additional 10 participants were previously confirmed as 'known' AF after a review of medical records), a 'known' BBB (4.8%, 4/84), a 'known' SR with AEBs (1.2%, 1/84), showed a normal SR on a recent ECG (1.2%, 1/84) or had a SR with mild bradycardia which

did not warrant a further investigation (1.2%, 1/84). One participant declined a $_{12L}$ECG and another four did not respond to the invitation (6.0%, 5/84).

Out of the six participants with 'Possible AF' who did undergo a $_{12L}$ECG (1.0%, 6/604), three were diagnosed with a 'new' AF (0.5%, 3/604). An additional case of AF was discovered in a participant with an 'Unclassified' diagnosis, producing a total yield of 'new', screening-detected AF of 0.7% (4/604). All four cases of 'new' AF qualified for anticoagulation, and three were initiated on OAC at the end of the study (0.5%, 3/604; two warfarin and one DOAC; *N.b.* one patient was not started on OAC due to an excessive risk of bleeding). In the absence of the interpreting cardiologist, all four patients with 'new' AF would have been screening-detected and referred for $_{12L}$ECG by either the KMD algorithm or the CP interpretation of $_{SL}$ECG (0.7%, 4/604). Three of the four cases would have been identified by pulse palpation alone (0.5%, 3/604).

Apart from four 'new' AF diagnoses, a further 28/604 participants with 'Possible AF' or 'Unclassified'/'Unreadable' diagnoses, who were referred to the GP (4.6%), were diagnosed with a 'new', non-AF cardiovascular condition. The common conditions included BBBs (2.0%, 12/604), SR with AEBs/VEBs (1.5%, 9/604) and the first-degree AVBs (1.3%, 8/604). As shown in **Figure 3.6**, some of the participants had more than one 'new' condition, including one AF patient who was discovered to have an undiagnosed chronic heart failure and was started on an appropriate diuretic treatment. Several other patients had their treatment adjusted as a result of screening (0.3%, 2/604): one patient with sinus bradycardia and AEBs had a reduction in the dose of their beta blocker whereas the other patient with sinus bradycardia, BBB, left anterior fascicular block and a pre-existing coronary heart disease had their beta blocker switched to a nitrate. Two more 'new', non-AF diagnoses were obtained from participants with 'Normal SR' diagnoses who did not need a $_{12L}$ECG follow-up. One had a new first-degree AVB noted by the cardiologist at the time of $_{SL}$ECG interpretation. The other one had their HR re-checked by the GP as recommended by the cardiologist leading to an incidental finding of hypertension, which was managed with a calcium channel blocker. In the absence of the cardiologist, the KMD algorithm, the CP interpretation of $_{SL}$ECG and pulse palpation would have correctly referred 24, 23 and 12 of the 30 patients who were subsequently diagnosed with a 'new' non-AF cardiovascular condition, producing the non-AF yields of 4.0%, 3.8% and 2.0%, respectively.

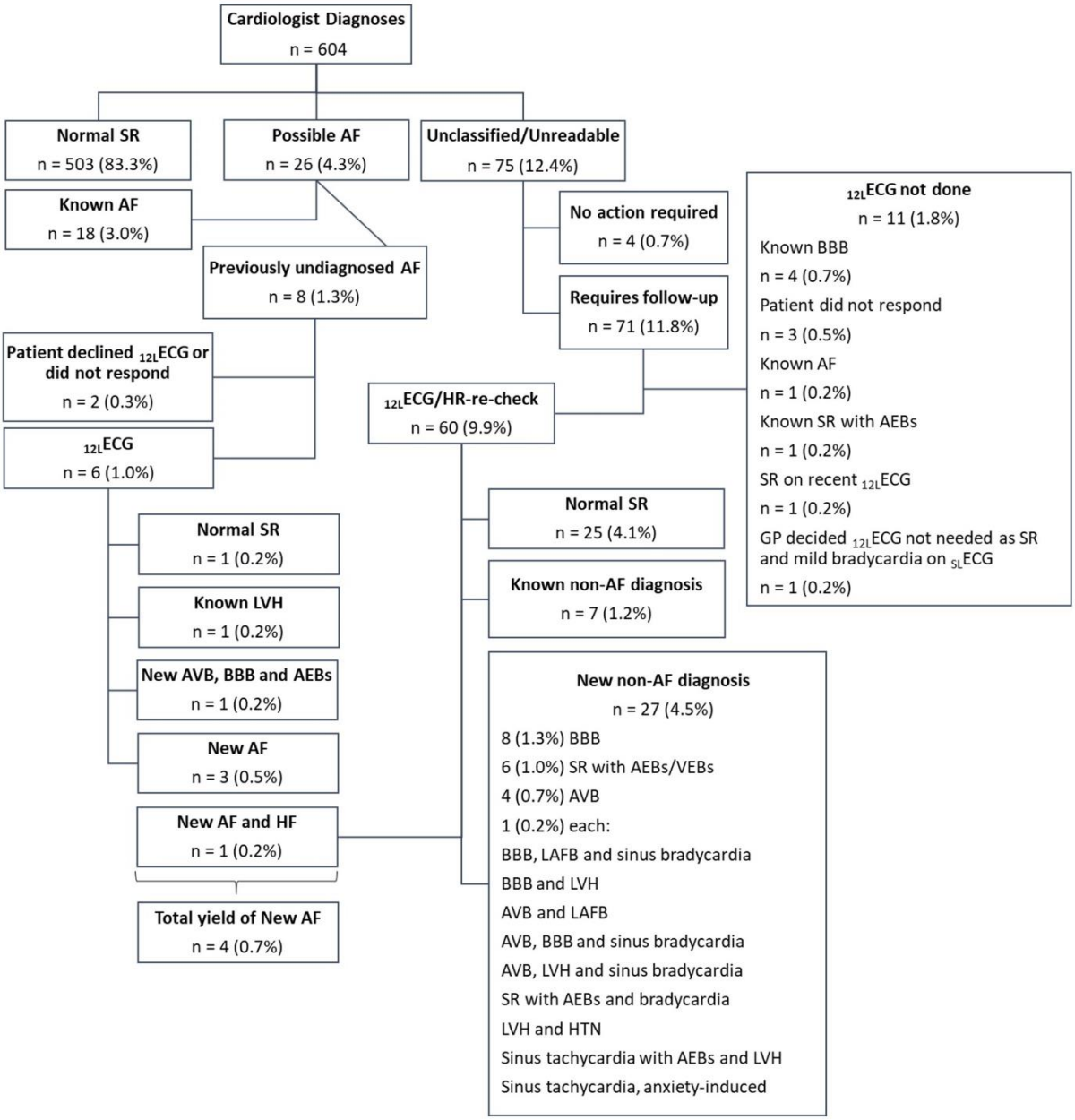


Figure 3.6 Follow-up outcomes of participants with cardiologist-confirmed 'Possible AF' and 'Unclassified/Unreadable' diagnoses

Adapted from: Savickas et al. (2020b). All variables are expressed as a number of participants (% total). Abbreviations: $_{12L}$ECG – 12-lead ECG; AEB – atrial ectopic beat; AF – atrial fibrillation; AVB – first-degree atrioventricular block; BBB – bundle branch block; GP – general practitioner; HF – heart failure; HR – heart rate; LVH – left ventricular hypertrophy; HTN – hypertension; LAFB – left anterior fascicular block; $_{SL}$ECG – single-lead electrocardiogram; SR – sinus rhythm; VEB – ventricular ectopic beat.

3.4.5 Stakeholder feedback

Participant feedback

A total of 422/604 (69.9%) participants completed the optional, anonymous feedback questionnaires following their AF screening appointment in GP surgeries (**Table 3.4**). The feedback received was overwhelmingly positive with all respondents rating the service received as either 'good' or 'very good' (100%, 409/409), and nearly all being in favour of attending a repeat AF screening the following year (99.0%, 404/408). The vast majority of respondents felt that AF screening was either 'important' or 'very important' (95.7%, 396/414), although less than a half were aware of either AF (47.2%, 195/413) or the associated health risks (46.6%, 192/412) before they were screened. Most participants were satisfied both with information received before (96.6%, 399/413) and after the appointment (99.0%, 410/414) with the CP. Respondents were largely pleased with a clear explanation provided by CPs in relation to pulse palpation (99.8%, 414/415) or $_{SL}$ECG (99.3%, 410/413), and the explanation of the test results alike (99.5%, 413/415). All patients rated the tests carried out by CPs as either 'good' or 'very good' (100%, 409/409) and agreed that CPs made them feel at ease during the appointments (100%, 403/403). They were almost unanimously satisfied with the length of the appointment (99.0%, 403/407), and most were happy to see a CP for other screening tests in the future (95.5%, 365/382).

The open-ended aspect of the question concerning other CP-led screening tests was completed by approximately a quarter of all respondents (26.5%, 112/422; *N.b.* some respondents indicated more than one test). Around 40% of these indicated that they would be willing to engage with any relevant screening tests provided by the CP (42.9%, 48/112). The most common choices of specific tests included diabetes (8.0%, 9/112), hypertension (5.3%, 6/112), cholesterol (4.5%, 5/112), prostate or any cancer (4.5%, 5/112 each), any heart screening (3.6%, 4/112), dementia/Alzheimer's disease (2.7%, 3/112) and cervical cancer (1.8%, 2/112). Interestingly, 27/112 respondents to this question (24.1%) specifically indicated that they were not aware of or were unsure as to what services CPs might be able to provide.

The majority of respondents were keen to provide additional comments concerning the likes/dislikes of the service or the improvement of the AF screening strategy proposed (65.2%, 275/422; **Figure 3.7**). Similar to close-ended questions, most responses to these three open-ended questions were positive (95.6%, 263/275). A number of respondents praised the professional (5.1%, 14/275), yet relaxed, friendly and *'at-ease'* nature of the CP-

led AF screening service (22.2%, 61/275). Participants were particularly pleased with the *'informative'* consultation where any information was presented clearly and in *'simple English'* (34.2%, 94/275). The screening process itself was perceived as simple, quick, efficient, effortless, painless, methodical and well-organised (31.3%, 86/275). A few participants were impressed with the size of the KMD and the *'incredible'* novelty of mobile technology (2.5%, 7/275). About one in ten felt that the service provided them with reassurance about their health status (10.2%, n = 28/275) and improved their access to healthcare by offering a local, convenient, opportunistic *'health check whilst attending surgery for something else'* (8.7%, 24/275). Patients were happy they could contribute to both the *'preventive medicine'* agenda and clinical research (11.6%, 32/275).

Table 3.4 Participant responses to closed-ended questions of the feedback questionnaire administered during AF screening in general practice surgeries

Data presented as a number of responses/total number of respondents (% total).

Question Item	Response	Number of respondents (n = 422)
From your experience of it, how important was the screening for you?	Very important/important	396/414 (95.7)
Were you aware of this condition before you were screened?	Yes	195/413 (47.2)
Were you aware of any of the health risks associated with this condition, before you were screened?	Yes	192/412 (46.6)
How satisfied were you with the information provided before the appointment?	Very satisfied/satisfied	399/413 (96.6)
Did the pharmacist clearly explain what was involved by having your pulse tested?	Yes	414/415 (99.8)
Did the pharmacist clearly explain what is involved in having an ECG?	Yes	410/413 (99.3)
Afterwards did the pharmacist clearly explain the results of the test to you?	Yes	413/415 (99.5)
How satisfied were you with the information provided after the appointment?	Very satisfied/satisfied	410/414 (99.0)
Please rate how well you thought the pharmacist carried out the tests	Very good/good	409/409 (100)
Did the pharmacist make you feel at ease?	Yes	403/403 (100)
How satisfied were you with the length of the appointment?	Very good/good	403/407 (99.0)
Overall how satisfied were you with the service that you received?	Very good/good	409/409 (100)
If the test was offered to you again next year, would you have it done?	Yes	404/408 (99.0)
Would you be happy to see the pharmacist for other screening tests in the future?	Yes	365/382 (95.5)

Figure 3.7 A word-cloud representation of free-text responses to participant feedback questionnaires

Includes free-text responses concerning the positive/negative aspects of the service and suggestions for improvement (n = 275)

A total of 12 participants (4.4%, 12/275) expressed somewhat less positive views about the service. Six participants (2.2%, 6/275) mentioned the lack of or incorrect pre-appointment information, meaning they *'had no idea'* as to what the appointment might involve. Three respondents (1.1%, 3/275) raised their concerns about internal communication issues between the surgery staff and the research team, for instance the receptionist responding that they *'have never heard of'* AF screening at the surgery. One respondent each (0.4%, 1/275) also criticised the ambiguity of questions within the questionnaire, the excessive noise levels inside the surgery, a delay in their appointment, the length of the appointment or the absence of *'personal introduction'* at the beginning of the clinic. Several respondents

proposed that the existing AF screening strategy could be improved by *'greater publicity'* (0.7%, 2/275), by making the feedback questionnaire clearer, by offering an opportunity for patients to self-screen, by organising AF screening annually, by including it into a *'regular personal screening plan*' or by ensuring the service was not run alongside the influenza vaccination clinics (0.4%, 1/275 each).

CP feedback

Four out of six CPs (66.7%, 4/6; two females) completed the end-of-study feedback questionnaires. The age of respondents and the number of years qualified as a pharmacist ranged 30-38 years and 6-14 years, respectively. Two CPs had worked in general practice for < 12 months whereas two other CPs had done so for 4 and 5 years, respectively. Three pharmacists were White British and one – Black/Black British/African. Respondents had mixed views about their pre-study knowledge of AF which was rated as either 'fair' (50.0%, 2/4), 'good' or 'poor' (25%, 1/4 each). An improvement was seen after the study with all respondents (100%, 4/4) rating their AF knowledge as 'good' or 'very good'. All four pharmacists (100%) also thought that the role of CPs in AF screening and general practice as a whole was either 'important' or 'very important'. Similarly, all four (100%) agreed that CPs were well-equipped with the knowledge and resources to screen for and detect AF. Three of the CPs (75.0%, 3/4) rated their access to study information, advice and resources as 'good' or 'very good' and all four (100%) concurred on the 'good' or 'very good' nature of the equipment used. All respondents (100%) indicated that their overall study experience was 'good' or 'very good' and all were 'satisfied' or 'very satisfied' with either the support from the research team or the support towards the interpretation of screening results. Three CPs (75.0%, 3/4) were also 'satisfied' or 'very satisfied' with the training they received and with the level of support from their GP.

The free-text comments conformed with favourable quantitative responses. One pharmacist suggested that CP involvement in AF screening may improve the utilisation of their skillset, *'free up'* GP time, provide a *'useful service to patient population'* and *'improve outcomes for patients'*. CPs enjoyed the learning experience, the interaction with service users, patient education and the simplicity of the device (25.0%, 1/4 each). As a point of improvement, one CP recommended delivering all of AF screening as pre-booked appointments, which would allow patients to *'read the information prior to the appointment'* and would make the process *'more streamlined'*.

The evaluation of CP training was conducted using a separate eight-point feedback questionnaire, which was completed by the same four CPs. In general, CPs found the

majority of training aspects either 'good (useful)' or 'excellent (very useful)' (**Figure 3.8**). This was particularly the case with regards to study introduction, clinical assessment – pulse palpation, the study protocol, screening in practice and personal reflection (100%, 4/4). Three out of four respondents (75.0%, 3/4) also rated the AF presentation, clinical assessment – ECG and consultation skills training as either 'good' or 'excellent'. One CP (25.0%, 1/4) indicated that they particularly enjoyed the *'mock screening and feedback'* including the explanation of the *'paperwork'*. On the other hand, they wished they had more adequately reviewed the Powerpoint presentation provided by the cardiologist before the start of the screening clinics.

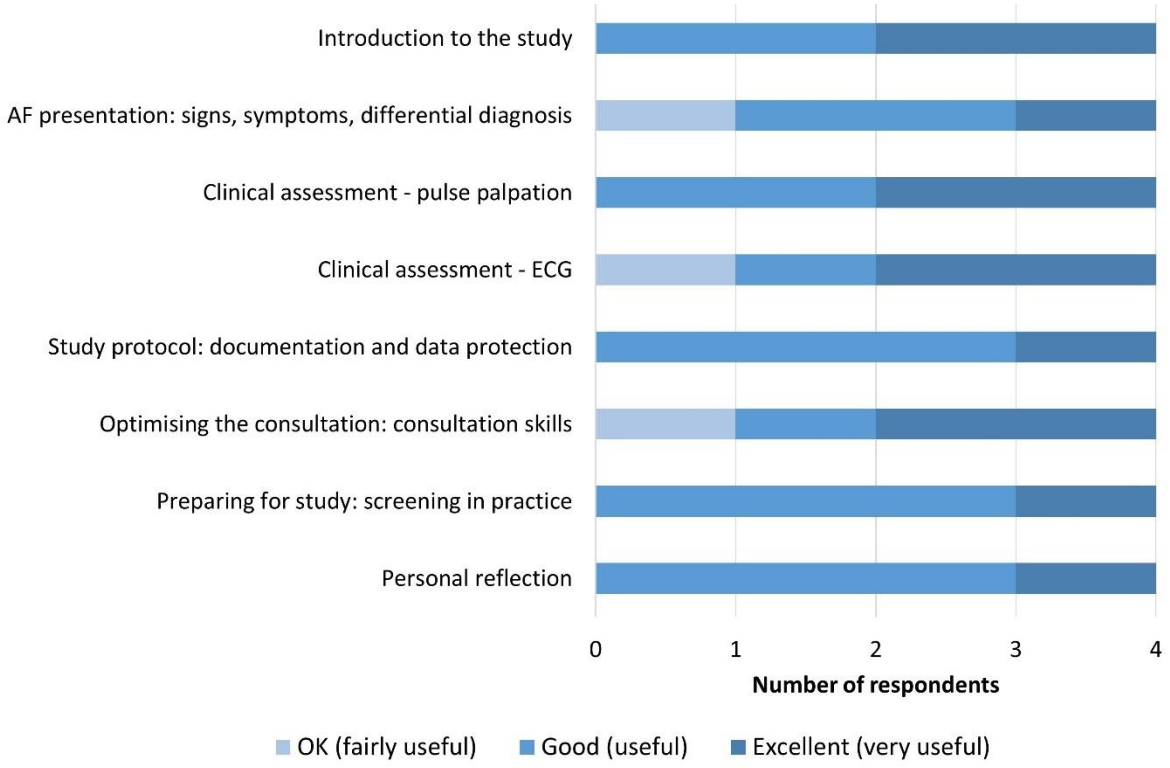


Figure 3.8 Training-specific feedback of clinical pharmacists delivering AF screening in general practice

Abbreviations: AF – atrial fibrillation, ECG – electrocardiogram.

GP feedback

A total of 12 GPs from two participating GP surgeries completed the feedback questionnaires. Nearly all of them felt that AF screening was either 'important' or 'very important' (91.7%, 11/12). All 12 GPs (100%) indicated that their surgeries were able to perform a $_{12L}$ECG, with HCAs (41.7%, 5/12) or nurses (33.3%, 4/12) commonly conducting the procedure, and GPs (100%, 12/12) interpreting the ECGs for AF. Most GPs thought that the AF screening service provided during the study was either 'good' or 'excellent' (83.3%, 10/12), and that it was received 'well' or 'very well' by both patients and staff (91.7%, 11/12). GPs liked the quick and simple *'gadget'* (25.0%, 3/12), the fact that the screening was conducted in an opportunistic manner during the influenza vaccination clinics (16.7%, 2/12), the *'quality of instant ECG trace'*, the professional nature of the service, *'clinical pharmacist leading on the screening'* and the positive reception by patients (8.3%, 1/12 each). One GP (8.3%, 1/12) suggested that the service could be improved by removing the *'need for patients to discuss past medical history in waiting room'*.

Three GPs agreed (25.0%, 3/12) that they would employ CPs to deliver AF screening in the future, and six (50%, 6/12) would 'possibly' do so. Those GPs who were unwilling to employ CPs to provide AF screening indicated the *'funding issues'* and *'cost'* as the main barriers (16.7%, 2/12). One respondent would employ a CP on a condition that they would also provide other services whereas another respondent thought that AF screening could be done by HCPs other than pharmacists, for instance the HCAs (8.3%, 1/12 each). The majority of responding GPs (91.7%, 11/12) concurred that they would at least consider commissioning CPs to perform other screening tests, such as those for bowel cancer, hypertension, diabetes or respiratory conditions (8.3%, 1/12 each). Last but not least, all 12 respondents (100%) agreed that they would want the AF screening service to be run at their surgery the following year with a promising potential of it developing into the national screening programme (83.3%, 10/12 rated the likelihood at ≥ 6 out of 10).

3.4.6 Economic analysis

Compared to the no-screening scenario, the CP-led AF screening strategy in GP surgeries was cost-effective regardless of the screening method, with a mean base-case ICER of £14,460 (95% CI, £2,255-£26,665)/QALY gained for the KMD algorithm and a slightly greater ICER of £16,678 (95% CI, £7,191-£26,164)/QALY gained for pulse palpation (**Table 3.5**). The ICERs remained below the WTP threshold of £20,000/QALY gained in 71.8% and 64.3% of the 100,000 simulations using the KMD algorithm and pulse palpation, respectively (**Figure 3.9**). The mean 10-year INB compared to the 'no-screening strategy' was £1,903/patient with AF and £120,084,946/all patients with 'new' AF across England

and Wales identified when screening with the KMD algorithm, and £946/patient with AF and £49,741,500/all patients with 'new' AF identified using pulse palpation.

The cost-effectiveness of AF screening strategies using either the KMD algorithm or pulse palpation was sensitive to the level of adherence to OAC therapy. At the lowest adherence level of 40%, the certainty of cost-effectiveness was modest as indicated by wider than the base case 95% CIs, although the mean ICER for AF screening using the KMD was still below the cost-effectiveness threshold (£19,957 (95% CI, -£15,292-£55,207)/QALY gained). In contrast, AF screening using pulse palpation at this adherence level was no longer cost-effective with an ICER of £23,030 (95% CI, -£80,292-£126,351)/QALY gained. At the highest tested adherence level of 80%, both screening methods were highly cost-effective producing approximately 51% lower mean ICERs than at 40% adherence to OAC of £9,824 (95% CI, -£7,167-£26,815)/QALY gained and £11,356 (95% CI, £5,794-£16,919)/QALY gained for the KMD algorithm and pulse palpation, respectively.

The adjustment in proportions of AF patients receiving DOAC and VKA therapies from the 56:44 ratio to the 29:71 ratio referred to by NICE (2014b), had little effect on the cost-effectiveness of KMD-based screening, producing the mean ICERs across the OAC adherence range on average only 2.1% (£282) lower than the base case and a mean ICER of £14,127 (95% CI, -£1,040-£29,293)/QALY gained at 55% adherence to OAC. The economic model was however strikingly sensitive to any adjustments in screening participation rate. Increasing the participation rate from 50% to 80% resulted in 38.4% (£5,270) lower mean ICERs across the adherence to OAC range, with an ICER of £8,902 (95% CI, -£9,661-£27,465)/QALY gained at 55% adherence level. Reducing the participation rate down to 30% produced on average 69.3% (£9,492) higher mean ICERs across the adherence to OAC range, with wider 95% CIs, and a mean ICER of £24,300 (95% CI, £6,982-£41,619)/QALY gained at 55% adherence level. Besides the improvement in screening participation, the cost-effectiveness of the base-case AF screening strategy was enhanced by halving the proportion of 'Unclassified'/'Unreadable' diagnoses to 6.7%. This adjustment led to an approximately 15.0% (£2,067) lower mean ICERs throughout the OAC adherence range, with a mean ICER of £12,286 (-£1,169-£25,741)/QALY gained at 55% adherence level. This effect was comparable to the effect observed when switching from AF screening using pulse palpation to the KMD algorithm, which produced on average 15.6% (£2,138) lower mean ICERs across the OAC adherence range.

Table 3.5 Findings of the cost-effectiveness analysis of AF screening strategy in a general practice setting

Incremental cost-effectiveness ratios (ICERs) are expressed as a mean (95% confidence intervals). Abbreviations: AF – atrial fibrillation; DOAC – direct-acting oral anticoagulant; VKA – vitamin K antagonist.

Base Case Assumptions	**Level of Adherence to Oral Anticoagulant Therapy (%)**				
	40	**55 (base case)**	**60**	**70**	**80**
• 3-monthly AF screening cost/participant £286.96 • Total prevalence of AF 4.3% • Prevalence of 'unknown' AF 1.3% • Rate of 'Unclassified'/'Unreadable' diagnoses 13.4% • Participation in screening rate 50% • Test sensitivity 92.3% • Test specificity 97.4% • %Patients on DOAC 56% • %Patients on VKA 44%	£19,957 (-£15,292-£55,207)	£14,460 (£2,255-£26,665)	£13,226 (-£1,288-£27,740)	£11,295 (£8,609-£13,981)	£9,824 (-£7,167-£26,815)
Deviations from Base Case					
• Pulse palpation instead of device • Rate of Unclassified/Unreadable diagnoses 2.2% • Test sensitivity 76.9% • Test specificity 92.2%	£23,030 (-£80,292-£126,351)	£16,678 (£7,191-£26,164)	£15,342 (£5,776-£24,907)	£13,046 (-£534-£26,627)	£11,356 (£5,794-£16,919)
• %Patients on DOAC 29% • %Patients on VKA 71%	£19,606 (£232-£38,981)	£14,127 (-£1,040-£29,293)	£12,956 (£5,634-£20,277)	£11,073 (-£32,704-£54,851)	£9,589 (£2,464-£16,713)
• Base-case assumptions • Screening participation rate 80%	£12,383 (£7,753-£17,012)	£8,902 (-£9,661-£27,465)	£8,164 (£85-£16,243)	£6,935 (£448-£13,421)	£6,026 (£366-£11,686)
• Base-case assumptions • Screening participation rate 30%	£33,494 (-£504-£67,493)	£24,300 (£6,982-£41,619)	£22,214 (£2,993-£41,434)	£19,609 (£10,450-£27,678)	£16,604 (£5,267-£27,941)
• Rate of Unclassified/Unreadable diagnoses 6.7%	£16,983 (£5,094-£28,872)	£12,286 (-£1,169-£25,741)	£11,225 (£3,091-£19,359)	£9,598 (-£7,832-£27,027)	£8,335 (-£9,500-£26,171)

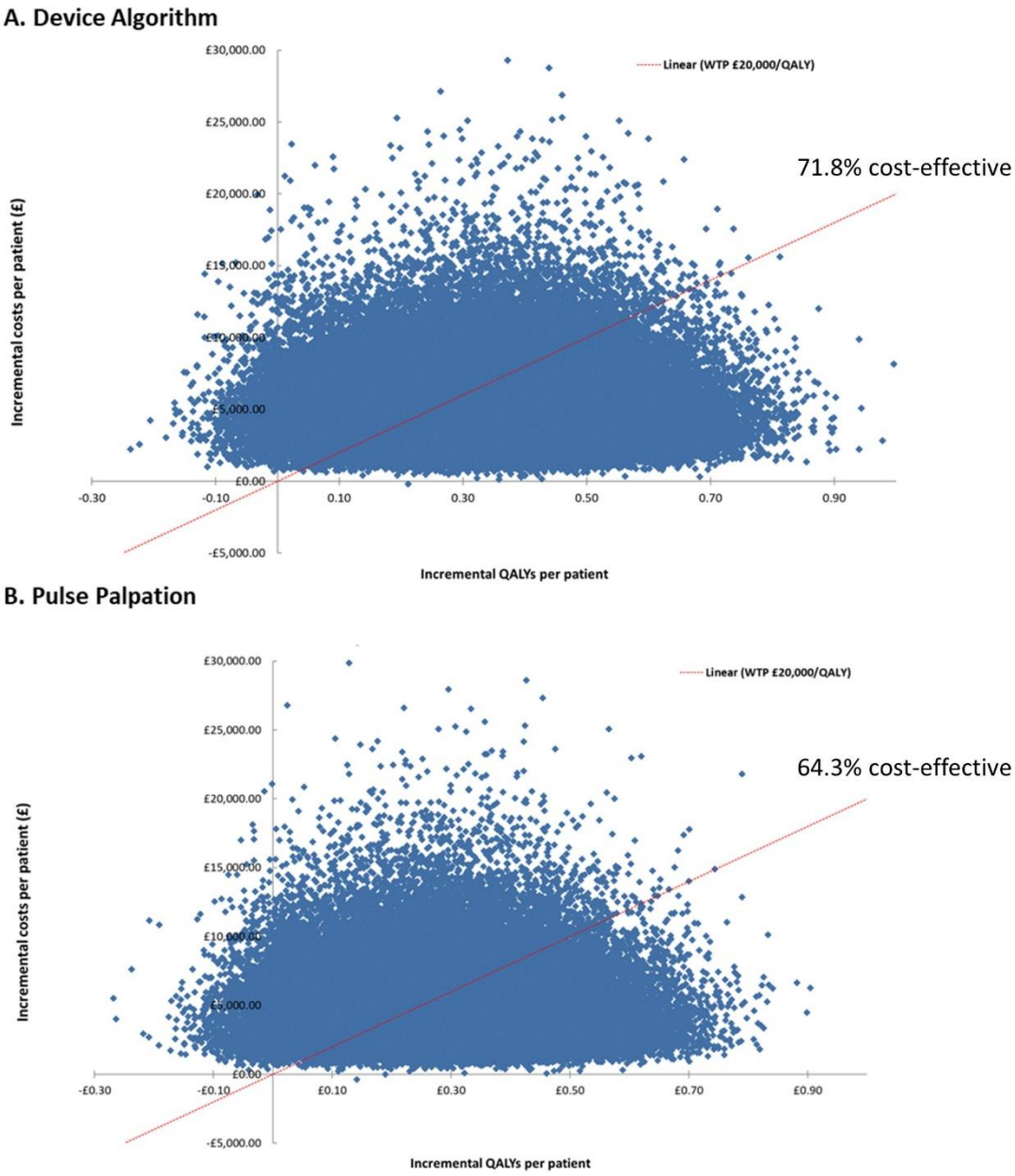


Figure 3.9 Incremental cost-effectiveness of AF screening within a general practice setting compared to no screening

Incremental cost-effectiveness planes show 100,000 pseudorandom Monte Carlo estimates of incremental costs and QALYs gained per patient with AF comparing: A. the base case of the AF screening strategy using KMD algorithm with no screening; B. the base case of the screening strategy using pulse palpation with no screening. Any points falling below the dotted line have an ICER < £20,000 per QALY gained. Abbreviations: AF - atrial fibrillation; ICER – incremental cost-effectiveness ratio; KMD – Kardia Mobile® device; QALY – quality-adjusted life year; WTP – willingness to pay [threshold].

3.5 Discussion

3.5.1 Comparison with existing literature

Recruitment and AF prevalence

This study investigated the feasibility of a cross-sectional, CP-led AF screening programme of individuals ≥ 65 years, delivered in GP surgeries using either pulse palpation or $_{SL}$ECG (KMD) during the influenza vaccination season. The desired sample size of 600 participants was reached over a period of seven months, spread across two influenza vaccination seasons. A total of 604 participants were included in the study, accounting for 3.1% of the ≥ 65-year-old population registered at the four participating practices (NHS Digital 2017b)). This level of recruitment efficiency was below those achieved by Kaasenbrood *et al.* (2016), Orchard *et al.* (2016) or Rhys *et al.* (2013) who screened approximately 3,000, 1,000 and 600 individuals attending influenza vaccination appointments over a single vaccination season. It however far exceeded the recruitment efficiency of most community pharmacy-based AF screening programmes (Lowres *et al.* 2014; Sandhu *et al.* 2016; Bacchini *et al.* 2019), and certainly that by Zaprutko *et al.* (2019) which screened only 525 pharmacy customers in 10 pharmacies over a period of 11 months. Whilst difficult to judge without the knowledge of comparative response rates, such differences in recruitment efficiency between community pharmacies and GP surgeries may reflect the more established general practice infrastructure, particularly the presence of routine clinical consultations and the universal medical record (NHS Digital 2009; NHS Digital 2020) which, as shown by this study, may enable either opportunistic or systematic AF screening. The somewhat limited population coverage of community pharmacy records (Chini *et al.* 2011; Torjesen 2019) may restrict the systematic recruitment whereas the AF screening itself may compete with the workflow of pharmaceutical services, thus reducing the service efficiency (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018). An exception to this hypothesis could be the AF awareness campaign-coupled initiatives in community pharmacies or other community settings, for instance the programme by da Costa *et al.* (2020) which recruited nearly 2,800 participants in 110 sites over one month, thereby demonstrating a similar recruitment efficiency to that observed in GP surgeries during this study.

Besides service efficiency, general practice offers routine access to a relevant population, with several AF screening studies within this setting reporting the ≥ 65-year-old prevalence of AF between 7% and 11% (Hobbs *et al.* 2005; Kearley *et al.* 2014; Ghazal *et al.* 2020). Although significantly below these figures as well as the 6.7% prevalence in Australian community pharmacies (Lowres *et al.* 2014), the 4.3% total prevalence of AF ascertained

by this study was close to the anticipated 5% mark (Sudlow *et al.* 1998b; Majeed *et al.* 2001; Morgan & Mant 2002), and echoed the 4.4% prevalence of AF in primary care or outpatient settings outlined in the systematic review by Lowres *et al.* (2013). It also resembled the AF prevalence of 3.7-4.5% detected by studies, which delivered single time point AF screening as part seasonal influenza vaccination clinics (Rhys *et al.* 2013; Orchard *et al.* 2016; Kaasenbrood *et al.* 2016). Similarly, the 1.3% prevalence of 'unknown' AF noted at the time of screening was nearly identical to the 1.4% reported by Lowres *et al.* (2013). It fell in the middle of the 1.1-1.5% prevalence presented by most individual general practice-based single time point AF screening studies (Morgan & Mant 2002; Hobbs *et al.* 2005; Kearley *et al.* 2014; Orchard *et al.* 2016; Kaasenbrood *et al.* 2016; Orchard *et al.* 2019b), and was close to the 1.3-2.4% prevalence range reported in community pharmacies (section **1.3.3**) (Sandhu *et al.* 2016; Zaprutko *et al.* 2019).

In case of an immediate pre- or post-AF screening confirmation by $_{12L}$ECG, the yield or prevalence of 'unknown' AF may be identical to that of the newly-diagnosed or 'new' AF (Hobbs *et al.* 2005; Kearley *et al.* 2014). In a real-world scenario, the diagnosis of AF by $_{12L}$ECG (NICE 2014a), particularly amongst asymptomatic patients, is unlikely to occur the same day as AF screening, meaning that up to 25% of all 'new' AF cases with a pattern of PAF may ultimately go undetected (Zoni-Berisso *et al.* 2014). The estimation of PAF prevalence was beyond the scope of the present study, however it is perhaps interesting to note that seven out of 100 participants, who were randomly selected for enhanced demographic comparison (7.0%), had a history of AF (including PAF), yet presented with 'Normal SR' at the time of screening. Not only does this finding confirm that the total prevalence of AF in ≥ 65s is likely to be above 5%, but it also suggests that a significant proportion of those with undiagnosed PAF may be undetected by conventional cross-sectional screening programmes. Indeed, as shown by the STROKESTOP study (Svennberg *et al.* 2015) or the recent initiative by Ghazal *et al.* (2020), a 14-day intermittent AF screening programme using $_{SL}$ECG devices may help discover and anticoagulate up to 3% of patients with 'new' AF. This yield of 'new', screening-detected AF in ≥ 65s is almost double that of 1.4% with single time point screening (Lowres *et al.* 2019). During the present study, the average time to $_{12L}$ECG was 16 days, after which only 0.7% of study participants were diagnosed with a 'new', screening-detected AF, and 0.5% were initiated on OAC therapy. Even though markedly lower than the yields reported by Lowres *et al.* (2019), or the $_{SL}$ECG yields of intermittent AF screening programmes (Svennberg *et al.* 2015; Halcox *et al.* 2017; Ghazal *et al.* 2020), the 0.7% yield of 'new' AF corresponded with the ≤ 1.0% follow-up $_{12L}$ECG yields discovered after the KMD-based AF screening in either community pharmacies (Lowres *et al.* 2014; Cunha *et al.* 2020) or GP surgeries (Orchard *et al.* 2016).

It was also not too dissimilar to the post-$_{12L}$ECG yield of 'new' AF (0.3%-0.6%) diagnosed after screening with pulse palpation in UK GP surgeries (Rhys *et al.* 2013) or with the HeartCheck® $_{SL}$ECG device in Canadian community pharmacies or GP surgeries (Sandhu *et al.* 2016; Quinn *et al.* 2018). At 0.5%, the proportion of $_{12L}$ECG-confirmed 'new' AF cases initiated on OAC therapy during the present study was slightly above the 0.3% reported by earlier AF screening studies in Australian community pharmacies or GP surgeries (Lowres *et al.* 2014; Orchard *et al.* 2016), but lower than the 0.8% encountered in a recent general practice study which utilised electronic screening prompts (Orchard *et al.* 2019b).

Despite the relatively low screening yield, the recruitment strategy of targeting individuals eligible for influenza vaccinations in GP surgeries proved valuable when identifying the relevant, at-risk group of patients with AF. Compared to participants with 'Normal SR', the 26 patients with cardiologist-confirmed AF were on average 10 years older, had a greater BMI, significantly more comorbidities and hence a higher CHA_2DS_2VASc score, which qualified all of them for stroke prevention with OAC therapy (NICE 2014a). Only two out of the 26 patients had a 'lone' or idiopathic AF with no other comorbidities (7.7%). These findings are consistent with the results of epidemiological studies which showed that 'lone' AF affects only 3-10% of AF sufferers, typically those aged < 60 years (Weijs *et al.* 2012; Oldgren *et al.* 2014), whereas the majority of AF cases are associated with one or more comorbidities, such as obesity, hypertension, diabetes, renal disease or heart failure (Benjamin *et al.* 1994; Watanabe *et al.* 2009; Staerk *et al.* 2018). Likewise, the majority of patients with AF identified by previous studies within the general practice influenza vaccination setting had at least one risk factor for AF and a CHA_2DS_2VASc score ≥ 2, thereby qualifying them for OAC therapy (Rhys *et al.* 2013; Orchard *et al.* 2016; Kaasenbrood *et al.* 2016). Together with evidence presented by the current study, these results suggest that the overlapping eligibility criteria for AF screening and influenza vaccination clinics (Kirchhof *et al.* 2016; Public Health England 2020a) may help identify the high-risk patients with AF who may benefit from post-screening interventions, such as the OAC therapy.

Diagnostic accuracy of AF detection methods

Few studies to date have compared the diagnostic accuracy of modern $_{SL}$ECG devices and conventional pulse palpation (Lowres *et al.* 2014; Quinn *et al.* 2018), which, despite concerns about the high FPR (Taggar *et al.* 2016a), remains the first-line option for the detection of symptomatic AF (NICE 2014a), and one of the choices for opportunistic screening to identify the silent AF (Kirchhof *et al.* 2016). Similarly, only three studies to date have evaluated the diagnostic accuracy of pharmacist-led AF detection (Lowres *et al.* 2014;

Zaprutko *et al.* 2019; Cunha *et al.* 2020), and none focused on the evolving role of general practice pharmacists. This study aimed to address both evidence gaps by comparing the diagnostic accuracy of CP-performed pulse palpation with the interpretation of $_{SL}$ECG by either the automated KMD algorithm, the CPs or the cardiologist (the reference standard). More than 90% of $_{SL}$ECG recordings produced during the study were of 'Excellent' or 'Acceptable' quality enabling the interpretation of 99% of $_{SL}$ECG traces by the cardiologist, the KMD algorithm or the CPs. These results conform with the 1.4% of uninterpretable $_{SL}$ECGs previously obtained using KMD in UK GP surgeries (Lown *et al.* 2018), and highlight the advantage of the relatively noise- or interference-free general practice consultation rooms. For instance, the proportion of uninterpretable $_{SL}$ECGs may be as high as 7-11% in busy supermarket or community pharmacy settings (Battipaglia *et al.* 2016; Zaprutko *et al.* 2019), possibly jeopardising the efficiency and value of AF screening.

During this study, the diagnostic classification by all three index tests differed significantly from that by the cardiologist (McNemar's test, $p < 0.05$). Despite this, the $_{SL}$ECG interpretation by the KMD algorithm or CPs showed a substantial inter-rater agreement with the cardiologist (0.72 and 0.69, respectively) which resembled that between the cardiologist's and trained technician's interpretations of $_{SL}$ECG during the community pharmacy-based study by Sandhu *et al.* (2016) (0.79). The two index tests also displayed an excellent agreement with each other (0.89), without any significant differences in diagnostic accuracy (McNemar's test, $p > 0.05$). More importantly, this study discovered significant differences between the diagnostic accuracy of pulse palpation and either of the other two index tests. Pulse palpation demonstrated a poor inter-rater agreement with the cardiologist (0.40) and a moderate agreement with either the $_{SL}$ECG interpretation by the KMD or CPs (0.52). In line with these findings, it had both inferior sensitivity and specificity for AF (77% and 92%, respectively) compared to the KMD algorithm (92% and 97%, respectively) or the CPs' interpretation of $_{SL}$ECG (89% and 97%, respectively). The diagnostic performance of the KMD algorithm was comparable to previous studies in primary care settings, where it demonstrated a sensitivity of 87-100% and a specificity of 91-99% (Lowres *et al.* 2014; Orchard *et al.* 2016; Lown *et al.* 2018; Himmelreich *et al.* 2019; Zaprutko *et al.* 2019). The sensitivity of pulse palpation was substantially lower than the 92% reported in the meta-analysis by Taggar *et al.* (2016a) or the 87-100% reported by earlier studies evaluating nurse-led pulse checks (Sudlow *et al.* 1998a; Somerville *et al.* 2000; Morgan & Mant 2002; Hobbs *et al.* 2005), but concurred with the 77% observed for pulse palpation by community pharmacists (Lowres *et al.* 2014). This low ability to identify AF positive patients may be attributed to the relative inexperience of CPs performing pulse palpation and is similar to the 72% sensitivity for frequent or continuous pulse irregularity

amongst nurses with minimal pulse palpation training (Morgan & Mant 2002). The relatively high FPR of pulse palpation (8%) compared to the other two tests (approximately 3% each) was not unexpected considering the data of previous studies in a general practice setting where pulse palpation displayed yet lower specificity of 71-86% (Sudlow *et al.* 1998a; Morgan & Mant 2002; Somerville *et al.* 2000; Hobbs *et al.* 2005). Interestingly, in the community pharmacy-based study by Lowres *et al.* (2014) the specificity of pulse palpation (93%) was comparable to that observed here (92%) but above the specificity of the KMD algorithm (91%). The greater specificity of the KMD ascertained by the present study (97%) may either be the result of a different screening environment (for instance, the lower noise levels in GP surgery consultation rooms compared to the community pharmacy), or the ongoing optimisation of the automated KMD algorithm (AliveCor 2019b).

Overall, compared to the cardiologist, $_{SL}$ECG interpretation by the KMD algorithm or CPs correctly classified 62% and 59% of the 'Possible AF' diagnoses by each test, respectively. This was comparably lower than the PPV of 83% reported for the KMD algorithm in a younger general practice cohort aged ≥ 18 years (Himmelreich *et al.* 2019), but echoed the 65% value when screening the ≥ 65s in community pharmacies (Zaprutko *et al.* 2019). The FDRs for $_{SL}$ECG interpretation by the KMD algorithm or CPs were 39% and 41%, respectively. These values mean that, out 604 participants attending AF screening, 39 would be given a provisional diagnosis of AF by the KMD algorithm or the interpreting CPs, but only 24 or 23 of them would actually have the condition. Whilst by no means insignificant, the FDRs associated with the KMD algorithm or CP interpretation were by far lower than the 69% estimated for pulse palpation. To put this into perspective, out of the total sample of 604 participants, 65 would be given a 'Possible AF' diagnosis by pulse palpation, even though 45 of these would not have the disease. The FDR of pulse palpation in previous literature ranges from the moderate 59% to an unacceptable 92%, meaning that up to 9 in 10 patients with pulse palpation-identified false AF may in fact not need any further investigation (Sudlow *et al.* 1998a; Morgan & Mant 2002; Hobbs *et al.* 2005; Rhys *et al.* 2013; Quinn *et al.* 2018). Not only may that cause unnecessary anxiety amongst patients with false positive AF diagnoses (Hafslund *et al.* 2012), but it may also overload the healthcare system due to unnecessary $_{12L}$ECG referrals (Lafata *et al.* 2004).

As discussed in section **1.2.2**, the alarmingly high rate of false positive discoveries due to pulse palpation is likely the result of non-AF irregularities, such as AEBs or VEBs (Cooke *et al.* 2006; Taggar *et al.* 2016a). Indeed, as shown by this and several other studies, such rhythm abnormalities, which may be falsely identified as AF by pulse palpation, can be successfully ruled out by the interpretation of $_{SL}$ECG (Lowres *et al.* 2014; Chan *et al.* 2017b;

Himmelreich *et al.* 2019). During this study, the cardiologist identified benign AEBs/VEBs in $_{SL}$ECG recordings of nine participants with false 'Possible AF' diagnoses due to pulse palpation (1.5%), but only in three (0.5%) and one (0.2%) participants who were issued a false 'Possible AF' instead of 'Normal SR' by the interpreting CPs or the KMD algorithm, respectively. Despite this, the KMD algorithm and CP interpretation of $_{SL}$ECG led to a considerably greater prevalence of 'Unclassified'/'Unreadable' diagnoses than observed with pulse palpation (approximately 13% vs. 2%, respectively). Therefore, paradoxically AF screening using pulse palpation produced up to eight fewer inappropriate referrals to the GP than screening using the KMD algorithm (33 and 41, respectively). The 8-17% prevalence of 'Unclassified'/'Unreadable' diagnoses with the KMD is well-documented (Orchard *et al.* 2016; Lown *et al.* 2018; Selder *et al.* 2019; Orchard *et al.* 2019b; Zaprutko *et al.* 2019; Cunha *et al.* 2020), and when added to the FPR of 2.6%, may at first appear to offset the benefits of using the device instead of pulse palpation. However, the sensitivity of the KMD algorithm for non-AF ECG abnormalities means that it may help identify those participants who require a $_{12L}$ECG yet would not otherwise be discovered by pulse palpation (e.g. those with BBBs). The use of the KMD algorithm during this study helped identify new, non-AF diagnoses in a total of 30 participants (5.0%), including an additional 12 patients (2.0%), who would have not been referred back to their GP after pulse palpation. This involved two patients with either new hypertension or sinus bradycardia who had their treatment adjusted as a result of AF screening.

Cost-effectiveness of the intervention

The superior diagnostic accuracy of the KMD algorithm over pulse palpation appeared to counter-balance the economic impact of additional referrals due to 'Unclassified'/'Unreadable' diagnoses. In line with previous cost-effectiveness studies amongst the ≥ 65s (Maeda *et al.* 2004; Lowres *et al.* 2014; Moran *et al.* 2016; Welton *et al.* 2017; Jacobs *et al.* 2018), both single time point AF screening approaches using the KMD algorithm and pulse palpation were cost-effective compared to the no-screening scenario, with base-case ICERs below the WTP threshold of £20,000/QALY gained (NICE 2012a). As anticipated from work by Lowres *et al.* (2014), the cost-effectiveness of the two screening methods improved with an increase in the level of adherence to OAC. Nonetheless, the use of the KMD algorithm was approximately 16% more cost-effective throughout the adherence to OAC range and remained cost-effective even at the lowest tested adherence level of 40%, the point at which pulse palpation was no longer cost-effective. Overall, at base-case assumptions, AF screening using the KMD algorithm and pulse palpation were cost-effective in 71.8% and 64.3% of the 100,000 iterations, respectively, which resembled the 60-80% chances of cost-effectiveness previously reported for opportunistic AF detection

using pulse palpation (Hobbs *et al.* 2005; Moran *et al.* 2016). Although the difference between the 72% and 64% may at first not appear significant, the INB extrapolation across the target population meant that the use of KMD algorithm instead of pulse palpation might have saved the health economy an additional £70 million over a period of ten years. This direct evidence contradicts the findings of two recent reviews which suggested that AF screening using pulse palpation may in fact be marginally more cost-effective than that using $_{SL}$ECG devices (Welton *et al.* 2017; Duarte *et al.* 2019). Whilst such a discrepancy may reflect differences in economic modelling, for instance an inclusion of studies from the pre-mobile $_{SL}$ECG era by Welton *et al.* (2017), it urges a large-scale re-evaluation of the economic benefits associated with each of the two AF detection methods.

The sensitivity analysis of the economic model echoed the findings by Welton *et al.* (2017), revealing that the cost-effectiveness of the PDAF intervention was largely insensitive to changes in the proportions of patients receiving warfarin or DOAC therapies. This finding was unexpected since the two models informing the present study both reported the markedly lower cost-effectiveness of DOAC-based scenarios compared to the warfarin-based ones (Lowres *et al.* 2014; Jacobs *et al.* 2018). Such differences may possibly be attributed to the variations in OAC acquisition and service costs between the Australian or Dutch and UK healthcare systems (NICE 2014b). Unlike reported by Lowres *et al.* (2014) or Moran *et al.* (2016) we also discovered that the economic model was highly dependent on the uptake of screening, resulting in average +69% or -38% fluctuations of ICER values when the participation rate was varied from 50% to 30% or 80%, respectively. According to Welton *et al.* (2017), the mean uptake of AF screening ranges from 54% to 73%, implying that the real-life economic impact of the PDAF intervention may lie between the ICERs associated with 50% and 80% of participation (£8,902 and £14,460, respectively). As shown by Lowres *et al.* (2015) and da Costa *et al.* (2020), pharmacists may have a crucial role in raising the awareness of AF or the screening services, thus potentially increasing the screening uptake. Besides the cost-effectiveness improvements due to the uptake of screening, in the present study, ICERs decreased by another 15% upon halving the proportion of 'Unclassified'/'Unreadable' diagnoses, suggesting that a degree of $_{SL}$ECG interpretation by a qualified HCP may help maximise the economic gains with the KMD.

Stakeholder feedback and acceptability

The added value of a HCP's presence during AF screening was also showcased in the responses to multi-stakeholder feedback questionnaires. Less than 50% of patient respondents were aware of AF or related health risks prior to being screened, perhaps not surprising considering that only seven out of 18 participants with 'known' AF were fully

aware of their condition at the time of screening. The issue of poor patient awareness of AF identified by this study has been recognised by previous AF screening initiatives (Orchard *et al.* 2014; Lowres *et al.* 2014; Sabater-Hernandez *et al.* 2018), and highlights the value of HCPs, such as pharmacists, who may use AF screening as an opportunity to provide healthcare education. Similar to the study by Lowres *et al.* (2015) in community pharmacies, almost a quarter of respondents were unsure as to what services CPs may be able to provide indicating that there is also room to raise awareness of the professional scope of pharmacists. Despite their limited knowledge of pharmacists, study participants praised the informative and user-friendly consultation with CPs, which improved their access to healthcare and provided immediate reassurance about their health status. The latter aspect may be particularly important for participants with 'Possible AF' or inconclusive diagnoses who may not be adequately informed and reassured if they were to be conducting the test themselves at home. Resembling the findings of previous AF screening studies in primary care (Orchard *et al.* 2014; Lowres *et al.* 2015; Orchard *et al.* 2016; Halcox *et al.* 2017), participants were also impressed with the convenience and speed of mobile $_{SL}$ECG technology, demonstrating the potential of using KMD as a multi-purpose screening and educational tool by future AF screening programmes. Most importantly, 99% of all responding participants agreed that they would take part in AF screening the following year, and some even asked for it to be made routine or integrated into personalised health checks, which would in principle agree with the Government's CVD agenda (Public Health England 2019c). Several respondents pointed out potential improvements to AF screening either by refining the pre-appointment information, by increasing the publicity of the service or by enhancing the communication between the research and clinical teams. All of these points may act as barriers to the implementation of a new service (Lowres *et al.* 2014; Orchard *et al.* 2014; Orchard *et al.* 2016), however as shown by the **AF S**creen, **M**anagement **A**nd guideline **R**ecommended **T**herapy (AF-SMART) programme in Australian GP surgeries, may be successfully addressed through appropriate leadership, multidisciplinary effort and an established care pathway (Orchard *et al.* 2019a; Orchard *et al.* 2019b).

Apart from the views of service users, the acceptability of the AF screening intervention was investigated via the questionnaires aimed at CPs conducting the screening and GPs working at the participating practices. CPs were pleased with the majority of aspects related to AF training received and their participation in the study as a whole. As in the community pharmacy study by Lowres *et al.* (2014), responding CPs felt that their knowledge of AF increased throughout the study and were positive about their role in AF screening, which was thought to benefit both the prospective patients and healthcare organisations. In

agreement with study participants, CPs enjoyed providing patient education and using the KMD, however made suggestions to improve the theory element of AF training and to pre-book all AF screening appointments in order to streamline the process. Unlike community pharmacists (Lowres *et al.* 2014; Sabater-Hernandez *et al.* 2018), responding CPs did not envisage any issues with regards to their professional relationships with GPs, indicating that this barrier may be setting-specific and does not necessarily apply in GP surgeries.

Quite the opposite was in fact observed, as GPs responding to feedback questionnaires valued the role of CPs leading on the screening and appreciated the additional service provided at their practice. As seen with the other two stakeholder groups and previous studies in general practice (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019a), GPs also complimented the instantaneous nature of AF screening using the KMD and its high acceptability by patients. Similarly, all GPs were positive about repeating the initiative the following year and most felt it could evolve into a national AF screening programme provided the barriers of patient confidentiality and funding could be overcome. Whilst the former concern may be study-specific, the funding barrier is not uncommon amongst GPS involved in AF screening programmes, which may directly affect the utilisation of their professional time (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019a). For instance, during the present study, all responding GPs indicated that themselves or their GP colleagues were solely responsible for $_{12L}$ECG interpretation at their surgeries. The success of AF screening programmes such as the PDAF intervention would therefore depend heavily on appropriate remuneration which would likely need to be more firmly integrated into the General Medical Services (GMS) contract (NHS England and BMA 2019a).

3.5.2 Strengths and limitations

A key strength of this study was its recruitment strategy, which utilised the matching age criteria for opportunistic AF detection and seasonal influenza vaccination clinics (Kirchhof *et al.* 2016; Public Health England 2020a). Not only did this approach help us recruit a relevant, at-risk group of individuals with AF, but it also facilitated a convenient and cost-effective option for opportunistic health testing within the familiar general practice environment, which was positively evaluated by stakeholders responding to feedback questionnaires. Furthermore, the general practice setting provided an advantage of an established in-house clinical infrastructure, which ensured a structured follow-up of most patients referred for a $_{12L}$ECG or a HR check, and an adequate support for those with new diagnoses. That may not always be the case in other primary care settings, such as community pharmacies, due to the less established communication channels or complex

inter-professional relationships between the community pharmacists and GPs (Lowres *et al.* 2014; Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020).

To our knowledge, this study was the first of its kind to evaluate the feasibility of CP-led AF screening intervention in a general practice setting, adding evidence to previous studies of AF screening by pharmacists in community pharmacies presented in section **1.3**. The evidence generated by this study comes at a crucial time of rapid CP role evolution and integration in the UK (Bradley *et al.* 2018; NHS England and BMA 2019b; Stewart *et al.* 2019), and demonstrates the vast potential of these qualified HCPs to expand their clinical scope beyond the traditional medicines-focused duties. Only two studies to date investigated the use of pulse palpation and modern $_{SL}$ECG devices alongside (Lowres *et al.* 2014; Quinn *et al.* 2018), therefore this research was also the first to directly compare both the diagnostic accuracy and cost-effectiveness of the two methods in a single study.

As appraised in section **2.4.1,** the prevalence-incidence bias of the single time point AF screening strategy (Delgado-Rodriguez & Llorca 2004) was perhaps the greatest limitation of this study, preventing the detection of those participants with PAF who were in SR at the time of screening. Although technically a limitation, this means that the yield of AF detection and hence the cost-effectiveness of the intervention are likely to be even higher than reported here provided the repeated or intermittent screening were to be implemented in the future (Aronsson *et al.* 2015; Welton *et al.* 2017). A large proportion of patients screened during this study had a previously diagnosed and treated AF, suggesting that they were possibly the pro-active type or the relatively 'healthy volunteers' who may not necessarily benefit the most from the intervention offered (Froom *et al.* 1999). Most participants were also registered at a single surgery (74%), and the AF screening programme as a whole had a limited coverage of the ≥ 65-year-old target population (3%). In turn, this AF screening programme may have overlooked those with limited access to conventional healthcare, such as the housebound, care home residents or the 10% of eligible individuals who simply choose not to attend the seasonal influenza vaccinations (Victor *et al.* 2018; Curtis & Price 2018; Public Health England 2019g). Unfortunately, some of these individuals, particularly the housebound and care home patients, are more likely to suffer from multiple comorbidities and are in most need of health testing, including the AF screening (Shah *et al.* 2011; Musich *et al.* 2015a). As shown by previous studies in UK and elsewhere, the prevalence of AF in long-term care settings may range from 7% to 19% (Reardon *et al.* 2012; Krüger *et al.* 2012; Gordon *et al.* 2014; Wiesel & Salomone 2017; Cunha *et al.* 2020), or up to eight times above the population average (Public Health England 2017a). The ongoing expansion of care home services provided by general practice-based CPs in

England offers a unique platform to deliver opportunistic AF screening during routine clinical visits (NHS England 2018b; NHS England and BMA 2019c).

Another limitation of this study was the under-representation of individuals from black, Asian and minority ethnic (BAME) groups, potentially limiting the generalisability of findings beyond the study sample. Nearly all of the study participants (97%) were of White British background compared to the diverse populations of England/Wales and Kent where BAME constitute 14% and 6%, respectively (Kent County Council 2013; Office for National Statistics 2018c). Some ethnic minority groups, such as individuals of South Asian ethnicity, display a greater than average risk of CVD (Gunarathne *et al.* 2008; British Heart Foundation 2010; George *et al.* 2017), however struggle to access GP services (NHS England 2018a). Expanding the AF screening programme evaluated here to these communities may therefore help to both improve the generalisability of study findings and possibly detect a greater yield of previously undiagnosed AF.

Apart from sampling and recruitment considerations, the study was limited by the real-world, open-label protocol, whereby both CPs performing the index test and the study cardiologist (reference standard) were not blinded to previous diagnoses, including those by the automated KMD algorithm. In some cases, CPs were also aware of participant's clinical information which, together with provisional diagnoses by the KMD algorithm, may have introduced a diagnostic review bias and over-estimated the diagnostic accuracy of CP interpretation of $_{SL}$ECG (Schmidt & Factor 2013). Similarly, despite additional training, the relative inexperience of CPs performing pulse palpation may have underestimated the accuracy of this technique, although this is possibly not too dissimilar to pulse palpation amongst the general public who are encouraged to self-test for AF by organisations, such as the AF Association (AF Association 2020). Last but not least, in the absence of direct evidence, the economic model constructed for this study was limited by key assumptions discussed in sections **2.8.3** and **3.3.11**, particularly an assumption that participants with screening detected AF displayed the same risk of ischaemic stroke and all-cause mortality as those diagnosed with AF during routine care. Whilst this is a common assumption (Lowres *et al.* 2014; Aronsson *et al.* 2015; Jacobs *et al.* 2018), it may have over-estimated the economic benefits of the intervention urging a caution when applying the findings to real-life practice.

3.6 Conclusion

This chapter outlined the quantitative results of the PDAF study in GP surgeries and provided evidence to support the feasibility of CP-led AF screening of individuals aged ≥ 65

years in this setting during the influenza vaccination season. The study findings suggested that the proposed AF screening programme was effective, cost-effective and displayed a high degree of acceptability amongst both service users and potential service providers. The recruitment strategy of targeting individuals in GP surgeries who are eligible for seasonal influenza vaccinations helped achieve the desired sample size over two vaccination seasons whilst providing access to the relevant and at-risk group of patients with AF. Trained CPs demonstrated an ability to detect AF using either the conventional pulse palpation or the KMD, leading to 'new' AF diagnoses in 0.7% of participants at the end of the study. The convenience of AF screening using the KMD was also positively appraised by study participants, CPs and GPs, whilst showing a potential to detect other non-AF cardiovascular conditions in up to a further 5.0% of individuals. Crucially, compared to the study cardiologist, the $_{SL}$ECG interpretation by the automated KMD algorithm displayed both superior diagnostic accuracy and cost-effectiveness than the conventional pulse palpation. Pending the results of several RCTs, particularly the **S**creening for **AF** with **E**CG to **R**educe stroke (SAFER) (ISRCTN Registry 2019) and the STROKESTOP II studies (Engdahl *et al.* 2017), this evidence encourages clinicians and decision-makers to review the current guidance for AF detection, moving away from historical but less accurate pulse palpation to modern and purpose-built technology, such as $_{SL}$ECG devices. The evidence of AF detection and cost-effectiveness compared to the no-screening scenario provided here also supports the case for systematic population or opportunistic AF screening presented in recent international white papers (Freedman *et al.* 2017; The Health Policy Partnership 2018).

The findings of this study raised several questions for future research. First of all, the narrow population coverage of this study makes it unclear as to how and to what extent the feasibility of the PDAF screening intervention may be extrapolated to other primary care settings and certainly to communities of different ethnic or socio-economic backgrounds. Such questions were addressed in this thesis by evaluating the adapted PDAF intervention to deliver AF screening in care homes (**Chapter 5**) or within the selected South Asian community (**Chapter 6**). Secondly, responses to multi-stakeholder feedback questionnaires identified several themes, including possible barriers to service implementation, which may need to be further explored to understand the underlying mechanisms and potential solutions. These elements were further investigated during the PDAF qualitative evaluation with patients, CPs and GPS from participating surgeries (**Chapter 4**). The feedback ascertained from GPs informed the development of a separate qualitative study to explore their views about the national AF screening programme (**Chapter 7**). One of the GPs responding to the questionnaire suggested that AF screening may be delivered by non-

pharmacist staff, such as the HCAs. This hypothesis was tested by utilising the trained pharmacy undergraduates to deliver AF screening under the supervision of a CP (**Chapter 6**). A question also stands as to whether or not the AF screening strategy proposed by the PDAF study or indeed any AF screening programme would translate into positive clinical outcomes/endpoints for patients, such as a reduction in the incidence of ischaemic stroke or all-cause mortality. Whilst indirect evidence provided by previous studies, including the England-wide AHSN initiative (Freedman *et al.* 2017; Wessex AHSN 2019), implies that this may be the case, the answer to this question remains a subject of future large-scale RCTs (discussed in section **8.5**).

Chapter 4: Pharmacists Detecting Atrial Fibrillation in General Practice Surgeries (Qualitative Evaluation)

4.1 Introduction

The MRC guidance for complex interventions outlined in section **2.2** recommends that behavioural phenomena, which may affect stakeholder engagement and thus the feasibility of the intervention (e.g. health awareness), should be explored using a mixture of quantitative and qualitative research methods (MRC 2006). The Australian GP-SEARCH pilot study was perhaps the first to report an enthusiastic reception of $_{SL}$ECG technology in AF screening as part of a semi-structured interview evaluation with practice patients, GPs, nurses and receptionists (Orchard *et al.* 2014). It also brought to light the confidence of nurses in conducting AF screening and the administrative staff's reluctance to engage in service provision. The subsequent feasibility study by the same research group combined AF screening with general practice influenza vaccination clinics, and conducted semi-structured interviews with GPs, practice nurses and practice managers (Orchard *et al.* 2016). The positive reception of $_{SL}$ECG devices and support for nurse-led services were both replicated in this study, which reported time limitations, IT issues and funding as the key hurdles to service implementation (Orchard *et al.* 2016). The concept of a 'designated champion' that may lead the local AF screening agenda in individual practices was also compiled and helped improve the uptake of the intervention during the subsequent AF-SMART programme (Orchard *et al.* 2019a). In turn, the mixed ethnographic and semi-structured interview evaluation of the latter initiative showcased the benefits of electronic health tools (e.g. prompts) in facilitating effective AF screening but highlighted the need for established protocols to ensure the follow-up of individuals with abnormal results.

Pending the findings of focus group interviews accompanying the SAFER study (ISRCTN Registry 2019), only one other UK-based AF screening study to date had been supported by qualitative research evidence. The evaluation of the **S**creening for **AF** Using **E**conomical and accurate **T**echnology (SAFETY) study, which screened individuals aged > 65 years using four different devices (PPG-capable tools, KMD and the WatchBP® mBPM), entailed semi-structured interviews with service users (Lown *et al.* 2018; Lown *et al.* 2020). Individuals interviewed were overall in favour of AF screening as a means to preventing stroke using any of the devices tested, however expressed a degree of confusion about AF as a condition and were somewhat anxious about prolonged screening taking over their lives. As shown by feedback from the PDAF study questionnaires (section **3.4.5**) and the qualitative studies in community pharmacies (section **1.3.3**), pharmacists may be well-

suited to educate the patients about AF and to explain the test results, thus potentially minimising the risk of health anxiety (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020). Nevertheless, community pharmacist-led AF screening may be limited by barriers, such as inadequate staffing, pharmaceutical workflow, the lack of remuneration and inadequate privacy (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018). The success of community pharmacy-based AF screening services may also be affected by complex relationships between the pharmacists and GPs, potentially jeopardising the effectiveness of referrals to general practice (Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020), and by patient misconceptions about the clinical role of pharmacists in public health (Lowres *et al.* 2015). Indeed, primary care staff interviewed during the qualitative evaluation of the AHSN's AF screening programme reported the uncertainty about processing $_{12L}$ECG referrals following AF screening by non-clinicians or those in community settings (Wessex AHSN 2019).

Several qualitative multi-stakeholder evaluations of CP-led services in GP surgeries suggested that their transition into this setting from traditional community pharmacy environment may positively alter the public perception about pharmacists' roles and help build the inter-professional trust (Tan *et al.* 2013; Ryan *et al.* 2018). This chapter presents the qualitative findings of the multi-stakeholder PDAF study evaluation which sought to explore the facilitators and barriers to CP-led AF screening service in GP surgeries (Savickas *et al.* 2020c), building on qualitative evidence presented above and data from stakeholder feedback questionnaires described in **Chapter 3**. It uses a structured, multidimensional TDF approach and a method of focus group interviews to probe into the perspectives of patients, CPs and GPS with regards to the impact of AF screening, the possible options for service design, and the inception of enhanced CP roles. The facilitators and barriers ascertained by previous qualitative evaluations in primary care settings are investigated alongside to determine their relevance to the development and implementation of the AF screening service proposed. This chapter therefore relates to the development, feasibility/piloting and evaluation elements of the MRC guidance for complex interventions (MRC 2006) (section **2.2**).

4.2 Aim and objectives

Aim:

To explore the facilitators and barriers to the development and implementation of the CP-led AF screening strategy in GP surgeries from the perspectives of patients, CPs and GPS participating in the PDAF study.

Objectives:

1. To ascertain the views and opinions of patients in relation to their pre-appointment expectations, information needs, the strengths and limitations of the screening strategy proposed, the modern AF screening technology and the CP's role in both AF screening and public health.
2. To ascertain the views and opinions of CPs regarding the strengths and limitations of the screening strategy proposed, the perceived reception of the study by other stakeholders, their satisfaction with training, support and involvement in the study, the role of pharmacists in AF screening and the use of $_{SL}$ECG technology.
3. To ascertain the views and opinions of GPS regarding the importance of AF screening, the strengths and limitations of the screening strategy proposed, the perceived reception of the study by other stakeholders, their satisfaction with communication and support from the study team and the role of pharmacists in AF screening.
4. To derive the key facilitators and barriers to the development and implementation of the AF screening strategy proposed within each stakeholder group and overall across all groups.
5. To map the key facilitators and barriers onto the TDF in order to determine the primary areas of concern to be addressed in the development and implementation of CP-led AF screening strategies in general practice.

4.3. Methods

4.3.1 Study design

This qualitative study was designed and delivered in a concurrent manner alongside the quantitative component of the PDAF study (Giddings & Grant 2006), using the TDF methodology adapted from Islam *et al.* (2012) and Atkins *et al.* (2017). The TDF approach and its application to qualitative studies included in this enquiry are appraised in section **2.4.2**. During this study, the TDF domains and component constructs informed the design of the topic guide and facilitated the qualitative data analysis. Considering the development and implementation-orientated study aim, the data collection method of focus group interviews (presented in section **2.6.2**) was selected to enable the dynamic exploration of shared issues and the generation of ideas or concepts that may drive the service development (Krueger & Casey 2000a; Breen 2006). The subtype of homogeneous focus groups with patients, CPs or GPS was utilised to minimise the impact of power relationships, thus encouraging participants to share their honest views. This method also facilitated a

comparison of qualitative themes ascertained from different stakeholder groups (Krueger & Casey 2000c; Hofmeyer & Scott 2007).

4.3.2 Design of topic guides

Flexible, semi-structured focus group topic guides for each stakeholder group were designed by three researchers (SC, EV and VS), using the themes retrieved from other qualitative studies of AF screening programmes (Orchard *et al.* 2014; Lowres *et al.* 2015; Orchard *et al.* 2016). The structure and questions of each topic guide were further refined using the TDF (Cane *et al.* 2012) and the data from the PDAF study feedback questionnaires. The topic guide for patients included a formal introduction, an icebreaker question and 10 open-ended questions that focused on their AF screening experience, the design of a screening service more generally, and the role of pharmacists in AF screening or public health services as a whole (**Appendix 30**). The topic guide for CPs and GPS consisted of an introduction followed by eight open-ended questions which explored the benefits of and barriers to AF screening, the role of CPs in AF screening and the varying aspects of service design from the perspectives of each stakeholder group (**Appendix 31**). Both topic guides contained a number of planned follow-up probes for each key question designed to explore the emerging views or concepts (Krueger & Casey 2015).

The topic guide for interviews with patients was piloted by VS during the first focus group, and since no further amendments were introduced, qualitative data from this interview were included in data analysis (Breen 2006). The final version of each topic guide was approved by the same three researchers. Whilst no formal changes were introduced to the topic guide for patients following the pilot, some of the significant themes emerging from earlier patient interviews, for instance the AF screening in community pharmacies, were iteratively explored or probed into by the facilitator during the subsequent sessions as described below (Krueger & Casey 2015).

4.3.3 Recruitment and informed consent

Prospective participants were recruited using a convenience sampling strategy (Saumure & Given 2008a). All patients participating in the PDAF study were eligible to take part regardless of their AF screening result unless they lacked a mental capacity to provide an informed consent. Similarly, all CPs conducting AF screening and all GPS working at surgeries participating in the PDAF study were eligible to take part provided they had a sufficient mental capacity to consent. During each AF screening appointment, CPs provided prospective patient participants with an invitation letter (**Appendix 32**), a PIL (**Appendix 33**), a consent form (**Appendix 34**) and an expression of interest form (**Appendix 35**) for

the focus group in a pre-paid envelope. All CPs involved in the PDAF initiative were emailed an invitation to participate (**Appendix 36**) accompanied by the PIL (**Appendix 38**), a consent form (**Appendix 40**) and an expression of interest form (**Appendix 41**) at the end of the study by VS. The gatekeeper at each GP surgery distributed internal email invitations to prospective GPS participants (**Appendix 37**) enclosing a PIL (**Appendix 39**), a consent form (**Appendix 40**) and an expression of interest form (**Appendix 42**) to all GPS.

All prospective participants who returned their expression of interest forms either via the post (for patients) or via the email (for CPs and GPS) were invited to participate. Prior to each focus group interview, the facilitator (VS or SC) explained the purpose of the study, the layout of the interview and the data management with reference to a relevant PIL as necessary. Each prospective participant was also given time to ask the facilitator any questions they might have. A written informed consent was then obtained from all participants by them physically signing the consent form in line with the ethical approval. One copy of the consent form was given to the participant and one was retained by the research team.

4.3.4 Facilitation and data collection

Focus group interviews with patients were conducted in seminar rooms at the University of Kent (Canterbury campus). The interview with GPS was held in a designated room at one of the GP surgeries whereas the interview with CPs was carried out in a secluded, quiet area of the local pub, which was considered to be the most convenient location by CPs involved. Prior to the commencement of each interview, all participants were advised that interviews, particularly those held at the surgery or the pub, might carry a small risk of being overheard by colleagues or patients.

Each focus group interview was led by either VS or SC (the PI for the study) with support of EV. VS was directly involved in the PDAF initiative as a CP and only facilitated two of the interviews with patients. SC facilitated the focus groups with patients, GPS and CPs, and acted as an assistant moderator during the interviews facilitated by VS. EV greeted the participants and provided them with information, for example by answering any questions they may have about the study. Prior to the interviews, SC helped VS prepare by reviewing the topic guides and briefing them about the layout/method of the focus groups. VS also familiarised himself with an appropriate moderating technique detailed by Krueger & Casey (2015). All focus group interviews facilitated by VS were observed by SC, who intervened where appropriate (e.g. to probe further into participants' answers) and provided VS with developmental feedback.

The layout of the focus group and the questioning route overall followed the topic guide and the structure adapted from Krueger & Casey (2000b). After obtaining an informed consent, the facilitator of each interview explained the purpose of the study and reminded participants about the necessity to maintain each other's confidentiality following the focus group. Afterwards, they asked participants a series of open-ended questions from the flexible topic guide using the probing techniques adapted from Krueger & Casey (2015). Briefly, this included an appropriate use of planned or unplanned prompts and probes into the answers, and five-second pauses to allow all willing participants to contribute after one another's comments. Some examples of probes used included: *'Would you explain further?'*, *'Can you give us an example?'* or *'Is there anything else?'*. Where needed, verbal shifting from more dominant to less dominant participants was used to involve them in the conversation and to obtain a wider variety of views (Krueger & Casey 2015).

All interviews were audio-recorded using Olympus® recorders provided by the MSOP. SC also maintained a diary of notes/observations during each interview as a source of supplementary information (Patton 1999; Krueger & Casey 2015). The audio recordings were transcribed verbatim by VS. The accuracy of transcription was confirmed by SC and EV.

4.3.5 Data coding and analysis

The coding and analysis of qualitative data was carried using NVivo (v12) and the structured deductive-inductive TDF approach adapted from Atkins *et al.* (2017) and Islam *et al.* (2012) as described in section **2.9**. Field notes taken by SC were consulted after the preliminary analysis to support the identification of key facilitators and barriers (Lincoln & Guba 1985b; Forero *et al.* 2018). VS conducted the coding and data analysis, which was then independently verified by SC. All qualitative themes were subsequently endorsed by SB who had extensive experience of qualitative research and by EV and AM who provided the less specialist views. The statistical analysis of patient demographic data was carried out using SPSS (v25) and all data were expressed using the principles outlined in section **2.7.1**.

4.3.6 Reflexivity

VS and SC were registered pharmacists and maintained a reflexive account to acknowledge the possible influence of their professional background (Hiller & Vears 2016). VS in particular acknowledged their personal bias due to direct involvement in the AF screening process as a CP (Stewart *et al.* 2007). This status may have subconsciously influenced some of the patient participants who were more inclined to provide the positive views about

the service due to the prior familiarity with the facilitator from their AF screening appointment (Korstjens & Moser 2018). The researchers' professional background as pharmacists may have also inadvertently led to the prioritisation of topics or themes pertaining to pharmacist's professional identity.

4.4 Results

4.4.1 Study participants

A total of 25 patients attended four focus group interviews, each of 80-90 minutes duration, in January 2018 and February 2019 (5-7 individuals per group) (**Table 4.1**). Participants from all four practices involved in the PDAF study were represented with 17 interviewees (68%) registered at one particular surgery. Those attending the interviews were overall younger than the main cohort of PDAF participants, were predominantly male and of White British ethnicity. One participant was White American and one – White European.

The majority of participants (84%, 21/25) had been confirmed by cardiologist as having a 'Normal SR' on their $_{SL}$ECG. The heart rhythm of three participants was 'Unclassified/Unreadable' and of one – 'Possible AF', thus requiring a further investigation either in a form of a $_{12L}$ECG or a HR re-check. With an exception of one participant who was screened on the same day as his other, non-influenza appointment, most underwent AF screening either during pre-booked appointments (68%, 17/25, i.e. systematic screening) or immediately before or after their influenza vaccination (28%, 7/25, i.e. opportunistic screening).

Four CPs and nine members of GPS participated in two separate focus group interviews which lasted approximately 40 minutes each. Two of the participating pharmacists were male and two – female with professional experience ranging from six to 15 years post-registration. All CPs held either a specialist (AFC Band 7) or senior/lead (AFC Band 8) positions at the at the Kent Community Health NHS Foundation Trust. All GPS attending the interview were female and worked at one of the surgeries involved in the PDAF study. Three were office support staff, two were receptionists and the remainder, a research administrator, a prescribing technician, a student nurse and an HCA. Five participants had no involvement in PDAF study. The attending HCA was responsible for performing some of the follow-up $_{12L}$ECG tests, the prescribing technician had experience of answering telephone enquiries about the study and one office support worker was involved in facilitating the influenza vaccination clinics. The research administrator held the overall

responsibility for the co-ordination of the PDAF screening and follow-up appointments at the surgery.

Table 4.1 Demographic characteristics of patients participating in focus group interviews compared with those of the main PDAF study cohort

*Continuous variables are expressed as a median [interquartile range]. Categorical variables are expressed as a number (percentage). *p = 0.023 as determined by Wilcoxon's signed rank test. Abbreviations: AF – atrial fibrillation; PDAF – Pharmacists Detecting AF; $_{SL}$ECG – single-lead electrocardiogram; SR – sinus rhythm.*

Characteristics	Focus Group Participants (n = 25)	All PDAF Participants (n = 604)
Age, years	71 [68; 73]*	73 [69; 78]*
Male	13 (52.0)	258 (42.7)
Ethnicity		
White British	23 (92.0)	585 (96.9)
Other	2 (8.0)	19 (3.1)
Test result (Device's algorithm)		
Normal SR	19 (76.0)	484 (80.1)
Possible AF	2 (8.0)	39 (6.5)
Unclassified/Unreadable	4 (16.0)	81 (13.4)
Test result (Pharmacist's interpretation of $_{SL}$ECG)		
Normal SR	22 (88.0)	487 (80.6)
Possible AF	2 (8.0)	39 (6.5)
Unclassified/Unreadable	1 (4.0)	78 (12.9)
Test result (Cardiologist's interpretation of $_{SL}$ECG)		
Normal SR	21 (84.0)	503 (83.3)
Possible AF	1 (4.0)	26 (4.3)
Unclassified/Unreadable	3 (12.0)	75 (12.4)
Appointment type (screening strategy)		
Pre- or post- influenza vaccination same-day (opportunistic)	7 (28.0)	183 (30.3)
Pre- or post- another appointment same-day (opportunistic)	1 (4.0)	48 (7.9)
Pre-booked appointment (systematic)	17 (68.0)	373 (61.8)

4.4.2 Key findings mapped onto the TDF

The coding and analysis of facilitators and barriers revealed the key TDF domains, which were expected to influence the development and implementation of the AF screening service proposed (**Figure 4.1**). **'Environmental context and resources'**, **'Goals'** and **'Social or professional role and identity'** appeared to be the cornerstone domains in the

interviews with all three stakeholder groups. Patients, GPS and CPs all discussed the need to prioritise the resources available for AF screening by choosing an appropriate setting, target population and HCPs to deliver the screening in the environment of increasing service pressures. All stakeholder groups also debated the role of pharmacists in the delivery of such screening initiatives. Patients and GPS identified the underutilised clinical role of pharmacists as a facilitator, however at the same time, emphasised the traditional commercial or supplier's perception of community pharmacies as a possible barrier to public engagement with AF screening. Patients felt that pharmacists' social and professional identity as clinical practitioners had to be developed and promoted in the eyes of the public, moving away from the traditional shopkeeper's role.

In turn, the discussion led by CPs was largely centred around their current and future professional roles, emphasising the need for better integration within the general practice infrastructure and the development of clinical skills. CPs appraised the inception of their clinical identity and specific roles in AF screening (e.g. the provision of information and education) as a key facilitator, but acknowledged their professional limitations, such as their limited experience of interpreting ECGs. Their discussion was also largely focused on the positive consequences of stakeholder (e.g. GP or commissioner) engagement and the use of $_{SL}$ECG devices compared to conventional pulse palpation.

Besides the awareness of pharmacists' roles, patients and GPS highlighted the necessity to increase the public's knowledge of AF and health services. These two stakeholder groups expressed a range of beliefs influenced by their shared social experience, such as the inaccessibility of general practice reported by patients or the poor patient engagement with services reflected upon by staff. GPS had their own agenda to facilitate behavioural regulation (i.e. patient engagement) and service implementation, stressing the importance of improved communication between themselves and service providers (i.e. the study team). They were willing to and felt capable of contributing to the running of the AF screening service either through service promotion or management.

As may be observed from the above, the key facilitators and barriers to service development and implementation were often supported by evidence from more than one stakeholder group. The majority of facilitators and barriers also spanned across two or more TDF domains, and are presented under the most relevant domains in **Table 4.2**. For instance, the facilitator *'presence of HCP'* was initially mapped onto both **'Behavioural regulation'** and **'Environmental context and resources'** domains of the TDF. It is however presented

under the latter to denote the impact of reassuring HCP presence on the screening environment, which may positively affect patient engagement with the service.

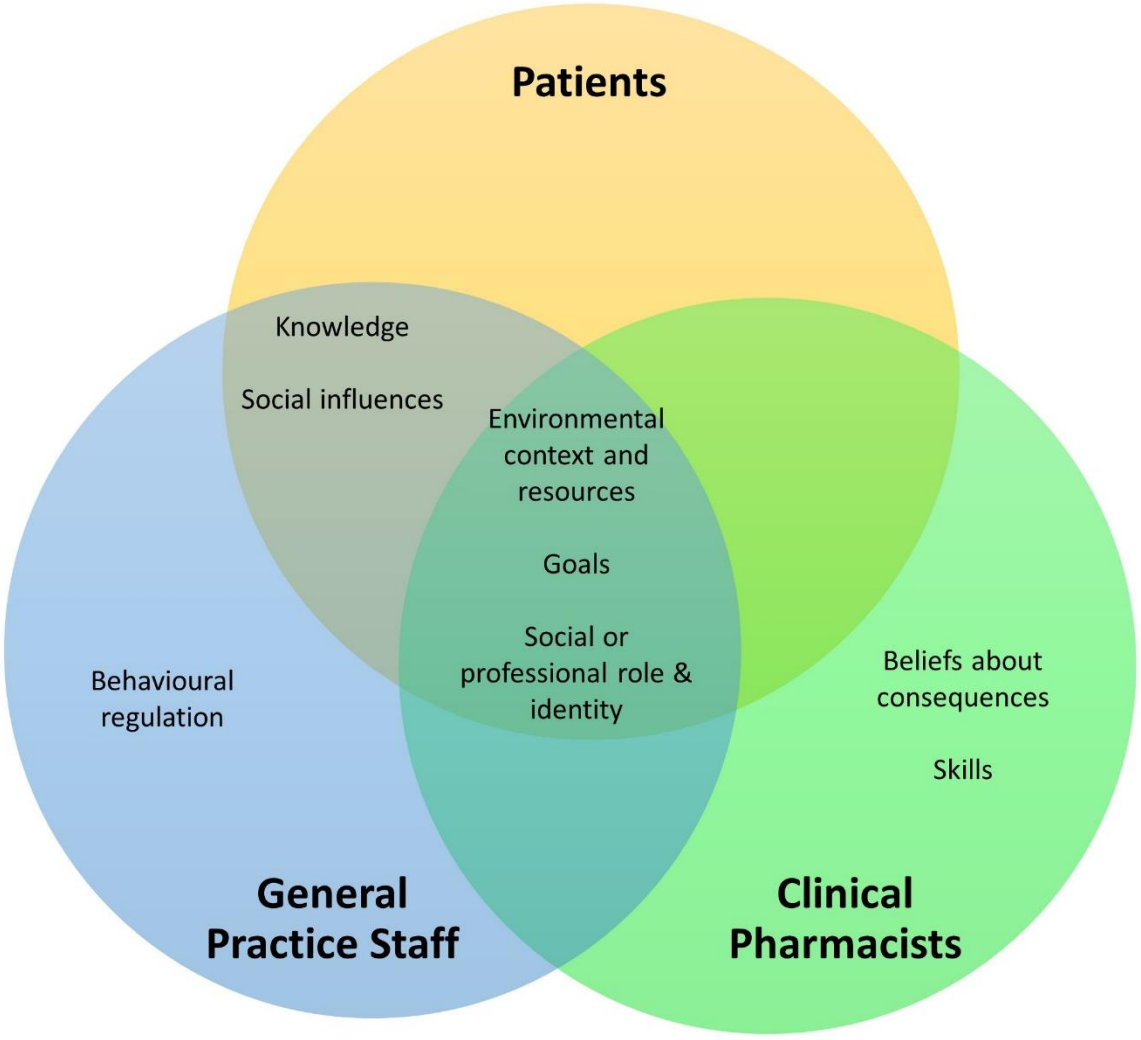


Figure 4.1 Venn diagram depicting the TDF domains most likely to influence the facilitators and barriers to service development and implementation

Most relevant domains for each stakeholder group were selected using the criteria by Islam et al. (2012) (n = 25 for patients, n = 9 for general practice staff and n = 4 for clinical pharmacists). Abbreviations: TDF – Theoretical Domains Framework.

The subsequent inter-domain analysis of the key TDF domains identified three overarching themes spanning across several domains: knowledge and awareness, prioritisation of resources and environmental considerations. These themes and the underlying subthemes are discussed below, referring to related facilitators and barriers in each case as appropriate.

Table 4.2 Key facilitators and barriers to AF screening service proposed mapped against the most relevant TDF domains

Abbreviations: AF – atrial fibrillation; ECG – electrocardiogram; GPS – general practice staff; HCP – healthcare professional; TDF - Theoretical Domains Framework.

TDF Domain(s)	Facilitators	Stakeholder Group(s)	Barriers	Stakeholder Group(s)
Environmental context and resources	Space and established general practice infrastructure	All	Busy clinic environment	All
	Advantages of single-lead ECG	Patients and pharmacists	Accessibility of community pharmacy	Patients and pharmacists
	Presence of HCP	Patients	Service costs and resources	Patients and GPS
			Variation in general practice culture and poor service integration	Pharmacists
			Variable access to care	Patients
			Logistics of same-day screening	
Goals	Prioritisation of at-risk groups	All	Screening led by other HCPs	Patients and pharmacists
	Flexible choice of appointment	Patients and GPS	Self-testing technology	Patients
	Engagement of stakeholders	Pharmacists		
Social or professional role & identity	Utilisation of pharmacists' skills	All	Misconceptions about pharmacists	Patients and GPS
	Development of pharmacists' roles	Pharmacists	Unconventional role of pharmacists	Pharmacists
Knowledge and social influences	Knowledge and awareness	Patients and GPS	Getting used to novel screening	Patients
	Staff inclusion in service provision	GPS	Lack of communication with staff	GPS
			Miscommunication with patients	

4.4.3 Knowledge and awareness

Awareness of AF and screening

Some patients (PT) openly admitted that they did not have much knowledge about AF prior to the screening procedure despite in some cases receiving treatment for other cardiovascular conditions, such as hypertension:

'*Although I've had hypertension for 25 years which is under good control, I wasn't particularly aware of this other than from our friend who had irregular heart beat, well I thought it's just an irregular heart beat, similar things.'* [PT9]

Similarly, GPS recognised a gap in their AF knowledge, which might have prevented a more active contribution during the study:

'I think as admin staff, I'm not sure how clued up we are on AF, I don't know how much we actually know about it … We know it's important, but we don't know the ins and outs of it.' [GPS5]

'I mean GPS6 knows more than I do, but, you know, I know nothing about AF. So I'm not wanting to give out the leaflets to anyone in case they come back and say, you know, 'what is it?' [GPS7]

One patient with an academic background felt that the issue of poor public awareness of AF might lie in the level of education received from clinical staff upon contact:

'Some of this this may come down to the way that doctors dummy it down because they think all the patients are thick. 'You've got an irregular heart beat, Mr Jones,' never mind what the technical terms might be.' [PT1]

Two other patients with a pre-study diagnosis of AF emphasised the need to educate the public about the condition and the risks associated with it:

'Do people know? I didn't know anything about AF until the age of 63. We all know about breast cancer and colon cancer, AIDS [acquired immune deficiency syndrome] and all kinds of other things where there's been promotion for people that need testing.' [PT7]

'I mean, how many people in the general public have actually heard of the condition and understand the significance of actually having it, which is stroke?' [PT11]

Participating patients were generally interested in their health status and were motivated to attend AF screening due to personal risk factors, such as older age and history of heart disease amongst their family/friends, or social responsibility:

'Whether after this, you know, I'd be called back for any further testing because as you get older all these things start to deteriorate, maybe my blood pressure will sort of go even higher.' [PT12]

'I got a friend who suffers from AF and I've taken that to the doctor a few times for warfarin tests when her husband has been working. So I knew what it was and I wanted to contribute.' [PT22]

'We need to take pressure away from hospitals and, as I said earlier, prevention is better than cure. If you know you've got a problem, you can have it treated at point A. You're not going to end up in point E where you're gonna spend three or four weeks in hospital.' [PT19]

Patients from all four cohorts acknowledged that the asymptomatic nature of AF was a particular challenge in engaging less motivated and/or less AF-aware individuals:

'I think if I turned up at the chemist routinely and they said, you know, 'do you want AF checked out,' I'd probably say 'no' because I would say to myself, 'there's no indication of anything wrong and I'm busy today anyway, you know, cause I always am.' [PT10]

As a consequence of such discussions, patients and GPS proposed numerous ways to raise public awareness of AF and to improve the uptake of screening, including using advertising boards, patient-friendly posters, the surgery's or Age Concern's websites, text messages, emails, mobile phone applications, AF awareness campaigns, TV and radio programmes:

'I'd start making posters you know with bullets, symptoms, nothing too terrifying, of course, but you know, just general. Just to indicate to people or arouse or communicate with them to see whether they do feel that they have got some of the symptoms. If they so far haven't been checked out…' [PT2]

'Cause quite often if they are coming for a flu jab, they are coming in and out quickly so to give them a bit of advanced warning or literature might be good for a patient. […] Website, leaflets, through to the maybe at-risk patients or things like that.' [GPS5]

Role of pharmacists

Both patients and GPS felt that the public often perceived pharmacists as 'shop assistants' or suppliers of medicines rather than HCPs who can play a role in public health services:

'Then people need to be made aware of what the pharmacists can do. Cause as far as I'm concerned, the pharmacist is just a guy in a local shop and I go seem him if I've got a

headache or a cold or something like that … But if you were made aware that the pharmacist could diagnose these problems, you might go to the pharmacist.' [PT3]

The association between medicines' supply and pharmacists' professional identity was so strong that one of the interviewees suggested any pharmacist-led services in GP surgeries should be coupled with their traditional role as a supplier:

'Well, if they are gonna be in the GP surgery, they need to be running a pharmacy, dispensing medication.' [PT10]

A few patients and staff also expressed their doubts about pharmacists' ability to provide novel services, for instance to interpret the test results or to manage long-term conditions:

'Does the pharmacist have the expertise to deal with type 2 diabetes or whatever?' [PT14]

'Can they answer the questions that patients have?' [GPS4]

However, engagement in AF screening appeared to modify patients' views about CPs, and several participants pointed out that public awareness of pharmacist-led services could indeed be raised by carrying out similar initiatives in the future:

'And it's only recently that it's been done with you, that you actually recognise that a pharmacist is a very, very skilled and trained person and has got an immense knowledge of a wide range of problems…' [PT14]

4.4.4 Prioritisation of resources

Effective use of novel technology

Patients participating in all four focus group interviews were fascinated by mobile technology, which according to them, made the AF screening process fast, non-invasive and painless. Interviewees were intrigued by the opportunity to observe a live recording of their ECG on a mobile phone and appreciated the presence of a CP, who provided them with an explanation of results and immediate reassurance:

'What impressed me about the test was really how simple it was and the fact that you could do it on your mobile phone with a little tiny pad. I was blown away by that, I was expecting a lot more technical equipment and, you know, probably have to take your shirt off.' [PT16]

'The guy that was talking to us said, 'do you realise that your heart works in more than just one way?' and when our recording came out with all these various times, and saying, 'this is this part of it working, this is this…' and that fascinated me the fact you go along usually and someone says you know, 'right, here's your heart and it goes bleep, yeah, it's all fine.' [PT14]

In turn, CPs reflected on patients' interest in the technology and the convenience of having a *'pocket'* device with them at all times. Despite some 'Unclassified/Unreadable' readings, they expressed a strong faith in KMDs which also helped identify suspected hearth rhythm disorders other than AF, and appeared to be more reliable than the traditional pulse palpation:

'I've got confidence again in [cardiologist], um, but there were a few patients where it came back and it was completely unreadable. But no, I would say I'm 95% confident in the device.' [CP3]

'I really didn't like doing the pulses because I found some people it was really hard to find their pulses … And, I just, I just found there was so much variability that actually that's why I did like the device was because having taken a lot of pulses now, you can see how things could get missed if you just rely on pulses.' [CP4]

Three of the CPs mentioned the limitations of $_{SL}$ECG, such as its inability to capture PAF or the inconclusive nature of diagnoses compared to $_{12L}$ECG:

'This is only going to tell us that at the moment this is not a problem. But if you're really worried because you're having a palpitation, you really need to go to your doctor to get that checked out because you need to have something done during a palpitation to measure that.' [CP4]

Considering the device's simplicity, several patients proposed self-testing for AF, questioning whether or not a HCP was required for screening to take place:

'Now without being disrespectful to you, anybody who has been trained for a day, could have operated a piece of equipment that you used that day. It doesn't actually need a pharmacist…' [PT5]

A few others proposed a mixed approach: either self-testing in a surgery followed by an appointment, or telehealth-based self-testing followed by the interpretation of the result and feedback from a central database monitored by HCPs:

'I know that in our surgery, in the waiting area there's just a machine stuck in the corner where you put your arm in, it does your blood pressure, and all you do is take the print out and give it to reception and they route it to your doctor. And that's just used up a couple of minutes of your waiting time so nothing lost at all.' [PT10]

'If you had a central bank of where it went to, then they would interpret it. You know, just like you do with your bank details when your transactions go through…' [PT13]

However, most patients remained cautious towards self-screening due to the fear of misdiagnosis in the absence of a HCP, which could lead to unnecessary stress and anxiety:
'The danger of doing things in that mind is that you might think you've got something very wrong and panic because of what you consider your findings on your computer.' [PT15].
'You know, it's all very well you're saying, well let's say, 'well if it's doing that, you're normal, if it's doing that, it's not, etc.' But I would rather have somebody who's more qualified than me, who's going, 'oh, yes, you've got a problem, sir.' [PT20]

Service costs and resources

In addition to technical resources, patients debated the overall economic value of the service proposed. Most participants considered opportunistic AF screening to be worthwhile as part of the broader preventative healthcare agenda, which despite initial investment, was thought to be cost-effective producing savings for the health service in the long-term:
'They were saying on the news about this blood test that can tell if you have pancreatic cancer … and the 10 types of cancer that it can find with a blood test for £250…I'd rather pay that annually and know that I was saving myself rather than…' [PT13]

Three patients were more sceptical and wondered if the screening programme proposed would actually result in substantial savings when compared to usual care:
'If you're notifying people, radio, TV, whatever, and you're hoping to identify lots of people who are potentially gonna get or have got AF, and then you can start giving them pills from a certain point, how does that stack up against the cost if you do nothing and then they go into AF and need to be hospitalised?' [PT6]

Some of these concerns were mentioned by GPS who identified the costs associated with equipment, pharmacy staff and follow-up as one of the key barriers to the implementation of the AF screening programme proposed:
'If it's funded, then probably. But I don't know if it wasn't because like they were saying all the equipment is going to cost money…' [GPS1]
'As well if the pharmacist were provided…' [GPS3]
'*And the time because you would have to follow them up so it would be a lot more for you, wouldn't it?'* [GPS6]

Patients and GPS also reflected upon the extra resources associated with same-day pre- or post-influenza vaccination opportunistic screening, such as the waiting time or unplanned parking costs. According to some participants, not only could these *'drop-in'* appointments result in a poor use of resources, but they may also compromise the recruitment process:

'Your parking ticket is about to run out or you planned to go somewhere else, you haven't got time to stop, then you would slip through the net. Whereas for us, because we were given a specific appointment, that we knew we could make we were not going to slip through the net.' [PT11]
'The only downside at the point when they come to reception was GPS7 and I found that, because the queue was so big at reception, a lot of people didn't want to queue up.' [GPS6]

For others, the efficiency and convenience of same-day AF screening seemed to counteract the poor use of resources compared to pre-booked appointments:
'It sort of went quite smoothly because it was done within flu clinic. I thought it was a really good opportunity to grab the people that are eligible while they are in the surgery.' [GPS1]
'My mind was based on the fact that I haven't had any of them done for seven years, and I thought, 'well actually I'm here, I haven't got to make an appointment, ok, I'm having my flu jab and then going straight in there, and that's the job done.' [PT14]

In light of conflicting thoughts about the choice of the appointment type or the screening strategy, three interviewees proposed a flexible system, giving individuals the option to wait or return for a pre-booked appointment:
'If you do it on the spot it's over and done with and all the records are there. And only if people know they want to do it and they've got their diaries with them, should you try to do one later.' [PT10]
'Some patients are not gonna come back, you gonna need to grab them when they're here. But other people will be prepared to come back to a clinic.' [GPS3]

While patient and GPS conversations were primarily focused around the monetary and time considerations, CPs touched upon the fundamental need to involve other stakeholder groups, such as GPs, clinical specialists or service commissioners. Getting GPs on board in particular was seen as essential to maximise the uptake of screening and to implement an effective follow-up process, particularly where future screening was to be conducted outside of the surgery, for instance in the supermarkets:
'But it works better when the GPs in the vaccination clinic said this would be a good thing… If the GPs didn't back it up then there was less up take … If you're outside of the GPs surgery then clearly it needs to be something that is a commissioned programme … local CCGs, area people to say this is what we will be doing.' [CP4]

GPS emphasised the importance of administrative or technical personnel's engagement in the development and/or delivery of the new service. Staff expressed their frustration with

poor internal communication from the research team, which despite their willingness to participate, precluded them from taking on a more active role in the initiative, e.g. by distributing promotional leaflets or identifying eligible individuals for screening:
'We were given some leaflets, 'can you hand these out? Can you explain that once they've had their flu jabs, they then have an opportunity to speak to some pharmacists at the end of that.' And that was it. It would have been quite nice if you know, going into it, we were given a little bit more understanding of what are we actually presenting to the patients.' [GPS7]

According to three members of staff, miscommunication during the study also affected the patients who in certain cases appeared to be confused about their test result or felt obliged to take part in optional AF screening:
'I was basically answering a lot of phone calls from people saying, 'I had this test done, I was speaking to pharmacist at the flu clinic, what is this and what is that?' [GPS6]

Targeting high-risk groups

All stakeholder groups agreed that the PDAF study was biased towards the pro-active, lower-risk patients, potentially overlooking those who did not regularly interact with healthcare and were likely at a higher-risk of CVD:
'People who don't attend the flu vaccine are probably ones who are more at risk because they're not looking after their health.' [CP4]
'But it'd be best if we targeted people that wouldn't come in, that we're missing out on.' [GPS6]
'We were all people who were having their flu vaccinations of course, we're that kind of person. Whereas my sister just refuses to have a flu vaccination.' [PT21]

In order to increase the coverage and benefits of the AF screening programme, a number of patients and CPs suggested targeting the less pro-active, at-risk individuals in public locations, such as the high street, supermarkets or gyms:
'*We used to stand there and drag the people off the street to have their blood pressure checked and some of them were an immediate, "Tom, we have to send you to hospital."'* [PT11]
'We should be inside of a supermarket doing people that are not engaged in health, they're maybe not buying the healthiest food, and actually that's where you need to be capturing these people.' [CP4]

Besides high-risk individuals encountered in public locations, CPs and GPS spoke about the housebound patients or care home residents who had limited access to healthcare despite being at-risk of CVD:

'Obviously, you're missing all of the housebound patients as well cause we don't go to search in care homes, there's gonna be actually quite a few in care homes.' [GPS6]

'They're not going anywhere so you've got a captive audience.' [CP3]

The consensus of the patient cohort was that, out of all high-risk individuals, AF screening programmes should prioritise the older persons. However, multiple patients thought that the eligibility criteria for AF screening could be broadened to include other at-risk groups, for instance the pregnant or the overweight:

'I did look at the people in the surgery and I thought, 'there is an awful lot of big people in here that possibly could have more heart problems than what I have and should you not be challenging those people as well?' [PT13]

Similarly, CPs and GPS suggested that opportunistic AF screening in GP surgeries could be extended to patients with long-term illnesses, such as diabetes or hypertension, or to individuals attending the NHS Health Checks:

'I've picked up a few patients that'd been diagnosed with AF through doing diabetic foot checks, listening to the foot pulses with a Doppler [ultrasonography] … And listening to irregular beats on the blood pressures on NHS health checks in particular. And then referred for an ECG that's picked up AF.' [GPS9]

The outcome of such discussions was the concept of a routine personalised health screening plan, repeatedly referred to by patients as the 'MOT' (reference to the annual UK Ministry of Transport check for motor vehicles):

'So if you could go in and have that test, then have, you know, whatever we are discussing now, so you have a sort of whole package.' [PT12]

'Like having an MOT.' [PT8]

'If your car is over a certain age and every year you go and have an MOT, then possibly we ought to be doing, thinking the same way.' [PT14]

Apart from including AF screening into a personalised health-check package, a few patients and CPs thought that the initiative could be delivered in combination with traditional pharmacy services, for instance by offering patients an AF check upon the collection of their repeat prescription:

'Pick up a prescription or go buy something at the pharmacy, they've got a private room to be offered it there and said, 'would you like to pop in and have this done?' [PT11]
'It would kind of be linked in to the pharmacy, but when you've got them waiting for their prescription, it's another thing that you can be like, 'oh, by the way.' [CP2]

Pharmacists as underutilised resource

Paradoxically, despite their public image as dispensers, most patients and GPS viewed pharmacists as highly qualified practitioners whose clinical knowledge and expertise were underutilised at the time of increased service pressures faced by GPs:
'The clinicians say they are terribly overstretched and anything that you can do … And you are not stupid, you are well-qualified people who have a good understanding certainly of pharmacology and medicines.' [PT1]
'Qualified pharmacists, you know, who have done like four-year degrees, obviously they've got huge knowledge on like the pathophysiology of humans.' [GPS8]

Patients believed that additional CP-led services, such as AF screening, would reduce GP workload and might improve their access to healthcare regardless of whether these were delivered in community pharmacies or GP surgeries:
'Because I think if pharmacists can take some of the work of GPs, i.e. either in the pharmacy or clinics themselves, I think it's a brilliant idea.' [PT18]
'Nurses work, doctors work, and you can look at the pharmacists who have got equal qualifications. Why weren't they being able to do this? … It opens another avenue where people can go and get checked.' [PT20]

The prescribing technician related CP-led AF screening to their educational role suggesting that, as substantial members of the multidisciplinary team (MDT), pharmacists were the ones to bridge the knowledge gap between patients and doctors:
'I think it's in the job cause it obviously educates the patients on why they are potentially taking this medication and what long-term effects it can have on them. I think, they kind of act as the middle ground between the GPs and the patients.' [GPS6]

Reflecting the trust placed in them by patients and GPS, CPs displayed some confidence in their newly developed AF screening role, particularly their ability to communicate the test result to the patient. This skill seemed be the distinguishing point between CPs as HCPs and technical personnel who may only be able to provide the result without an adequate explanation:

'The feedback I got instantly from people was like, 'of wow that's brilliant you know. That's really given me some extra information about a potential condition that I don't have or I do have, just more understanding about the body.' [CP1]
'You've got to give information about what this result means because you get it there on the screen, they can see it there … So you need more than an untrained professional to be able to give that advice because they are worried.' [CP2]

CPs perceived the structured training provided by the cardiologist as a catalyst to the development of their new AF screening role. They appreciated the ongoing support throughout the study, but wished for more training relating to ECG interpretation, which was not covered in depth at the beginning of the AF screening programme:
'That came from having the second lot of training with [cardiologist]. That really helped, because before we were like, it must be AF, but … so having that again helped.' [CP2]
'What we really needed was to have sat down with ECGs … We did a couple of quizzes at varying times, but we needed to have done that and more.' [CP4]

Other HCPs

Whilst CPs were viewed by the majority as vastly underutilised, patients were not apprehensive towards AF screening models led by other HCPs. Interestingly, some patients either had no preference as to who conducted the screening or demonstrated an indiscriminate faith in all HCPs:
'I think I'm generally interested if any doctor or nurse, pharmacist, I think white coat kinda all the same, so you put your life in their hands.' [PT7]

Several others spoke about utilising practice-based nurses or opticians. Optician-led services were perceived as more trustworthy than those provided by community pharmacists whereas nurses were valued due to their intrinsically clinical, *'hands-on'* skills, relatively low cost of services and superior accessibility compared to GPs:
'Could not a nurse do that? Sometimes you go for a regular blood pressure check or something … she could say, 'Have you got a couple of minutes? I'll just check that.' [PT6]
'The reason I mentioned X [opticians] is that they've extended what they do into hearing, and they do employ professionally qualified people obviously, in both of those areas. I think I trust what they are doing more than the retailer.' [PT21]

CPs did not shy away from the higher cost of their services compared to nurses or HCAs. Instead, one CP reminded the interviewees that nurse practitioners with a clinical interpretive ability may be equally as expensive as CPs:

'We are more expensive than some nurses, but I think the nurses who feel competent to interpret a $_{12L}$ECG are probably going to be comparable in cost to some of the pharmacists.' [CP4]

4.4.5 Environmental considerations

General practice

The great majority of patients spoke favourably about the welcoming, informal and relaxed environment within the consultation. Participants were unaffected by anxiety or *'mental block'* which could occur with traditional health check-ups, and according to one of the participants, had previously influenced their test results:

'Went into the hospital having my pre-tests and they took my blood pressure, it was rocketingly sky high. And then, referred back to my GP, GP said, 'I suspect this was the scenario', took my blood pressure and said, 'it's perfectly ok.' And, you know, went in for this … and there's no anxiety, the difference that you get in the recording is huge. So we walked away actually feeling quite satisfied.' [PT14]

A few patients, GPS and CPs, complained about the co-running of AF screening with busy influenza vaccination clinics. Patients and CPs felt that, the busy clinic environment prevented CPs in some cases from providing participants with comprehensive pre-appointment information about the screening. GPS added to these thoughts explaining that that the stressful influenza clinic environment might also affect staff themselves leading to an increased risk of errors:

'*I think one of the problems though is that there are so many of us filing through having our flu jabs and then wanting to get on and do the shopping or whatever it is, there's not really much time for verbal explanation.'* [PT16]

'You have such a limited amount of time to get people beforehand, so you're sort of telling them while they're anxiously trying to await their appointment which they haven't got a slot assigned for.' [CP2]

'*Because we were speaking to the patient and we could have potentially missed a patient going round and getting their flu jab and then not coding that they've had it…'* [GPS6]

Discussions which ensued during the CP and patient focus groups explored some of the possible contributing factors towards the unfavourable clinic environment in general practice. CPs focused on the variation in practice culture and the barriers of infrastructure preventing effective service integration, recruitment and screening:

'One of the health centres was less welcoming and less set up for us to be there. The other one was much more accommodating and although you were made to feel quite welcome when we were there outside of the vaccination clinics I felt a little bit more like I was, just kind of visiting rather than part of the scheme … And the [Town A] one was again a little bit ad-hoc and the room we had wasn't ideal.' [CP4]

The focus of patient discussion was the *'post code lottery'* nature of access to healthcare services in GP surgeries. For instance, participants registered at one of the surgeries were automatically invited for their seasonal influenza vaccinations whilst those based at a different surgery of the same town had to enquire themselves:
'PT13's [wife's] sister and brother in law they live down there, they've been for their flu jabs and they've been informed by their GPs. This is why I came back in, called back and said, 'we haven't been informed.' 'Ah, but you haven't had the five prescriptions in a year which would automatically trigger us to ask you to come down.' [PT14]

In spite of the generally well-established infrastructure and clinical environment, surgeries were overall widely perceived as inaccessible due to ongoing staff shortages, the convoluted referral system and excessively long appointment waiting times:
'My wife's family have a history of diabetes so she thought she likes to be regularly checked. And the palava!...That your GP surgery gonna make an appointment with a nurse, and if she's not happy, you gonna make another appointment with a doctor.' [PT1]
'It's not your fault or the GP's fault, you pick the phone up and you say, 'hi, I can see you in 2021 type of thing', I think, 'well, I think I'd give that one up.' [PT14]

Two participants who were issued with a provisional 'Unclassified'/'Unreadable' diagnosis following AF screening related the inaccessibility of general practice to their own situation whereby they were not provided with adequate information by the surgery or their follow-up appointment was significantly delayed:
'*The first time I phoned up, they said, 'we are full for the next 3 weeks,' which took me to when I was going on holiday. And I phoned them when I came back, and oh yes, and they couldn't, their diary wouldn't run that far ahead.'* [PT8]

Community pharmacy

A large number of patients viewed community pharmacies as more accessible than GP surgeries and considered the implementation of the AF screening programme in this setting a viable alternative option. Not only was this attributed to the difficulty of booking appointments at the surgery, but also to the approachability of community pharmacists, who

due to their immediate presence behind the counter, were perceived as more available than HCPs in general practice:
'I might go into the pharmacy wanna pack of aspirin, it might be the pharmacy that serves me so I get to see him face-to-face. The doctor is always shut in … And so that puts a sort of a bit of distance between. And I think that's part of a plus for the pharmacist that he's there and much more available and much more visible to the average person.' [PT16]

Despite acknowledging the advantage of community pharmacy's accessibility over GP surgeries, some of the same participants viewed pharmacies as a setting which lacked clinical infrastructure or physical space to conduct the AF screening consultations:
'In Town B, the pharmacy is small, one table outside, there wouldn't be room in that corner … Surgery B has rooms of that size so that's perfect. But the pharmacy is not big enough.' [PT7]

A few patients were concerned about the confidentiality of consultations in community pharmacy, which in some cases resembled a shop rather than a healthcare institution:
'The one thing psychologically against going to pharmacist is that basically they are like shops. You don't think, 'oh, well if they ask me to do something, is it going to be here in front of people buying their soap?' … I know there is a little room round the back somewhere, I don't know about the pharmacy.' [PT8]

Apart from space considerations, practice infrastructure was described as superior to that of community pharmacy due to a complete access to patients' medical records. Compared to the free-of-charge infrastructure within surgeries, the commercial nature of community pharmacy also influenced several participants' level of trust in services offered in this environment and made them question whether or not they would be charged for such services, including the AF screening:
'I suppose one of the dividing lines going to your pharmacist and going to your doctor's is your medical record. A pharmacist would not have that, even if he gave you some kind of treatment, it would not be on the record.' [PT2]
'Well they charge for flu jabs, don't they? … They are obviously aimed at people who want a flu jab, who don't qualify for the free one.' [PT22]
'Yeah, I think it probably would colour people's [opinion] if they had to pay.' [PT23]

Referring to their past experience, patients and CPs were not convinced that a typical community pharmacy had a sufficient number of staff, particularly pharmacists themselves, to facilitate additional public health initiatives, such as AF screening. Some were unsure as

to how community pharmacists would find the time to undertake new clinical duties without compromising their traditional supply function:

'I think that's the crux of the matter when we've using pharmacists is, how they could devote that amount of time to screening as opposed to actually doing their dispensing.' [PT11]

'It wouldn't work because of CP2's point, is that even with accuracy checking technicians, you still need a screening of the prescription.' [CP4]

Deficiencies of infrastructure and staff capacity were translated into the hectic community pharmacy environment. Patients referred to *'rude staff*', long queues when waiting to collect their prescriptions and felt that the identification of individuals suitable for AF screening in such a busy environment might be nearly impossible. The less busy waiting areas of general practice on the other hand were thought to provide HCPs with sufficient time to identify and approach eligible patients:

'If you were to do it in a local pharmacy, how would you identify people that you wanted? Because our pharmacy is very busy. People come in there all the time whereas if you were at the surgery, there's people sitting and waiting and you can sort of observe the type of person you're looking for perhaps.' [PT3]

As a deviation from this consensus, two patients reported their positive experience of medication reviews in the community pharmacy, which were conducted in a timely manner and in an appropriate consultation room:

'I phoned and booked an appointment, went to see him, and that was brilliant: 10 minutes and answered all my questions, I was very pleased … They have an interviewing room in there which is very good.' [PT18]

4.5 Discussion

4.5.1 Comparison with existing literature

This study utilised a TDF methodology and the method of focus group interviews to ascertain the key facilitators and barriers to the development and implementation of the CP-led AF screening strategy in GP surgeries from the perspectives of service users (patients), service providers (CPs) and the GPS. The preliminary analysis identified five main TDF domains, which were expected to influence the development and implementation of the intervention. From these, three major themes relating to knowledge/awareness, prioritisation of resources and environmental considerations were identified.

As expected from pre-existing evidence (Lane *et al.* 2006; Kaufman *et al.* 2018) and questionnaire data presented in section **3.4.5**, which showed that less than 50% of patients were familiar with AF or its risks, the lack of AF awareness was highlighted amongst the three major qualitative themes discussed here (**Figure 4.2**). Poor public awareness of AF was also identified as one of the primary barriers to the uptake of AF screening by several qualitative studies evaluating the AF screening programmes in UK or Australian primary care (Orchard *et al.* 2014; Sabater-Hernandez *et al.* 2018; Lown *et al.* 2020). One of the academic patients participating in the current study, thought that the public were largely unaware of AF as a result of clinicians bypassing the term 'atrial fibrillation' during the consultations and instead referring to the condition as 'irregular heart beat'. This finding echoes that by Sabater-Hernandez *et al.* (2018) who discovered that even those individuals with pre-existing AF might be unsure about their condition, attributing this to the inadequate explanation of the non-user-friendly medical term 'atrial fibrillation'. The task of conveying complex healthcare information to patients may be challenging since up to one in five people display inadequate health literacy, which is an independent predictor of poor AF awareness (Reading *et al.* 2017). As highlighted by patients interviewed during this study, the 'silent' nature of AF might further compromise the public knowledge of the condition preventing the engagement of the less pro-active, asymptomatic individuals. In turn, it appears that patients in 'emotional distress' or those who experienced 'frightening symptoms' of AF may be likely to exhibit increased awareness of the condition (Sabater-Hernandez *et al.* 2018). During the present study not only patients but also some of the administrative or technical GPS were unaware of AF, suggesting that the lack of AF awareness may be a widespread public health issue. In the Australian GP-SEARCH pilot, trained general practice receptionists undertaking AF screening were uncertain about the aim of the screening or the risks associated with the condition (Orchard *et al.* 2014).

The combined views of patients and staff interviewed here hinted that the barrier of poor AF and service awareness may be overcome through the delivery of a structured, multifaceted programme consisting of advertising materials, patient education and widespread public health campaigns. Similar 'layered' approaches to raising AF and service awareness were proposed by community pharmacy-based AF screening studies (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020). Lowres *et al.* (2015) advocated for community pharmacists to directly approach patients eligible for AF screening or to facilitate the health promotion events (Lowres *et al.* 2015), whereas Sabater-Hernandez *et al.* (2018) and da Costa *et al.* (2020) also emphasised the importance of public-friendly educational materials, pharmacist-led demonstrations and the involvement of PPOs, such as the Arrhythmia Alliance. Several independent research groups reported the favourable

outcomes of structured AF educational programmes for patients, including a significant increase in AF-related knowledge, QOL and adherence to OAC therapy, while reducing the risk of stroke and anxiety/depression scores (Clarkesmith *et al.* 2013; Vinereanu *et al.* 2017; Guo *et al.* 2017). The recently completed **H**ome-based **E**ducation and **L**earning **P**rogram for **AF** (HELP-AF) trial evaluating the nurse- or pharmacist-led educational home visits aims to add to this evidence by displaying a meaningful reduction in hospital admissions and all-cause mortality (Hendriks *et al.* 2019). Nevertheless, it is worth noting that programmes involving the basic provision of educational information are unlikely to be successful (Lane *et al.* 2006), and any future interventions would almost certainly require a multidisciplinary effort with regular follow-up, monitoring and feedback (Clarkesmith *et al.* 2013; Vinereanu *et al.* 2017; Guo *et al.* 2017).

The significance of a multidisciplinary collaboration in the delivery of AF screening service was pointed out by both GPS and CPs participating in this qualitative evaluation. Contrary to findings by Orchard *et al.* (2014), whereby surgery's receptionists were reluctant to engage in the new service, our GPS were keen to become more involved in AF screening, for example by helping recruit the patients. However, their willingness to contribute was affected not just by poor AF awareness but also by the lack of communication or information from the research team. The latter was anticipated from patient feedback questionnaires (section **3.4.5**) where several respondents identified the "broken" internal communication between the receptionists and the study team as a barrier to service delivery.

Whilst impaired staff communication may be transient due the novelty of the service or its status as a research initiative, it may also be a part of pre-existing general practice culture, and may ultimately lead to an inefficient use of resources or compromised patient care (Vermeir *et al.* 2015). The variation in practice culture and environment was mentioned as a barrier to service integration by participating CPs. It was also one of the core concepts of the recent review into inter-professional teamwork in primary care, which reflected on the gap in communication between the frontline and the *'back office'* professionals (Levesque *et al.* 2017). Levesque and co-workers (2017) stated that such relational aspects of teamwork may be improved through the development of shared working vision led by practice managers who may act as 'champions' of new initiatives. Furthermore, stakeholders interviewed by several qualitative evaluations of AF screening interventions agreed that the success of the novel AF screening service depended heavily on the pro-active actions of the screening champions (Orchard *et al.* 2016; Orchard *et al.* 2019a; Wessex AHSN 2019; da Costa *et al.* 2020). Likewise, CPs interviewed here indicated that the uptake of AF screening was greater where GPs encouraged prospective participants to

take part. Pharmacists also stressed the essential engagement of other stakeholders, particularly service commissioners, thereby, together with staff, drawing a multidisciplinary image of the 'new' AF screening service, involving practice managers/GPs ('champions'), GPS (service promoters/effectors of follow-up) and CPs (service providers).

Aside from stakeholder engagement, CPs appreciated the use of $_{SL}$ECG devices, which was a major enabler for AF screening initiatives and patient education. This finding was not a surprise considering the published evidence concerning the poor diagnostic accuracy of pulse palpation (Cooke *et al.* 2006; Taggar *et al.* 2016a) and the superior diagnostic accuracy of KMD discussed in **Chapter 3**. Patients were overwhelmingly fascinated by the technology and interested in learning more about their heart rhythm. Several "tech-savvy" patients were even brave enough to propose a complete or partial self-screening service. Different to studies by Sabater-Hernandez *et al.* (2018) and Lown *et al.* (2020), the majority of patients interviewed here were not concerned about being *'over-servised'* by the self-monitoring technology, but were instead worried about the possibility of a misdiagnosis or a positive diagnosis whilst carrying out the test at home.

Unsurprisingly, patients participating in all four focus groups appreciated the reassuring presence of a qualified HCP during the screening appointment, in some cases, without attaching any particular significance to who the chosen professional might be. This lack of differentiation between HCPs was not unanticipated considering the "blurring" between the roles of primary care HCPs who at times struggle to identify the realms or boundaries of each other's clinical competence (Oxtoby 2009; Niezen & Mathijssen 2014). When speaking specifically about the value of CPs, both patients and GPS praised their currently underutilised clinical skillset. Resembling the previous qualitative studies of AF screening in community pharmacies (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018), educational and advisory skills of CPs were at the centre of these discussions, and were a distinguishing feature between the skilled HCPs and the less clinically-qualified staff, such as HCAs. General practice-based CPs' ability to conduct effective patient consultations had previously been favourably appraised by both service users and other HCPs, and leads to improved patient satisfaction and practice capacity (Wilcock & Hughes 2015; Tinelli *et al.* 2015; Ryan *et al.* 2018). Yet, several reports indicate that the relatively new role of practice-based CPs warrants further structured training and/or additional support mechanisms to help them develop the advanced clinical skills to complement their traditional advisory duties (Butterworth *et al.* 2017; Bradley *et al.* 2018).

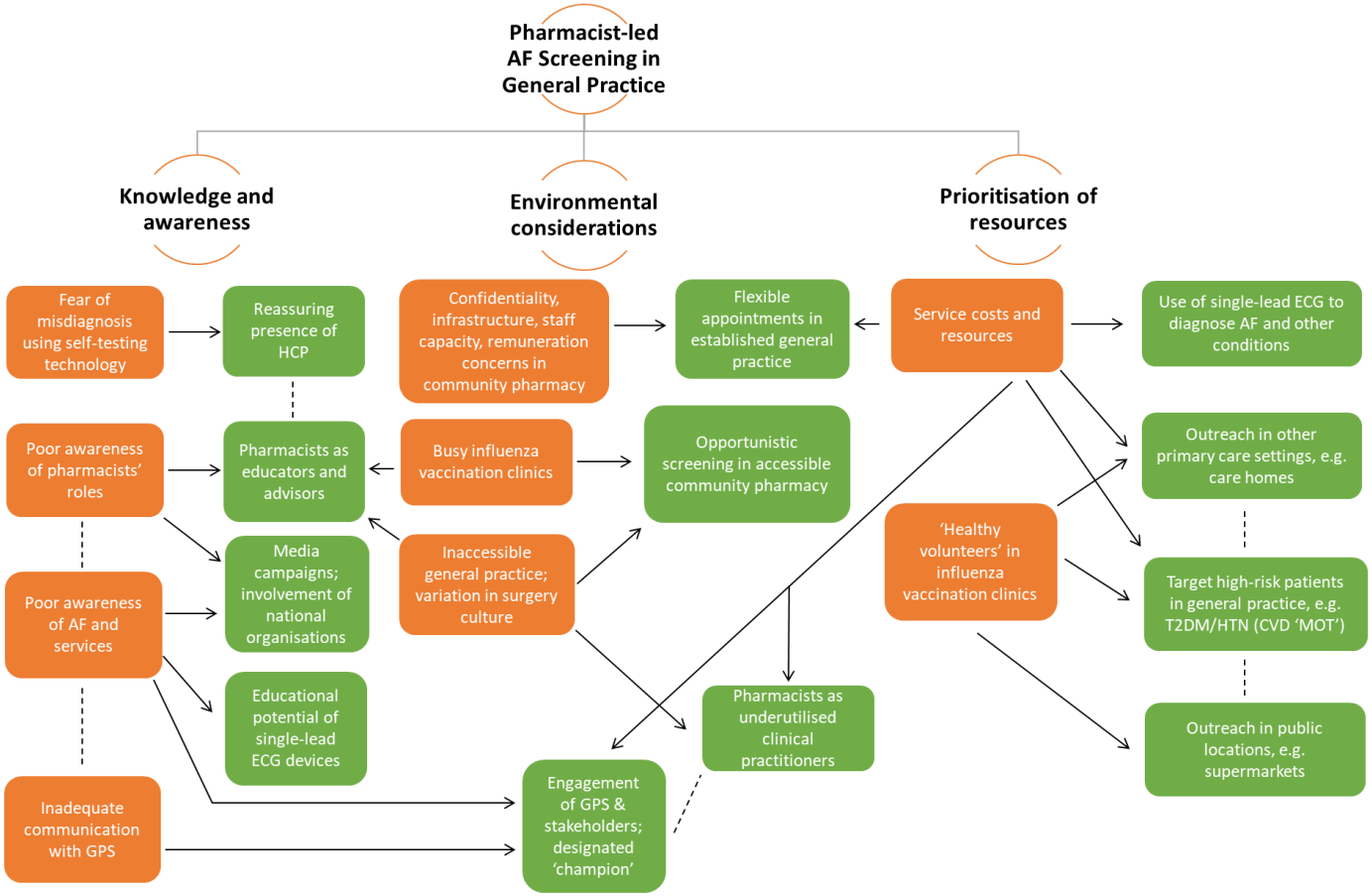


Figure 4.2 Key barriers (orange) and facilitators (green) in relation to the AF screening service proposed

Presented under the three main qualitative themes identified during the present study. The arrows emerge from each barrier and point towards a facilitator which may be used to overcome the respective barrier. Dotted lines relate to a potential relationship between the relevant barriers or facilitators. Abbreviations: AF – atrial fibrillation; CVD – cardiovascular disease; ECG – electrocardiogram; GPS – general practice staff; HCP – healthcare professional; HTN – hypertension; MOT - Ministry of Transport [car inspection]; T2DM – type 2 diabetes mellitus

These ideas were not alien to CPs participating in the PDAF initiative who appreciated the clinical education received in their study evaluation questionnaires (section **3.4.5**), but openly requested more practical training, particularly concerning the interpretation of ECGs, during the focus group interviews.

Perhaps due to their inherently clinical skills and historic role in health testing, practice nurses were considered by patients and CPs themselves as a substitute to pharmacists to conduct AF screening. The success of nurse-led AF screening in primary care had been documented both in the UK (Morgan & Mant 2002; Lown *et al.* 2018) and elsewhere (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019b). Respective qualitative evaluations presented positive multi-stakeholder feedback and high confidence of nurses in carrying out the screening, who similar to CPs, enjoyed the interaction with patients and visualised themselves as advisors or educators (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019a). A recent England-wide survey however showed that, as observed for CPs during this study, over 80% of nurse practitioners requested more training related to ECG interpretation (Taggar *et al.* 2016b). Furthermore, only 29% of nurse practitioners and even fewer nurses (16%) or HCAs (3.7%) considered themselves to have sufficient knowledge to decide on the management of the newly diagnosed AF post-ECG (Taggar *et al.* 2016b).

This is an area where practice-based CPs may use their medicines expertise to optimise the treatment for patients with AF by increasing adherence to anticoagulation guidelines and reducing the inappropriate use of antiplatelets (Virdee & Stewart 2017; Public Health England 2019e; Chahal *et al.* 2019). Encouraged by such reports, the collaboration funded by the NHS England's *'Test Bed Programme'* established a pathway for one-stop AF clinics, facilitated by community pharmacists at the screening stage and arrhythmia nurses/anticoagulation pharmacists at the management stage (Care City 2019). The preliminary findings were positive, identifying 'new' AF in 1.6% of participants, and ensuring that all patients were anticoagulated within 30 days (Antoniou *et al.* 2019). Following the success of this pilot, community pharmacists have become central to the Government's agenda for the detection of undiagnosed AF (Department of Health and Social Care 2019; Royal Pharmaceutical Society 2019). However, several substantial questions remain unanswered and would need to be considered by future developers of community pharmacy-based AF screening services. First of all, the current model of one-stop clinics involves three HCPs (community pharmacist, arrhythmia nurse and a practice-based CP), therefore questioning the cost-effectiveness of the intervention, which could otherwise be comfortably undertaken within a single location by a single, AF-trained specialist CP. More

importantly, the current model does not address the logistics of community pharmacy-related concerns raised by previous AF screening studies in this setting, including the management of concomitant workflow, inadequate staffing, service remuneration and risks to patient confidentiality (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018).

All of these concerns were voiced by patients interviewed during the present study who were not eager to engage in AF screening within the *'shop'* environment of community pharmacies and preferred the less accessible but more trusted GP surgeries. As reported by Lowres *et al.* (2015), some participants were also surprised by the fact that AF screening was delivered by CPs and struggled to separate the historic supplier's role of pharmacists in community pharmacy from their newly developed clinical identity. It appears that the Government's efforts to increase the public's awareness of pharmacists (NHS England 2018d; NHS England 2019d), have created an image of qualified and underutilised HCPs, yet have not removed the perceptions of their primary role as dispensers. This shared perception of pharmacists may be affected by numerous factors ranging from the retail nature of community pharmacy environment to the confusion between the roles of pharmacists and pharmacy technicians (Gidman *et al.* 2012; Kelly *et al.* 2014). Interestingly, when viewed separately from the community pharmacy context, CPs were largely perceived by patients and GPS as competent HCPs albeit a *'waste of talent'*. The positive shift towards the recognition of pharmacist's qualifications and clinical role amongst patients was particularly evident following the study appointment, thus highlighting how similar initiatives could raise the profile of practice-based CPs in the future. Indeed, several qualitative studies exploring the general practice integration of CPs described a promising journey from initially poor understanding of their role amongst multiple stakeholders to the refinement of their professional expertise within the MDT and the increased appreciation by patients/staff several months later (Tan *et al.* 2013; Ryan *et al.* 2018). The widespread integration of practice-based CPs into the emerging PCNs gives this branch of the profession hope that they will assume an increasing public health role in primary care, perhaps by incorporating AF screening as part of combined interventions for target patient groups (NHS England 2019d; NHS England and BMA 2019b).

The appropriate selection of target group(s) and setting of recruitment for AF screening were considered by all three stakeholder groups to be as important as the choice of a HCP. Similar to the feasibility study by Orchard *et al.* (2016), the combination of seasonal influenza vaccinations and AF screening during the PDAF initiative may have attracted the annual surgery visitors. However, patients, GPS and CPs all agreed that most participants attending influenza vaccinations were likely the mobile, motivated and pro-active *'healthy*

volunteers' (Froom *et al.* 1999) who did not display a significant risk of CVD. Instead, interviewees suggested targeting the "hard-to-reach" groups of individuals who may be at risk of CVD but do not regularly visit their GP surgery, such as the housebound patients, care home residents or individuals at the shopping centres. Reports from care homes show that the prevalence of undiagnosed AF in this setting may be up to nine-fold above the population average (Public Health England 2017a; Wiesel & Salomone 2017; Chaskes *et al.* 2018; Khan *et al.* 2020), signifying the potential to benefit this overlooked group of individuals at the time when practice-based CPs play an ever-increasing role in the delivery of care home services (NHS England and BMA 2019c; Savickas *et al.* 2020a) (see **Chapter 5** for the PDAF study extension in care homes). As another alternative, rather than changing the setting of screening, interviewees proposed targeting at-risk individuals within the surgery by developing a tailored cardiovascular 'MOT' screening package. In line with the CVD 'ABC' agenda of the *'NHS Long-term Plan'* (NHS England 2019d), this may include screening individuals without an established CVD attending the NHS Health Checks (NHS 2019b) and/or focusing on those with risk factors for CVD and AF, for instance by screening patients attending annual diabetes or hypertension reviews (Benjamin *et al.* 1994; NHS England and BMA 2019a). As discussed in section **1.3.4** the concept of pharmacist-led AF screening within a CVD 'MOT' package is not a novelty in community pharmacies (Lowres *et al.* 2015; Twigg *et al.* 2016; Sandhu *et al.* 2016; da Costa *et al.* 2020), but future studies are yet to explore its implementation in GP surgeries.

4.5.2 Strengths and limitations

The method of focus group interviews was one of the key advantages of this qualitative evaluation, enabling researchers to probe into the shared perspectives concerning the most significant facilitators and barriers to AF screening service within each stakeholder group (Tausch & Menold 2016). It also allowed for the diverging opinions of some participants to be shared in a safe and more natural environment (Krueger & Casey 2000a). The result of this process was the emergence of primary shared concepts, such as the CVD 'MOT' and the AF awareness-driven engagement in the new service, whilst identifying the areas with conflicting views, for instance the use of self-testing technology. The participation of multiple stakeholders enriched these concepts further by exploring them from the angles of each service contributor: from service users to service providers and largely objective GPS, few of whom were directly involved in the AF screening initiative.

The convenience sampling strategy employed in the recruitment for this evaluation may have overlooked those with limited interest in or access to healthcare initiatives, such as the housebound, thereby limiting the transferability of findings to other settings (Saumure &

Given 2008a). However, albeit slightly younger, the sample of patient participants was overall representative of the PDAF study sample (**Table 4.1**), suggesting that the views obtained here were likely a reflection of the main study group. One should also note that the majority of patient participants were registered at a single surgery, and it is possible that their views affected the themes derived despite the facilitators' attempts to take the perspectives of all participants into account. Yet once again, the percentage of study participants registered at this surgery (68%) was close to the total proportion of PDAF participants screened at the same surgery (74%; section **3.4.1**).

The lack of GP or senior manager participation in this qualitative study was another limitation considering their significance in clinical leadership, commissioning and service implementation. Nevertheless, the absence of senior GPS during the interviews may have turned into an advantage by minimising the impact of any hierarchical relationships on group dynamics (Hofmeyer & Scott 2007). Following on from this evaluation, a separate semi-structured interview study was conducted to help triangulate the data presented here by exploring similar themes relating to the national AF screening programme from the perspectives of GPs (**Chapter 7**). The homogeneity of the focus groups may have had a further positive effect on group dynamics by reducing the influence of distinct participants' demographics (Krueger & Casey 2000c), although such a positive methodological step may have been counterbalanced by the moderators' professional background as pharmacists. Not only may this characteristic have created a degree of hierarchical relationship (Hofmeyer & Scott 2007), but it may have also introduced a personal bias thereby unintentionally steering some of the discussions and the subsequent data analysis towards the pharmacist- or pharmacy-orientated themes (Stewart *et al.* 2007).

Lastly, the deductive TDF approach to data analysis is not without limitations. While it serves the purpose of a structured, reliable approach to exploring a particular behaviour or a healthcare intervention for implementation (Islam *et al.* 2012; Lawton *et al.* 2016; Atkins *et al.* 2017), this framework analysis lacks the open-mindedness and depth of the more inductive approaches, such as the grounded theory, and the depth of meaning observed with phenomenology (Gale *et al.* 2013). Therefore, the specific primary concepts, facilitators and barriers to the AF screening intervention proposed will likely need to be explored and refined in more detail by future qualitative investigations (MRC 2006).

4.6 Conclusion

This chapter presents the qualitative evidence supporting the feasibility of the CP-led AF screening strategy in GP surgeries proposed by the PDAF study. It evaluated this complex

intervention by exploring the facilitators and barriers to its development and future implementation. Qualitative data discussed here suggests that much work is required to improve the public awareness of AF, healthcare services and the clinical role of pharmacists. According to interviewees, at the time of general practice workforce crisis, qualified yet underutilised pharmacists are in an ideal position to conduct AF screening, which may give an opportunity to educate the public about the condition and improve patient access to healthcare. Despite the poor accessibility of GP surgeries, patients interviewed during this study preferred to attend AF screening in this setting rather than in the community pharmacies, where concerns of confidentiality, commercialisation and inadequate staff capacity were raised. All three stakeholder groups agreed that the development of future AF screening programmes should prioritise the resources by targeting at-risk groups of patients, such as those with limited access to healthcare (e.g. housebound patients) or those with multiple comorbidities, including hypertension and diabetes mellitus. The result was a concept of a personalised, combined CVD 'MOT' check. As emphasised by CPs and GPS such a service should be a multidisciplinary effort between CPs, GPS, GPs and commissioners, a model which corresponds well with the plans for more integrated care within the PCNs. Data presented in this chapter also concurred with quantitative data discussed in **Chapter 3**, showing the superior service-user and service-provider acceptability of $_{SL}$ECG devices compared to conventional pulse palpation, which was perceived by CPs as unreliable and inaccurate, urging the future guideline review into the first-line methods for AF screening.

This qualitative evaluation of the PDAF study intervention raised several research questions for future investigations. Some of these were subsequently addressed by studies discussed in **Chapters 5-7**. **Chapters 5 and 6** build on the qualitative finding, which suggested that the PDAF study may not have captured some of the high-CVD risk groups of patients with limited access to healthcare, for instance patients in care homes (**Chapter 5**) or patients from the ethnic minority groups (**Chapter 6**). **Chapter 7** contributes to this study by exploring the themes discussed here from the perspectives of GPs across the UK. Future studies may add to the results of this qualitative study by conducting qualitative and quantitative evaluations of specific facilitators and/or barriers discussed here. This may include evaluating the feasibility of alternative service designs, for instance AF screening in public locations, AF screening led by HCPs other than nurses or pharmacists, or opportunistic/targeted AF screening during the CVD clinics for other conditions, for instance, the diabetic foot checks.

Chapter 5: Pharmacists Detecting Atrial Fibrillation in Care Homes

5.1 Introduction

The PDAF study in GP surgeries demonstrated the feasibility of CP-led AF screening of individuals aged ≥ 65 years during the influenza vaccinations season. Both quantitative and qualitative components of the PDAF study (**Chapters 3 and 4**, respectively) however highlighted the fact that the AF screening strategy proposed excluded those within the target population who did not attend seasonal influenza vaccination clinics or those who had limited access to routine care provided in GP surgeries.

One such group of individuals may be care home residents who constitute 3% of the total ≥ 65-year-old population of England and Wales (Office for National Statistics 2014). Approximately 72% of all care homes in England are residential (also referred to as care homes without nursing), and provide individuals with accommodation and support for activities of daily living, such as washing or taking medicines (Care Quality Commission 2019; NHS 2019a). The remaining 28% are nursing homes (or care homes with nursing), which are typically reserved for individuals with severe physical or cognitive impairment, and these in addition to residential care, provide clinical support from qualified nurses (Care Quality Commission 2019; NHS 2019a). In 2011, 83% of care home residents were aged ≥ 65 years, and 59% were over the age of 85 (Office for National Statistics 2014). Since the burden of long-term illnesses increases with age (Bhatnagar *et al.* 2016; Xu *et al.* 2018; Kingston *et al.* 2018), it is perhaps not surprising that UK care home residents live with an average of six comorbidities, including cerebrovascular disease, type 2 diabetes and IHD (Gordon *et al.* 2014). All of these conditions are associated with an increased risk of developing AF (Ball *et al.* 2013), and together with advances in age, contribute to the cumulative risk of ischaemic stroke (Olesen *et al.* 2011). The reported prevalence of AF in the care home population is therefore significantly above the 2.5% population average (Public Health England 2017a), ranging from 7% to 19% (Reardon *et al.* 2012; Krüger *et al.* 2012; Gordon *et al.* 2014; Wiesel & Salomone 2017).

The high prevalence of AF and the elevated cardiovascular risk profile implies that care home residents are likely to benefit from timely AF detection and OAC therapy (Rich 2012). Nevertheless, the evidence pertaining to AF screening programmes in this setting has been scarce, and none of the studies to date have been conducted in the UK. The AF screening studies in US nursing homes reported the unprecedented yields of ‘new’ AF from 6.9% to

7.4% (Wiesel & Salomone 2017; Chaskes *et al.* 2018; Khan *et al.* 2020), which were more than five-fold above the yields of single time point AF screening amongst the ambulant ≥ 65s in primary care or community/outpatient settings (Hobbs *et al.* 2005; Lowres *et al.* 2014; Lowres *et al.* 2019) and approximately two-to-three-fold above the yields observed in the same population following the intermittent screening (Svennberg *et al.* 2015; Halcox *et al.* 2017; Ghazal *et al.* 2020). An even greater yield of 'new' AF (13%) was discovered by the recent feasibility study in a Portuguese nursing home (Cunha *et al.* 2020). Although identifying a high proportion of those with previously undiagnosed AF, the feasibility of AF screening in care homes poses particular challenges and requires a further exploration. For instance, the study by Khan *et al.* (2020), which utilised KMDs to record $_{SL}$ECGs in US nursing homes, was limited by an excessive number of inconclusive diagnoses (26%), resulting in a sub-optimal diagnostic sensitivity of 72%. The authors concluded that this poor diagnostic performance may have occurred due to challenges in $_{SL}$ECG recording amongst the population with underlying physical and cognitive comorbidities (Khan *et al.* 2020).

Cognitive impairment including dementia affects up to 58% and 73% of individuals in residential and nursing homes, respectively, making their access to conventional medical interventions or routine care challenging (Alzheimer's Society 2014). Despite suffering from an average of six comorbidities, some care home residents may only have three contacts with NHS services per year (Victor *et al.* 2018), leading to a significantly lower quality of care compared to community dwellers of the same age (Shah *et al.* 2011). Apart from high prevalence of undiagnosed AF, limited access to healthcare services may also affect the quality of stroke prevention in those care home residents with 'known' AF (Shah *et al.* 2011). Together with the perception that the risk of OAC-related bleeding in old and frail care home residents outweighs the risk of ischaemic stroke this poor access to healthcare leads to inadequate stroke prevention in over 50% of eligible individuals with AF within this setting (Rich 2012; Alcusky & Lapane 2018).

The need to improve the healthcare access and quality of care received by people residing in care homes has been recognised by national organisations, urging the development of more integrated, multidisciplinary models of care (British Geriatrics Society 2016; NHS England 2018c; NHS England 2019d). This effort culminated in the development of the *'Framework for Enhanced Health in Care Homes'* (EHCH), which aimed to reduce the divide between the primary care and community services for care home residents whilst aligning such services with the emerging PCNs (NHS England 2020b). The delivery of structured medication reviews for care home residents was identified as one of the central care components within the EHCH framework (NHS England 2020b). In turn, the success of the

CPGP pilot and the co-running of the *'Medicines Optimisation in Care Homes'* (MOCH) programme (Mann *et al.* 2018; NHS England 2018b) helped CPs become the HCPs of choice to deliver medication reviews in care homes as part of their PCN roles (NHS England and BMA 2019b). Alongside medication reviews, the effective prevention and management of influenza was yet another important component of the EHCH framework, encouraging each care home to deliver a seasonal influenza vaccination programme (NHS England 2020b).

The high prevalence of undiagnosed AF, the regular presence of a CP and the focus on seasonal influenza vaccinations in care homes across England suggests that the adoption of the PDAF AF screening strategy in this setting may be a viable and beneficial service. This chapter relates to the PDAF study extension in care homes and presents the quantitative evidence in support of the CP-led AF screening service within this setting during the influenza vaccination season. It maps onto the feasibility/piloting and evaluation elements of the MRC guidance for complex interventions (MRC 2006) (section **2.2**), by investigating the feasibility of AF screening from the perspectives of participant recruitment, diagnostic accuracy and economic impact. The preliminary account of study findings underlying this chapter has been published previously (Savickas *et al.* 2019).

5.2 Aim and objectives

Aim:

To assess the feasibility, accuracy and economic impact of CP-led AF screening in care homes using either pulse palpation or $_{SL}$ECG during the influenza vaccination season.

Objectives:

1. To determine the proportion of care home residents that could be screened for AF using pulse palpation and/or $_{SL}$ECG devices.
2. To measure the total prevalence of AF in the study sample as determined by the study cardiologist, including the prevalence of 'known' and 'unknown' AF cases, and the proportion of each that may qualify for OAC therapy.
3. To measure the prevalence of 'Unclassified' and 'Unreadable' provisional diagnoses in the study sample ascertained by the CP using pulse palpation or the $_{SL}$ECG device compared to the study cardiologist.
4. To determine the prevalence of non-AF comorbidities amongst participants with 'Possible AF'.
5. To determine the quality of $_{SL}$ECG recordings produced by the CP.

6. To determine the accuracy of AF screening by a trained CP compared to the study cardiologist.
7. To compare the accuracy of AF screening using pulse palpation with either the $_{SL}$ECG interpretation by the CP or the automated algorithm.
8. To ascertain the proportion of screened individuals who were referred to the GP and were followed-up, including the yield of 'new' AF and non-AF diagnoses after an appropriate follow-up action.
9. To estimate the financial impact of the AF screening strategy proposed for the healthcare system.
10. To compare the participant demographics, diagnostic accuracy of index tests and the economic impact of the intervention in care homes with the equivalent parameters/measures observed during the PDAF study in GP surgeries.

5.3 Methods

5.3.1 Study design

This research utilised a multi-site, prospective, cross-sectional diagnostic accuracy study design adapted from the PDAF study in GP surgeries (Veale *et al.* 2018) (**Chapter 3**). A systematic population AF screening strategy (Welton *et al.* 2017) was used to screen a population of care home residents aged ≥ 18 years who were eligible for seasonal influenza vaccinations and were registered at one of the GP surgeries participating in the PDAF study. Systematic opportunistic screening was also offered to prospective participants receiving their seasonal influenza vaccinations at the care home on the day of screening (Welton *et al.* 2017). Participants with provisional AF or inconclusive diagnoses were followed-up to determine any diagnoses and further actions by the GP. The screening was conducted over a single influenza vaccination season (2018-2019).

The index tests selected for the study were as described for the PDAF study in GP surgeries (section **3.3.1**) and as appraised in section **2.6.1**, including pulse palpation, $_{SL}$ECG interpretation by the automated algorithm of the KMD and $_{SL}$ECG interpretation by the CP. The accuracy of index tests was compared against the reference standard of $_{SL}$ECG interpretation by the cardiologist.

5.3.2 Study setting and sites

The study was conducted in a care home setting. The selection of care homes was based on their affiliation to the four GP surgeries participating in the PDAF study and their proximity relative to the MSOP. A total of four care homes hosting 112 residents agreed to take part

in this initiative: three residential homes and one mixed residential and nursing home. Three care homes were located in the Faversham area and one in the Canterbury area of Kent.

5.3.3 Selection and training of the CP

Considering the relatively small size of the population eligible for screening, only one CP was selected to conduct AF screening in participating care homes using a convenience sampling method (Martínez-Mesa *et al.* 2016). This CP (VS) was an AFC Band 7 pharmacist with seven years post-registration experience. They were also a PhD researcher at the MSOP and previously delivered AF screening as one of the CPs during the PDAF study in GP surgeries. The CP underwent all fundamental training to conduct AF screening using the index tests and the PDAF protocol as described in section **3.3.3**. In order to facilitate an effective eligibility assessment and AF screening in a care home environment, they also completed the following specific training:

- *'Care homes: supporting people, optimising medicines (2018)'* by the Centre for Pharmacy Postgraduate Education
- *'Mental Capacity Act (2018)'* by the Medway NHS Foundation Trust and
- *'Safeguarding Adults at Risk Combined Level 1 & 2 (2018)'* by Care Shield®.

During the visits to each care home, the CP was accompanied by the GP from one of the surgeries participating in the PDAF study who was also a clinical researcher at the University of Kent. The GP administered seasonal influenza vaccines, helped recruit prospective participants and assessed each individual's mental capacity to provide informed consent.

5.3.4 Outcome measures

Primary outcome

The proportion of all care home residents (%) who are recruited and undergo AF screening using pulse palpation and/or $_{SL}$ECG device (KMD).

Secondary outcomes

1. The total prevalence (%) of AF in the study sample, including the prevalence of 'known' and 'unknown' AF as determined by the reference standard (cardiologist's interpretation of $_{SL}$ECG).

2. The proportion (%) of individuals with 'known' and 'unknown' AF who may qualify for OAC therapy (defined as males with a CHA_2DS_2-VASc score of ≥ 1 or females with a score of ≥ 2 (NICE 2014a)).
3. The prevalence (%) of 'Unclassified' and 'Unreadable' diagnoses ascertained through pulse palpation or $_{SL}$ECG interpretation by CPs or the KMD algorithm compared to the reference standard.
4. The prevalence of non-AF comorbidities amongst participants with reference standard-determined 'Possible AF'.
5. The quality of $_{SL}$ECG recordings produced by the CP using the KMD, defined as proportions (%) of $_{SL}$ECG recordings classified by the CP as 'Excellent', 'Acceptable', 'Poor' or 'Unreadable'.
6. The diagnostic accuracy of CP-led AF screening using pulse palpation compared to the reference standard. The diagnostic accuracy measures used for this and other secondary outcome measures included: sensitivity, specificity, accuracy, PPV, FDR and FPR. The complete definitions of each measure are provided in section **2.7.2**.
7. The diagnostic accuracy of CP-led AF screening using the KMD compared to the reference standard. The diagnostic accuracy of $_{SL}$ECG interpretation by the CP and the automated KMD algorithm were both estimated as part of this outcome measure.
8. The comparative diagnostic accuracy of:
    a. Pulse palpation by the CP and either the $_{SL}$ECG interpretation by the CP or the KMD algorithm
    b. $_{SL}$ECG interpretation by the CP and the KMD algorithm.
9. The inter-rater agreement (Cohen's kappa) between the:
    a. Pulse palpation by the CP and the reference standard
    b. $_{SL}$ECG interpretation by the CP or the KMD algorithm and the reference standard
    c. Pulse palpation by the CP and either the $_{SL}$ECG interpretation by the CP or the KMD algorithm.
    d. $_{SL}$ECG interpretation by the CP and the KMD algorithm
10. The proportion (%) of screened individuals who were referred to the GP and were followed-up, including the yield of 'new' AF and non-AF diagnoses after the confirmation by $_{12L}$ECG.
11. The cost-effectiveness of the AF screening strategy proposed using the KMD algorithm compared to the no-screening scenario. The cost-effectiveness of the intervention compared to no-screening was defined as an ICER < WTP of £20,000/QALY gained and a positive INB (NICE 2012a; Welton *et al.* 2017).

12. Statistically significant differences between the participant demographics of individuals recruited in care homes and GP surgeries during the main PDAF study.
13. Absolute differences in diagnostic accuracy of index tests and the economic impact of the intervention in care homes versus the equivalent measures/parameters in GP surgeries during the main PDAF study.

5.3.5 Sample size

The target sample size for this study was informed by the pilot AF screening study in a US nursing home, which recruited 101 participants out of the total of 261 residents (38.7%) over a period of two months (Wiesel & Salomone 2017). Therefore, the present study anticipated to screen a minimum of 43 out of the 112 individuals residing in participating care homes. This empirical sample size was in line with the NIHR guidance for feasibility studies which recommended a minimum sample size of 24-50 participants (NIHR Research Design Service London 2020).

5.3.6 Eligibility criteria

Inclusion criteria

- Age ≥ 18 years
- Eligible for seasonal influenza vaccination
- Resident at one of the participating care homes
- Registered at one of GP practices participating in the PDAF study.

Exclusion criteria

- Age < 18 years
- Patients fitted with a pacemaker or defibrillator
- A lack of mental capacity to provide a written informed consent with reference to the criteria outlined in the Mental Capacity Act 2005 (The National Archives 2005)
- Severe co-existing medical condition which a researcher considers to be the reason to exclude the patient from the study (e.g. terminal illness with life expectancy under 1 month).

5.3.7 Recruitment and informed consent

Study participants were recruited using a convenience sampling approach, which included consecutively enrolling all eligible individuals (Martínez-Mesa *et al.* 2016). Prospective participants were recruited during a single influenza vaccination season, between October 2018 and January 2019. Interested eligible individuals were identified and approached by

care home staff, the CP or the GP delivering seasonal influenza vaccinations, using the list of care home residents registered at surgeries participating in the PDAF study (**Figure 5.1**). Alternatively, care home residents were able to self-refer by responding to study advertisement, which included the PILs (**Appendix 43**) distributed by staff at each participating care home. Prospective participants were approached or were able to self-refer for AF screening either before or after their influenza vaccination. Those residents who chose not to have an influenza vaccination were still offered to take part in AF screening.

Prior to their enrolment onto the study, the GP assessed each individual's mental capacity to provide informed consent in line with the principles outlined in the Mental Capacity Act 2005 (The National Archives 2005). Prospective participants who were considered to possess sufficient mental capacity on the day of AF screening were then assessed against the rest of the eligibility criteria by either the GP or CP. The GP or CP provided eligible participants with a PIL (**Appendix 43**) which contained the relevant study information detailed in section **3.3.7**. They also offered a brief verbal explanation about the study, the screening process and the data management with reference to the PIL. Each prospective participant was given as much time as they needed to decide whether or not to take part, and were offered an opportunity to ask the GP or CP any questions they may have. Those interested could choose to undergo opportunistic AF screening the same day as their influenza vaccination or at a more convenient time. A written informed consent to take part was obtained from all participants immediately before the screening procedure by the CP, with one copy of the consent form (**Appendix 18**) retained by the research team and one copy given to the participant. In line with the HRA (2020b), a process was developed for the GP to seek advice from a personal or nominated consultee (e.g. a relative or a carer) in a form of a signed declaration (**Appendix 44**) where a prospective participant displayed a fluctuating level of mental capacity but was deemed to benefit from AF screening (*N.b.* none of the participants were entered into the study following the advice of a consultee).

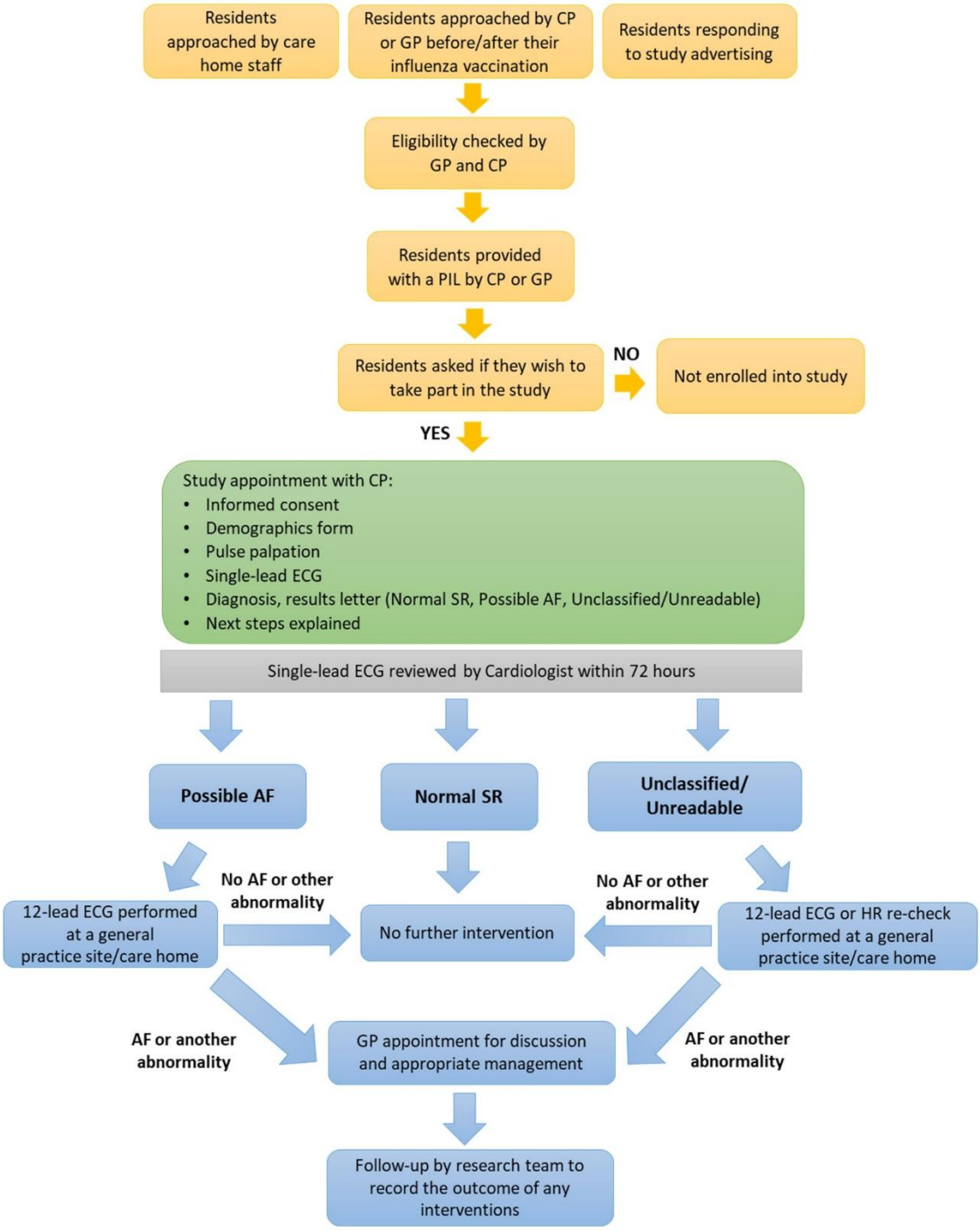


Figure 5.1 The flowchart of the Pharmacists Detecting Atrial Fibrillation (PDAF) study in care homes

The figure includes details of recruitment, informed consent, screening procedure and the post-appointment processes. Abbreviations: AF – atrial fibrillation; CP – clinical pharmacist; ECG – electrocardiogram; GP – general practitioner; HR – heart rate; PIL – participant information leaflet; SR – sinus rhythm.

5.3.8 Screening protocol and follow-up

The AF screening process and follow-up were conducted as shown in **Figure 5.1** and as described for the PDAF study in GP surgeries (section **3.3.8**). Briefly, after obtaining consent, the CP completed a short demographic questionnaire (**Appendix 19**) with participant's assistance and then carried out a manual radial/ulnar pulse palpation over 60 seconds followed by a 30-second $_{SL}$ECG recording using the KMD. They noted down the quality of each $_{SL}$ECG recording ('Excellent', 'Acceptable', 'Poor' or 'Unreadable') as well as the provisional diagnoses of pulse palpation, the KMD algorithm and their own interpretation of $_{SL}$ECG (**Appendix 20**), providing the participant with an appropriate letter of results (**Appendices 21, 22 and 23**) and information about the follow-up steps. All $_{SL}$ECG recordings were overread by the cardiologist within 72 hours and participants with confirmed 'Possible AF' or 'Unclassified/'Unreadable' diagnoses were referred to their GP for further action, such as a $_{12L}$ECG. The research team followed up all patients referred to the GP, and obtained the details of their enhanced demographic data and any follow-up outcomes accordingly (**Appendix 25**). Contrary to the PDAF study in GP surgeries, participants were not asked to complete the post-screening feedback questionnaires nor were they invited to take part in the focus group interviews. This decision was guided by logistical difficulties of travel arrangements and the high prevalence of physical/mental impairments in the target population.

5.3.9 Quantitative data analysis

The quantitative data analysis followed the fundamental statistical considerations and assumptions outlined in section **2.7**. The data were analysed and presented as for the PDAF study in GP surgeries (section **3.4**).

5.3.10 Economic analysis

The economic model was developed as a Markov cohort simulation which compared the costs and utilities of two hypothetical cohorts of patients with AF aged ≥ 65 years, derived from the total population of care home residents across England and Wales (a population of 291,000) (Office for National Statistics 2014): the 'intervention cohort' or the 'screening strategy' (who underwent the screening) and the 'control cohort' or the 'no-screening strategy (who did not undergo the screening). The detailed rationale for this method and the breakdown of key model assumptions is provided in section **2.8.**

The baseline transition probabilities between the health states were obtained from major OAC trials and were age-adjusted for probabilities of ischaemic stroke and major bleed amongst care home residents according to the hazard ratios reported by the Swedish

investigation into CHA_2DS_2-VASc and HAS-BLED scores (Friberg *et al.* 2012). The baseline mortality rate was also age-adjusted for mortality observed in care home residents (Office for National Statistics 2014) as well as the increased mortality following an ischaemic stroke or a major bleed (Jacobs *et al.* 2018; Eikelboom *et al.* 2006) (**Appendix 45**). In addition to general model assumptions (section **2.8.3**), the base-case economic analysis assumed the following:

- The prevalence of total and 'unknown' AF of 13.5% and 9.6%, respectively as determined by the reference standard.
- The rate of 'Unclassified'/'Unreadable' diagnoses of 32.7% as determined by $_{SL}$ECG interpretation using the KMD algorithm.
- The sensitivity and specificity of the KMD algorithm with regards to the reference standard of 57.1% and 100%, respectively.
- That all participants with 'new' AF were eligible for OAC (a CHA_2DS_2-VASc score of ≥ 2 for females, or ≥ 1 for males).

The general costs of the base-case model were as outlined in section **2.8.4** and **Appendix 45**, and included the purchasing cost of KMDs, the CP time (9 minutes/appointment) (NHS Employers 2019), relevant medical interventions ($_{12L}$ECG/GP interpretation and GP/cardiologist appointments for 'new' AF) (NHS Improvement 2017; Welton *et al.* 2017), the cost of OAC therapy, ischaemic strokes/major bleeds (NICE 2014b) and false positive AF and 'Unclassified'/'Unreadable' diagnoses by the KMD algorithm. The purchasing cost of the KMD included 166 devices with reference to the AHSN initiative in England, adjusted for the population size of care home residents (The AHSN Network 2019a; AliveCor 2019c).

The PSA employed a Monte Carlo simulation generating 100,000 iterations of the model and tested the deviations from the base case outlined for the PDAF study in GP surgeries (sections **2.8.5** and **3.3.11**). However, instead of testing the cost-effectiveness of pulse palpation as a deviation from the base case scenario, this study compared the cost-effectiveness of AF screening using the KMD algorithm in care homes versus the GP surgeries, under the assumptions for AF screening in this setting provided in section **3.3.11.** The mean INBs were calculated per care home resident with AF and per all care home residents with 'new' AF detected using the KMD algorithm across England and Wales (Office for National Statistics 2014).

5.4 Results

5.4.1 Study participants

A total of 53/112 (47.3%) of care home residents were enrolled onto the study and underwent AF screening with the CP between October 2018 and January 2019 (**Figure 5.2**). All eligible residents agreed to take part in the study. The remaining 59/112 (52.7%) of residents could not be screened either due to severe underlying physical comorbidities or the lack of mental capacity as assessed by the GP. All participating residents (100%) were registered at two of the GP surgeries involved in the PDAF study, and 32/53 (60.4%) of them were recruited in two of the four care homes. As shown in **Table 5.1**, the median age of care home participants was 91 [86; 94] years, and they were on average 18 years older than participants of the main PDAF cohort recruited in GP surgeries (73 [69; 78] years; Mann-Whitney U test, $p < 0.001$). Compared to individuals in general practice, a significantly greater proportion of care home residents were female (75.5%, 40/53 vs. 57.3%, 346/604; Chi-square test, $p = 0.01$). Similar to the main cohort, nearly all participants were of White British ethnicity (98.1%, 52/53). Less than a half of care home residents stated that they drank alcohol (47.6%, 10/21), and those that did consumed on average five fewer units of alcohol per week than participants in GP surgeries (1.0 [1.0; 6.5] units vs. 6 [2.0; 14.0] units; Mann-Whitney U test, $p = 0.011$). In contrast to the general practice sample, none of the care home residents were smokers (0%, 0/50 vs. 8.9%, 54/604; Fisher's exact test, $p = 0.027$). Both cohorts of participants had a comparable BMI.

The $_{SL}$ECG recordings using the KMD were performed in 52/53 (98.1%) of care home participants. In one instance $_{SL}$ECG could not be recorded due to severe hand and arm tremor experienced by a participant with Parkinson's disease who displayed a 'Normal SR' on pulse palpation. The follow-up of this participant was left at the discretion of their GP, and they were excluded from the analyses of screening outcomes and diagnostic accuracy presented below. Out of the participants who underwent AF screening using the KMD, over 80% only had one $_{SL}$ECG recording (80.8%, 42/52), with ≥ 2 recordings performed in the remaining 10/52 (19.2%) of participants who displayed an 'Unreadable' or poor-quality recording (vs. 15.2%, 92/604 in GP surgeries; Chi-square test, $p > 0.05$). The median appointment length was 9 [8; 12] minutes, on average two minutes shorter than PDAF appointments in GP surgeries (11 [10; 15] minutes; Mann-Whitney U test, $p < 0.001$; *N.b.* appointment times in care homes did not account for the initial eligibility assessment by the GP).

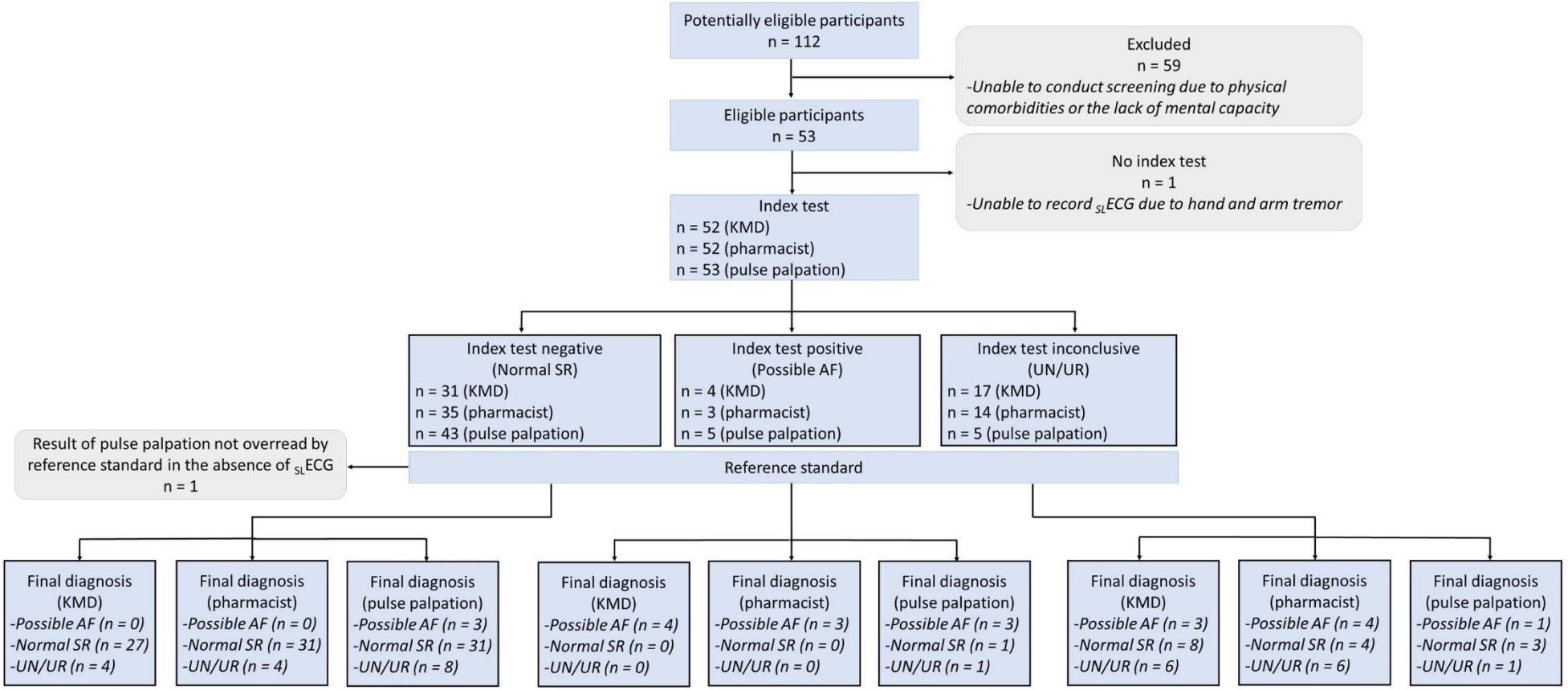


Figure 5.2 STARD flow diagram for the PDAF study in care homes

The figure was adapted from Cohen et al. (2016), and displays the inclusion/exclusion of study participants and the diagnostic classification by each index test (KMD interpretation of SLECG, pharmacist's interpretation of SLECG or pulse palpation) and the reference standard. Abbreviations: AF – atrial fibrillation; KMD – Kardia Mobile® device; PDAF – Pharmacists Detecting Atrial Fibrillation; SLECG – single-lead electrocardiogram; SR – sinus rhythm; STARD - Standards for Reporting Diagnostic Accuracy Studies; UN – Unclassified; UR – Unreadable.

Table 5.1 Demographic characteristics of participants screened in care homes compared to the main cohort in GP surgeries

*Results from Chapter 3 included for direct comparison. Continuous variables are expressed as a median [interquartile range]. Categorical variables are expressed as a number of participants (% total of the group). *One participant was of Sri Lankan ethnicity. Between-group differences were determined using a Mann-Whitney U test for numerical variables and a Pearson's Chi-square or Fisher's exact test with Freeman-Halton extension and Bonferroni correction as appropriate for categorical variables. Abbreviations: BMI – body mass index; bpm – beats per minute; GP – general practitioner.*

Characteristics	Care Homes (n = 53)	GP Surgeries (n = 604)	P value (2-sided)
Age, years	91 [86; 94]	73 [69; 78]	< 0.001
Male	13 (24.5)	258 (42.7)	0.010
Ethnicity			
White British	52 (98.1)	585 (96.9)	1.000
White Irish	0 (0.0)	3 (0.5)	1.000
Other	1 (1.9)*	16 (2.6)	1.000
Current alcohol drinker	10 (47.6) (n = 21)	380 (62.9)	0.173
Alcohol, units/week	1.0 [1.0; 6.5] (n = 9)	6 [2.0; 14.0] (n = 372)	0.011
Current smoker	0 (0.0) (n = 50)	54 (8.9)	0.027
BMI, kg/m^2	25.1 [20.9; 29.2] (n = 38)	26.1 [23.5; 29.3] (n = 585)	0.099
Heart rate device, bpm	76 [68; 82] (n = 52)	72 [65; 81]	0.157

5.4.2 Screening outcomes

Participants with 'Possible AF'

The study cardiologist was able to decipher $_{SL}$ECG recordings of all 52 participants (100%) who underwent AF screening using both index tests (**Figure 5.3**). Seven participants (13.5%, 7/52) were classified as 'Possible AF' at the time of screening resulting in a total AF prevalence of 13.5% (95% CI, 5.6-25.8). Out of these, 6/52 (11.5%) of participants with 'Possible AF' reported no previous history of AF and were referred for a confirmatory $_{12L}$ECG. The seventh participant (1.9%, 1/52) was unsure as to whether they had a diagnosis of AF and therefore required confirmation by review of their medical records. These confirmed that the participant was known to have AF, but was receiving aspirin instead of the OAC because they previously declined anticoagulation therapy. An additional participant who was referred for a $_{12L}$ECG was also discovered to have a history of AF and took a DOAC. This resulted in a 3.8% prevalence of 'known' AF (2/52). The remaining 5/52

participants had no recorded history of AF in their medical notes and formed the 9.6% prevalence of 'unknown' or previously undiagnosed AF.

Compared to participants with 'Possible AF' diagnoses recruited in GP surgeries, more care home residents with cardiologist-confirmed AF were female (57.1%, 4/7 vs. 42.3%, 11/26). They were also significantly older (90 [87; 94] vs. 82 [73; 85] years; Mann-Whitney U test, p = 0.001) and had a significantly lower BMI (23.8 [19.9; 26.9] kg/m^2 vs. 28.5 [24.2; 33.5] kg/m^2; Mann-Whitney U test, p = 0.048; **Table 5.2**). Five out of seven care home residents (71.4%) suffered from hypertension, 3/7 (42.9%) – from renal disease and 2/7 (28.6%) – from diabetes mellitus. Whilst the prevalence of most non-AF comorbidities was similar in both samples, care home participants with AF were more likely to suffer from peripheral vascular disease (28.6%, 2/7 vs. 0%, 0/26; Fisher's exact test, p = 0.04). The median number of non-AF comorbidities was comparable in both cohorts (2.0 [1.0; 2.0] vs. 2.0 [1.0; 3.0] for participants with AF in care homes and GP surgeries, respectively). All care home residents with cardiologist-determined AF (100%, 7/7) had a CHA_2DS_2VASc score of ≥ 3, qualifying them for OAC therapy, although their median score was not dissimilar from that of participants with AF encountered in GP surgeries (3.0 [3.0; 6.0] vs. 3.0 [3.0; 4.3], respectively). Their risk of bleeding, indicated by the HAS-BLED score, was however half of that observed amongst the general practice sample (1.0 [1.0; 2.0] vs. 2.0 [2.0; 3.0]; Mann-Whitney U test, p = 0.012).

Participants with non-AF diagnoses

A total of 35/52 (67.3%) of participants were deemed by the cardiologist to display a 'Normal SR' at the time of their $_{SL}$ECG recording and did not require any further follow-up action. Besides those with 'Possible AF' diagnoses, a further 10/52 (19.2%) of care home participants were assigned an 'Unclassified' diagnosis by the cardiologist and were referred for a $_{12L}$ECG procedure. The reasons for 'Unclassified' diagnoses included inconsistent or unidentifiable p waves (9.6%, 5/52), the presence of left or right BBB (7.7%, 4/52) and a possible atrial flutter (1.9%, 1/52).

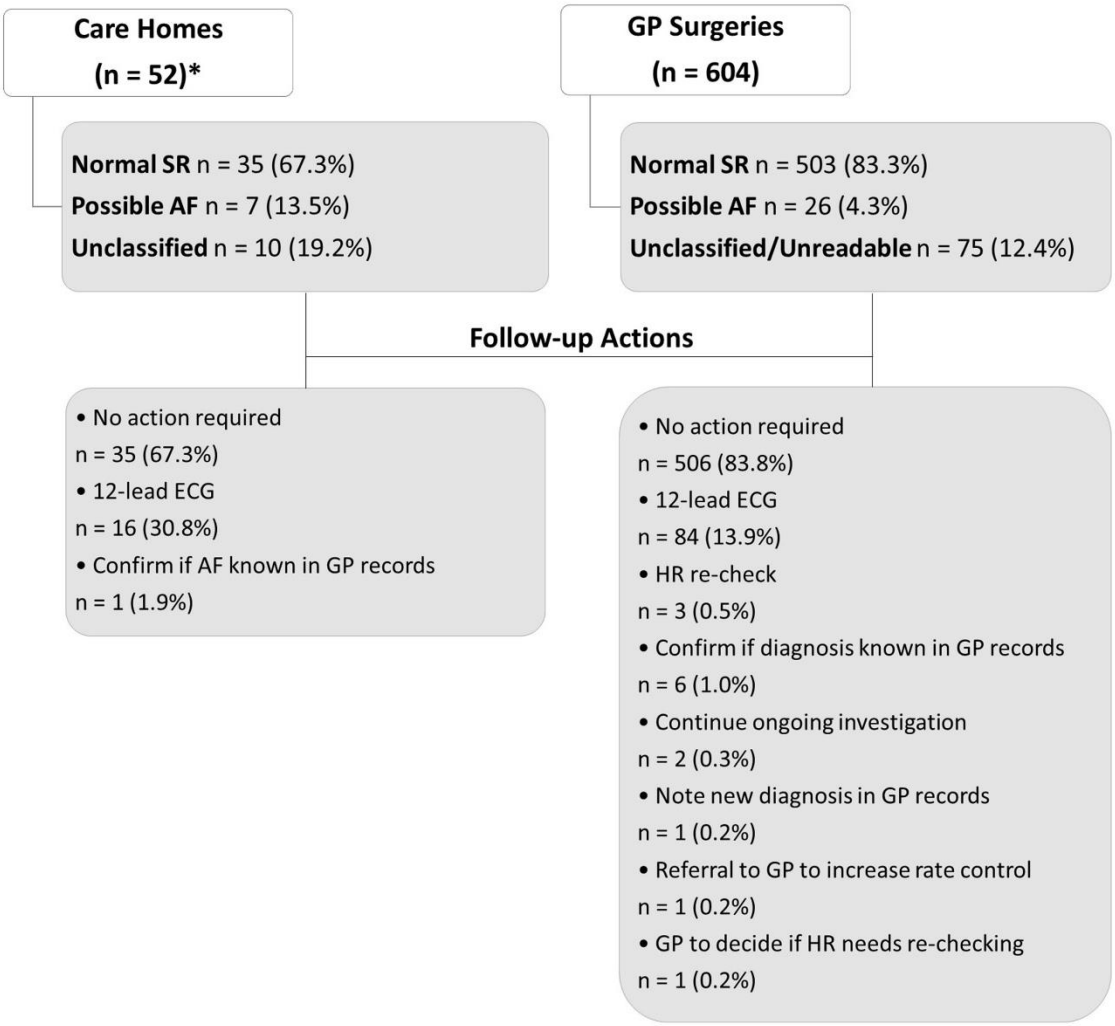


Figure 5.3 Cardiologist's diagnoses and recommended follow-up actions based on the interpretation of $_{SL}$ECG recordings of participants in care homes compared to those in GP surgeries

*Results from Chapter 3 included for direct comparison. All variables are expressed as a number of participants (% total). *One care home participant did not have a $_{SL}$ECG recording and their follow-up was left at the discretion of the GP. Abbreviations: AF – atrial fibrillation; ECG – electrocardiogram; GP – general practitioner; HR – heart rate; $_{SL}$ECG – single-lead ECG; SR – sinus rhythm.*

Table 5.2 Demographic comparison of cardiologist-confirmed 'Possible AF' cases in care homes and GP surgeries

*Results from Chapter 3 included for direct comparison. Continuous variables are expressed as a median [interquartile range]. Categorical variables are expressed as a number of participants (% total of the group). Between-group differences were determined using a Mann-Whitney U test for numerical variables and a Fisher's exact test for categorical variables. *too few respondents for an adequate statistical comparison. Abbreviations: AF – atrial fibrillation; BMI – body mass index; COPD – chronic obstructive pulmonary disease; GP – general practitioner.*

Characteristics	Participants with Possible AF in care homes (n = 7)	Participants with Possible AF in GP surgeries (n = 26)	P value (2-sided)
Age, years	90 [87; 94]	82 [73; 85]	0.001
Male	3 (42.9)	15 (57.7)	0.674
Current alcohol drinker	0 (0.0) (n = 1)	16 (61.5)	0.407
Alcohol, units/week	0 (0.0) (n = 1)*	10.0 [2; 14] (n = 16)	N/A
Current smoker	0 (0.0)	3 (11.5)	1.000
Height, cm	177.8 [161.1; 180.0]	167.5 [162.5; 177.5]	0.417
Weight, kg	69.0 [61.4; 80.0]	78.3 [69.7; 97.0]	0.143
BMI, kg/m^2	23.8 [19.9; 26.9]	28.5 [24.2; 33.5]	0.048
CHA_2DS_2VASc score	3.0 [3.0; 6.0]	3.0 [3.0; 4.3]	0.620
HAS-BLED score	1.0 [1.0; 2.0]	2.0 [2.0; 3.0]	0.012
Hypertension	5 (71.4)	18 (69.2)	1.000
Renal disease	3 (42.9)	11 (42.3)	1.000
Diabetes mellitus	2 (28.6)	8 (30.8)	1.000
Thyroid disease	1 (14.3)	4 (15.4)	1.000
Transient ischaemic attack	1 (14.3)	3 (11.5)	1.000
Ischaemic heart disease	0 (0.0)	3 (11.5)	1.000
Heart failure	0 (0.0)	2 (7.7)	1.000
Intracranial bleed	0 (0.0)	1 (3.8)	1.000
Peripheral vascular disease	2 (28.6)	0 (0.0)	0.040
COPD	0 (0.0)	2 (8.0)	1.000

5.4.3 Diagnostic accuracy

SLECG interpretation by the KMD algorithm

The KMD algorithm assigned 31/52 (59.6%) of care home residents a diagnosis of 'Normal SR', 4/52 (7.7%) – a diagnosis of 'Possible AF' and 17/52 (32.7%) – a diagnosis of 'Unclassified' nature (**Figure 5.4**). Compared to the reference standard, the KMD algorithm correctly classified four out of seven cases of 'Possible AF' without producing any false positive diagnoses. It however failed to identify three participants with cardiologist-

confirmed AF who were falsely assigned an 'Unclassified' status. This resulted in a perfect specificity and PPV (100% each) at the expense of a low sensitivity (57.1%), which was far below the mean value of 92.3% displayed in GP surgeries (**Table 5.3**). Despite the poor sensitivity, the overall diagnostic accuracy (94.2%) and the inter-rater agreement of the KMD algorithm with the cardiologist (0.70) were reasonably high, and comparable to those observed in general practice (97.2% and 0.72, respectively).

Whilst the KMD algorithm did not produce any false positive AF diagnoses, it issued eight false positive 'Unclassified' diagnoses, which would have led to unnecessary referrals in those participants that were thought by the cardiologist to display a 'Normal SR' (15.4%, 8/52). Where indicated by the cardiologist, this occurred due to the presence of AEBs or VEBs (5.8%, 3/52).

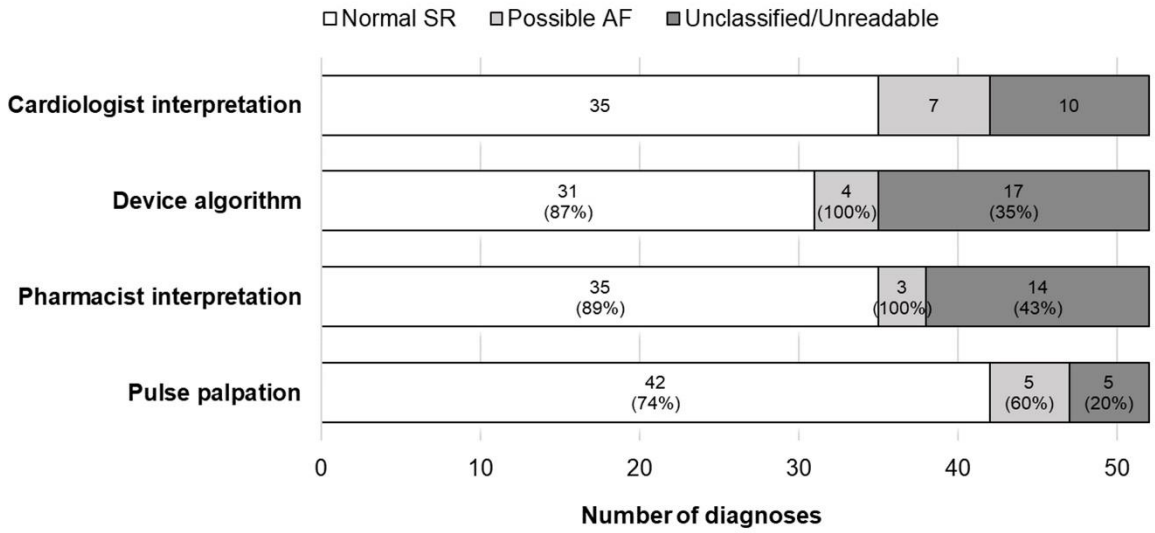


Figure 5.4 Diagnostic breakdown by index tests compared to the reference standard when conducting AF screening in care homes

Pulse palpation, KMD algorithm and clinical pharmacist's interpretation of $_{SL}$ECG (index tests) are compared to the cardiologist's interpretation of the $_{SL}$ECG (reference standard). All data are expressed as the number of cases in each diagnostic category (% mean PPV). Abbreviations: AF – atrial fibrillation; KMD – Kardia Mobile® device; PPV – positive predictive value; $_{SL}$ECG – single-lead electrocardiogram.

Table 5.3 Diagnostic accuracy of index tests for the detection of AF in care homes and GP surgeries

Results from Chapter 3 included for direct comparison. The accuracy of $_{SL}$ECG interpretation by the KMD algorithm or clinical pharmacist, and pulse palpation (index tests) when compared to the cardiologist's interpretation of $_{SL}$ECG (reference standard). All measures are expressed as a mean (95% confidence intervals). Abbreviations: FDR – false discovery rate; FPR – false positive rate; GP – general practitioner; KMD - Kardia Mobile® device; PPV – positive predictive value.

Diagnostic Accuracy Measures	**Index Tests**		
	KMD algorithm	*Pharmacist interpretation*	*Pulse palpation*
Care Homes			
Sensitivity	57.1 (18.4-90.1)	42.9 (9.9-81.6)	42.9 (9.9-81.6)
Specificity	100	100	95.6 (84.9-99.5)
Accuracy	94.2 (84.1-98.8)	92.3 (81.5-97.9)	88.5 (76.6-95.7)
FPR	0	0	4.4 (0.5-15.1)
PPV	100	100	60.0 (14.7-94.7)
FDR	0	0	40.0 (5.3-85.3)
Cohen's Kappa	0.70 (0.38-1.01)	0.57 (0.20-0.93)	0.44 (0.06-0.81)
GP Surgeries			
Sensitivity	92.3 (74.9 -99.1)	88.5 (69.9-97.6)	76.9 (56.4-91.0)
Specificity	97.4 (95.8-98.5)	97.2 (95.5-98.4)	92.2 (89.7-94.3)
Accuracy	97.2 (95.5-98.4)	96.9 (95.1-98.1)	91.6 (89.1-93.7)
FPR	2.6 (1.5-4.2)	2.8 (1.6-4.5)	7.8 (5.7-10.3)
PPV	61.5 (44.6-76.6)	59.0 (42.1-74.4)	30.8 (19.9-43.5)
FDR	38.5 (23.4-55.4)	41.0 (25.6-57.9)	69.2 (56.6-80.1)
Cohen's Kappa	0.72 (0.60-0.85)	0.69 (0.56-0.82)	0.40 (0.27-0.53)

$_{SL}$ECG interpretation by the CP

In addition to noting down the diagnoses by the KMD algorithm, the CP performing AF screening in care homes was asked to provide their own interpretation of $_{SL}$ECG recordings. The interpreting CP identified 35/52 (67.3%) of care home participants as displaying a 'Normal SR', 3/52 (5.8%) – as a 'Possible AF' and 14/52 (26.9%) – as 'Unclassified'. With reference to the cardiologist's interpretation of $_{SL}$ECG, the CP assigned the correct diagnosis to three out of seven participants with 'Possible AF'. Although their interpretation did not produce any false positive AF diagnoses, the CP missed one additional case of cardiologist-confirmed AF compared to the KMD algorithm, by assigning them a false 'Unclassified' status. This resulted in a total of four false negative diagnoses and hence an even lower mean sensitivity for AF of 42.9% (vs. 88.5% in GP surgeries). As with the KMD algorithm, the specificity and the PPV of the CP's interpretation were both at 100%, leading to an overall good diagnostic accuracy of 92.3%, which was not far from the 96.9%

encountered in GP surgeries. At 0.57, the Cohen's Kappa between the $_{SL}$ECG interpretation by the CP and the cardiologist was however moderate and below the substantial agreement of 0.69 observed when screening in general practice.

There were no statistically significant differences between the diagnostic accuracy of the KMD algorithm and the $_{SL}$ECG interpretation by the CP (McNemar's test; $p > 0.05$), generating an excellent inter-rater agreement of 0.85 (95% CI, 0.55-1.14). On the other hand, compared to the KMD algorithm, CP's interpretation of $_{SL}$ECG resulted in four fewer false positive 'Unclassified' diagnoses and thus four less unnecessary referrals in participants with cardiologist-determined 'Normal SR' (7.7%, 4/52). All four false positive 'Unclassified' diagnoses matched the ones misclassified by the KMD algorithm, and as before, three of them occurred due to the presence of AEBs/VEBs (5.8%, 3/52).

According to the CP, close to three quarters of participants (73.1%, 38/52) had $_{SL}$ECGs corresponding to either 'Excellent' (21.2%, 11/52) or 'Acceptable' (51.9%, 27/52) quality. Both proportions were significantly below the $_{SL}$ECG quality observed when conducting AF screening in GP surgeries, where 60.1% (363/604) and 32.9% (199/604) of participants had 'Excellent' and 'Acceptable' quality recordings, respectively (Fisher's exact test, $p < 0.001$ and $p = 0.046$, respectively). Similarly, despite the absence of 'Unreadable' $_{SL}$ECGs, AF screening in care homes was associated with a significantly greater proportion of 'Poor' quality recordings than the screening in GP surgeries (26.9%, 14/52 vs. 5.3%, 32/604; Fisher's exact test, $p < 0.001$).

Pulse palpation by the CP

Pulse palpation by the CP designated 42/52 (80.8%) of participants as 'Normal SR' and 5/52 (9.6%) each as either 'Possible AF' or 'Unclassified'. The HR derived through pulse palpation was statistically lower than that obtained using the KMD algorithm, although with a limited clinical difference between the means (70 [64; 76] vs. 76 [68; 82] bpm, respectively; Wilcoxon signed-rank test, $p < 0.001$). Compared to the reference standard, pulse palpation identified the same three out of seven true positive cases of 'Possible AF' as the CP's interpretation of $_{SL}$ECG, producing a sensitivity of 42.9% – still notably below the sensitivity for AF in GP surgeries (76.9%). The four false negative cases due to pulse palpation matched the ones by the CP's interpretation of $_{SL}$ECGs, although contrary to the latter, three out of four patients were given a false 'Normal SR' diagnosis and only one was deemed to be 'Unclassified'. In contrast to either the $_{SL}$ECG interpretation by the KMD or the CP, pulse palpation also gave rise to two false positive AF diagnoses, one of which was confirmed as 'Normal SR' and one as 'Unclassified' by the cardiologist. This led to a lower specificity of

95.6%, an FPR of 4.4% and an FDR or 40.0%, with the FPR and FDR values markedly below the ones computed for AF screening using pulse palpation in GP surgeries (7.8% and 69.2%, respectively). The overall accuracy of pulse palpation was to an extent lower than that of either of the other two index tests (88.5%) and was slightly below the accuracy of pulse palpation itself during the screening in general practice (91.6%). As noted in GP surgeries, the Cohen's Kappa between the pulse palpation and the reference standard was once again rather poor, or moderate at best (0.44).

The relatively small absolute differences between the diagnostic accuracy of pulse palpation and $_{SL}$ECG interpretation by either the KMD algorithm or the CP were not statistically significant (McNemar's test, $p > 0.05$). This effect was reflected in substantial inter-rater agreements: 0.64 (95% CI, 0.26-1.02) between pulse palpation and the KMD algorithm, and 0.73 (95% CI, 0.38-1.08) between pulse palpation and the CP's interpretation of $_{SL}$ECG. There were also no statistically significant differences in the diagnostic classification between the cardiologist and any of the three index tests. Despite the general indifference of diagnostic accuracy, pulse palpation produced fewer false positive 'Unclassified' diagnoses in participants with cardiologist-determined 'Normal SR' than observed with the KMD algorithm or the CP's interpretation of $_{SL}$ECG (5.8%, 3/52 vs. 15.4%, 8/52 and 7.7%, 4/52, respectively). Only one false positive 'Unclassified' diagnosis by pulse palpation matched those by either of the other two index tests and occurred due to the presence of VEBs (1.9%, 1/52). Considering the additional false positive AF diagnosis by pulse palpation in a resident with a 'Normal SR', this number of 'Unclassified' false positives led to the same number of unnecessary referrals as would have occurred after the CP's interpretation of $_{SL}$ECG (7.7%, 4/52) and four fewer referrals than with the KMD algorithm (15.4%, 8/52).

5.4.4 Follow-up outcomes

After the AF screening and the cardiologist's interpretation of $_{SL}$ECG, a total of 16/52 (30.8%) of care home residents with 'Possible AF' or 'Unclassified' diagnoses were referred for a $_{12L}$ECG investigation. The $_{12L}$ECG was performed in 10/16 (62.5%) of care home participants with a median time to the procedure of 24.5 [15.5; 50.8] days, which was significantly longer than the 16.0 [11.0; 24.0] days experienced by participants of the PDAF study screening in GP surgeries (Mann-Whitney U test, $p = 0.045$). Two participants did not require a $_{12L}$ECG because they either had a 'known' BBB or a 'known' AF and were anticoagulated accordingly (6.3%, 1/16 each). One resident died (6.3%, 1/16) and a further 3/16 (18.8%) of participants did not respond to an invitation.

Out of the 10 participants who underwent a $_{12L}$ECG investigation, one was diagnosed with a 'new' AF and was prescribed a DOAC (1.9%, 1/52). This participant was thought by the cardiologist to display a 'Possible AF' at the time of screening yet was falsely assigned a 'Normal SR' diagnosis by pulse palpation and an 'Unclassified' status by the KMD algorithm or the CP's interpretation of $_{SL}$ECG. Five other participants were found to be in SR at the time of the procedure (9.6%, 5/52). The recordings of the other four residents displayed a BBB (5.8%, 3/52) or an AVB (1.9%, 1/52), which were all previously diagnosed. The participant who was issued a 'Normal SR' diagnosis after pulse palpation but could not have a $_{SL}$ECG recording due to severe hand/arm tremor, did not undergo a $_{12L}$ECG as advised by their GP.

5.4.5 Economic analysis

Compared to the no-screening scenario, the base case of the CP-led AF screening strategy using the KMD algorithm in care homes was cost-effective with an ICER of £6,223 (95% CI, -£14,992-£27,438)/QALY gained, which was more than two-fold (132.4% or £8,237) below the £14,460 (95% CI, £2,255-£26,665)/QALY gained estimated for the same screening strategy in GP surgeries (**Table 5.4**). At base case, the cost-effectiveness of the intervention in care homes was maintained below the WTP threshold of £20,000/QALY gained in 89.3% of 100,000 iterations compared to only 71.8% of cases for AF screening in GP surgeries (**Figure 5.5**). This level of cost-effectiveness translated into the mean 10-year INBs of £3,937 and £1,903/patient with AF when conducting AF screening in care homes and GP surgeries, respectively. The INB of AF screening in care homes reached £31,396,719 when extrapolated to the total number of care home residents with 'new' AF which may be detected as a result of the screening strategy proposed in England and Wales.

The PSA of the model demonstrated that the mean cost-effectiveness of the intervention in care homes was sustained at any level of adherence to OAC therapy, and improved by approximately 50.2% (£4,295) from an ICER of £8,552 (95% CI, -£5,307-£22,412)/QALY gained at 40% adherence to an ICER of £4,257 (95% CI, -£1,156-£9,669)/QALY gained at 80% adherence. The cost-effectiveness advantage of AF screening in care homes over GP surgeries was maintained throughout the OAC adherence range with on average 132.2% (£7,835) lower mean ICERs. In contrast, the cost-effectiveness of the model was only mildly affected by changes in the proportions of care home residents with AF receiving the VKA and DOAC therapies. When switching from the VKA:DOAC ratio of 44:56 to the 29:71 previously referred to by NICE (2014b), the ICERs were on average 6.5% (£383) lower across the OAC adherence range, with a mean ICER of £5,834 (95% CI, £934-£10,734)/QALY gained at the 55% adherence to OAC therapy.

Table 5.4 Findings of the cost-effectiveness analysis of AF screening strategy in a care home setting

Results from Chapter 3 included for direct comparison. Incremental cost-effectiveness ratios (ICERs) are expressed as a mean (95% confidence intervals). Abbreviations: AF – atrial fibrillation; DOAC – direct-acting oral anticoagulant; ECG – electrocardiogram; OAC – oral anticoagulant therapy; VKA – vitamin K antagonist.

Base Case Assumptions	**Level of Adherence to Oral Anticoagulant Therapy (%)**				
	40	**55 (base case)**	**60**	**70**	**80**
• 3-monthly AF screening cost/participant £207.98 • Total prevalence of AF 13.5% • Prevalence of 'unknown' AF 9.6% • Rate of 'Unclassified'/'Unreadable' diagnoses 32.7% • Participation in screening rate 50% • Test sensitivity 57.1% • Test specificity 100% • %Patients on DOAC 56% • %Patients on VKA 44%	£8,552 (-£5,307-£22,412)	£6,223 (-£14,992-£27,438)	£5,682 (-£9,368-£20,752)	£4,874 (£2,139-£7,609)	£4,257 (-£1,156-£9,669)
Deviations from Base Case					
• Assumptions for PDAF study in general practice	£19,957 (-£15,292-£55,207)	£14,460 (£2,255-£26,665)	£13,226 (-£1,288-£27,740)	£11,295 (£8,609-£13,981)	£9,824 (-£7,167-£26,815)
• %Patients on DOAC 29% • %Patients on VKA 71%	£8,009 (-£2,844-£18,863)	£5,834 (£934-£10,734)	£5,338 (-£14,909-£25,584)	£4,530 (-£3,371-£12,431)	£3,961 (£1,058-£6,865)
• Base-case assumptions • Screening participation rate 80%	£5,328 (-£2,016-£12,672)	£3,874 (£1,136-£6,612)	£3,539 (-£458-£7,535)	£3,021 (£897-£5,146)	£2,637 (-£798-£4,477)
• Base-case assumptions • Screening participation rate 30%	£14,375 (-£10,448-£39,198)	£10,358 (-£23,877-£44,592)	£9,583 (£1,891-£17,275)	£8,165 (£-38,584-£54,914)	£7,101 (-£5,970-£20,172)
• Rate of Unclassified/Unreadable diagnoses 16.4%	£7,691 (-£11,557-£26,939)	£5,588 (-£10,941-£22,118)	£5,125 (-£4,791-£15,042)	£4,382 (-£12,019-£20,783)	£3,821 (-£456-£8,098)

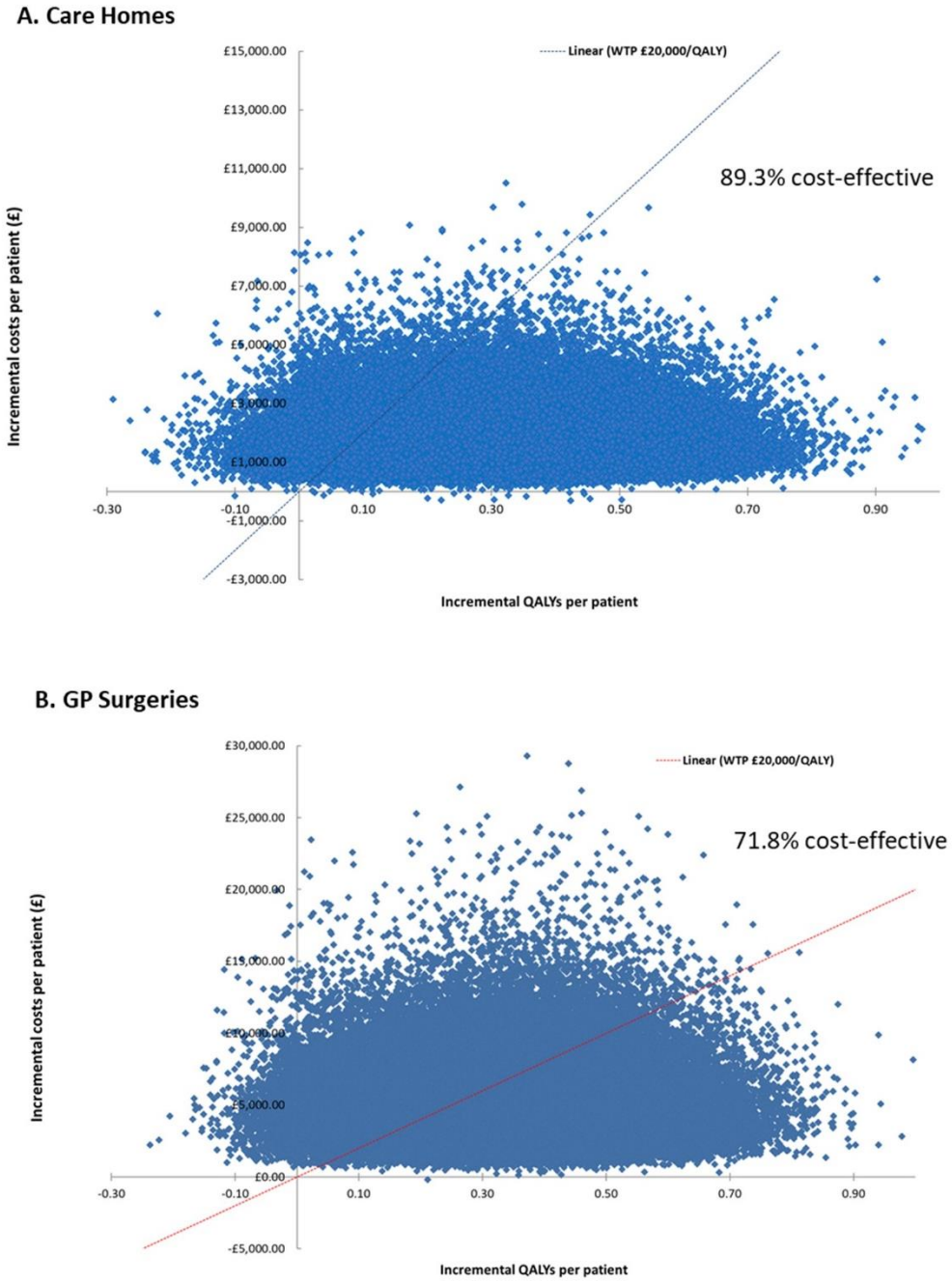


Figure 5.5 Incremental cost-effectiveness of AF screening in care homes or GP surgeries compared to no screening

Results from Chapter 3 included for direct comparison. Incremental cost-effectiveness planes show 100,000 pseudorandom Monte Carlo estimates of incremental costs and QALYs gained per patient with AF comparing: A. the base case of the AF screening strategy using the KMD algorithm with no screening in care homes; B. the base case of the screening strategy using the KMD algorithm in GP surgeries with no screening. Any points falling below the dotted line have an ICER < £20,000 per QALY gained. Abbreviations: AF – atrial fibrillation; GP – general practitioner; ICER – incremental cost-effectiveness ratio; KMD – Kardia Mobile® device; QALY – quality-adjusted life year; WTP – willingness to pay [threshold].

The model was highly sensitive to changes in the AF screening participation rate. Improving the uptake of screening from 50% to 80%, produced an average of 37.8% (£2,238) lower ICERs throughout the adherence to OAC range, with an ICER of £3,874 (95% CI, £1,136-£6,612)/QALY gained at the 55% OAC adherence. On the other side of the spectrum, decreasing the uptake of the intervention to 30%, led to an average of 67.5% (£3,999) higher ICERs, which at 55% OAC adherence rose to £10,358 (95% CI, -£23,877-£44,592)/QALY gained. Indicating the lack of certainty, the decrease in screening participation rate to 30% was also accompanied by 95% CIs which were wider than observed with any other deviations from the base case. The adjustment in the rate of 'Unclassified'/'Unreadable' diagnoses from 32.7% to 16.4% did not have such a notable influence on the cost-effectiveness of the intervention, although the ICERs were reduced by 10.1% (£596) across the adherence to OAC range, resulting in an ICER of £5,588 (-£10,941-£22,118)/QALY gained at the 55% adherence to OAC therapy.

5.5 Discussion

5.5.1 Comparison with existing literature

Recruitment and AF prevalence

This research adapted the PDAF study protocol tested in GP surgeries to investigate the feasibility of the CP-led AF screening programme in a UK care home setting during an influenza vaccination season. A total of 53 care home residents were screened by a single CP in four participating care homes over a period of three months, constituting approximately 47% of all available care home residents. The remaining 53% of residents were unable to participate either due to pronounced physical or mental impairments. One participant was deemed eligible by the GP to undergo AF screening, and was screened using pulse palpation but was unable to hold their hands steady enough for a $_{SL}$ECG recording to take place due to severe tremor. As such only 52 residents (46%) could be screening using both pulse palpation and the KMD. The low rate of recruitment due to underlying comorbidities in this group of patients was not unexpected. A population study in UK residential and nursing homes by Gordon *et al.* (2014) recruited 70% of available individuals, however amongst these, 62% suffered from dementia and 30% had a history of cerebrovascular disease. The burden of these comorbidities would have likely affected their physical and/or mental capacity should they have participated in AF screening offered during the present study. The average prevalence of dementia was even higher in a Norwegian nursing home setting (77%), and only 37% of all residents scheduled for a $_{12L}$ECG were able to undergo the procedure (Krüger *et al.* 2012) – close to the 46% of care

home residents who were screened using the $_{SL}$ECG here. Three of the AF screening studies in US or Portuguese nursing homes to date did not report their recruitment or participant exclusion rates (Chaskes *et al.* 2018; Khan *et al.* 2020; Cunha *et al.* 2020) whereas the study by Wiesel & Salomone (2017) excluded the uncooperative individuals, managing to recruit 43% of all nursing home residents. Whilst this was comparable to the proportion of care home residents recruited by the current study, one should note that the majority of individuals excluded by Wiesel & Salomone (2017) were those under the age of 65 rather than those suffering from dementia or physical comorbidities.

Similar to the PDAF study in GP surgeries, the coupling of AF screening and seasonal influenza vaccinations during this research in care homes provided access to the relevant and at-risk group of individuals. All 53 participants were aged ≥ 65 years and hence eligible for opportunistic AF screening according to the ESC guidance (Kirchhof *et al.* 2016). Since the burden of AF increases with age (Ball *et al.* 2013), the total prevalence of AF amongst the care home residents was 13.5% or more than three-fold above the prevalence observed in significantly younger PDAF participants from GP surgeries (4.3%), and five-fold above the population average of 2.5% (Public Health England 2017a). This prevalence was in fact closer to the total prevalence of 12.3% identified amongst the Swedish 75-76-year-olds with intermittent AF screening during the STROKESTOP study (Svennberg *et al.* 2015), even though it also corresponded well with the 13.4-14.0% prevalence recorded for UK care home residents (Shah *et al.* 2011; Gordon *et al.* 2014). Reflecting the effects of geographical variation, the total prevalence of AF seen here fell in between the 11-14% and 19% reported in US and Norwegian nursing homes, respectively (Reardon *et al.* 2012; Krüger *et al.* 2012; Ghaswalla *et al.* 2012).

Out of the seven cardiologist-determined AF cases amongst care home participants of this study, five had no prior history of the condition (9.6%), which produced a seven-fold greater prevalence of ‘unknown’ AF than noted for the main cohort of the PDAF study participants in GP surgeries (1.3%). This level of ‘unknown’ AF was above the 6.9-7.4% prevalence determined using the KMD in US nursing homes (Wiesel & Salomone 2017; Chaskes *et al.* 2018; Khan *et al.* 2020), and even greater than the 2.6-3.8% ascertained through intermittent AF screening strategies of ≥ 65s in primary care or community settings (Svennberg *et al.* 2015; Halcox *et al.* 2017; Kemp Gudmundsdottir *et al.* 2019; Ghazal *et al.* 2020), although this may once again be skewed by differences in age. Only two AF screening studies in a care home setting to date reported the yields of $_{12L}$ECG-confirmed ‘new’ AF, which was detected in 5/101 (4.9%) of the US nursing home residents (Wiesel & Salomone 2017) and 3/23 (13.0%) of those residing in a Portuguese nursing home (Cunha

et al. 2020). During the current study, after a median follow-up time to $_{12L}$ECG of 24.5 days, only one out of five care home residents with 'unknown' AF was diagnosed with a 'new' AF and anticoagulated accordingly (1.9%). Whilst only a fraction of yields reported by Wiesel & Salomone (2017) or a smaller study by Cunha *et al.* (2020), this yield of 'new' AF was markedly above the 0.7% ascertained through PDAF screening in GP surgeries and higher than the average yield of 1.4% reported for single-time point screening of ≥ 65s in the review by Lowres *et al.* (2019).

More importantly however, six out of seven care home residents with cardiologist-determined 'Possible AF' had at least one non-AF comorbidity, and all seven displayed a CHA_2DS_2VASc of ≥ 3, which qualified them for stroke prevention with the OAC therapy (Kirchhof *et al.* 2016). The median CHA_2DS_2VASc score of the sample was comparable to that of the main PDAF cohort (3.0 [3.0; 6.0] and 3.0 [3.0; 4.3], respectively), once again pointing at the effectiveness of the overlapping AF screening and influenza vaccination criteria (Kirchhof *et al.* 2016; Public Health England 2020a) when recruiting the at-risk group of AF patients. Whilst CHA_2DS_2VASc scores were not officially reported by previous AF screening initiatives in US care homes (Wiesel & Salomone 2017; Khan *et al.* 2020), the advanced age and high prevalence of comorbidities amongst the study participants suggested that their risk of stroke would be comparable to that reported here. This assumption was confirmed by Cunha *et al.* (2020) who found that all nursing home residents with screening-detected AF had a CHA_2DS_2VASc of ≥ 2, and a large population-based study in US nursing homes which ascertained that 93% of residents with AF qualified for stroke prevention with an OAC (Ghaswalla *et al.* 2012). The initiation of OAC therapy in older persons aged ≥ 75 years is also supported by the results of the **B**irmingham **AF T**reatment of the **A**ged (BAFTA) study, which demonstrated an approximate 50% relative reduction in the risk of stroke without an increase in bleeding amongst those receiving warfarin instead of aspirin (Mant *et al.* 2007).

These promising findings may on the other hand not be replicated in a care home population, which appears to differ from their community-dwelling age-matches due to the higher prevalence of cognitive impairment, physical comorbidities and polypharmacy (Kaufman *et al.* 2002; Bernstein & Remsburg 2007; Shah *et al.* 2011; Onder *et al.* 2012). As a result, in the absence of direct evidence, a large proportion of clinicians have historically been cautious about initiating OAC therapy in care home residents, primarily because of the high perceived risk of bleeding (Abel Latif *et al.* 2005; Rich 2012; Alcusky & Lapane 2018). During the present study, only 2/7 (28.6%) of eligible residents with suspected AF were prescribed OAC at follow-up, and one other participant (14.3%)

continued to take aspirin instead. The proportion of residents with AF receiving OAC therapy was substantially below the 21/27 (77.8%) registered at the PDAF study follow-up in GP surgeries, and echoed the 20-46% range reported by previous studies in a nursing home setting (Abel Latif *et al.* 2005; Ghaswalla *et al.* 2012; O'Caoimh *et al.* 2017).

It is worth noting that factors, such as advanced age or the history of stroke, which are included in the commonly used bleeding risk assessment scores, for example HAS-BLED, overlap with those of the CHA_2DS_2VASc score (Lip *et al.* 2011; Olesen *et al.* 2011). Therefore, according to the ESC, a high bleeding risk score should generally not be a sole reason for withholding OAC therapy in patients with AF who would otherwise qualify for stroke prevention (Kirchhof *et al.* 2016). In order to compare the risks of ischaemic stroke and bleeding amongst the PDAF study participants in care homes with those in GP surgeries, this project compiled the CHA_2DS_2VASc and HAS-BLED scores for both groups. Contrary to the popular belief, even though both groups displayed a similar risk of ischaemic stroke, the average HAS-BLED score was lower in the care home sample (1.0 [1.0; 2.0] vs. 2.0 [2.0; 3.0]). Although this finding was likely influenced by greater alcohol consumption in the general practice group and should be interpreted cautiously, it highlights the fact that care home residents with AF should not be automatically excluded from OAC therapy without a comprehensive assessment of their individual stroke versus bleeding risk balance. Other factors, which are not included in common risk scores, such as the patient's nutritional status, weight/BMI, the level of frailty and general life expectancy may all play a role in this holistic assessment (Shinohara *et al.* 2019; Anaszewicz & Budzyński 2017; Bauersachs & Herold 2020). Indeed, during the present study care home residents with AF were found to have a significantly lower BMI compared to those in GP surgeries (23.8 [19.9; 26.9] and 28.5 [24.2; 33.5] kg/m^2, respectively). In light of the possible relationship between the low body weight/BMI and the elevated risk of bleeding with OAC therapy (Park *et al.* 2017; Shinohara *et al.* 2019), these results reiterate the need to weigh the individual's bleeding risk and adjust the doses of anticoagulation accordingly.

Diagnostic accuracy of AF detection methods

As with the PDAF study in GP surgeries, the feasibility of CP-led AF screening in care homes was evaluated from the perspective of diagnostic accuracy, using either pulse palpation or the KMD. The quality of $_{SL}$ECG recordings produced using the KMD was 'Excellent' or 'Acceptable' in over 70% of cases, however 'Poor' quality was reported for $_{SL}$ECGs of 27% of patients. This proportion was more than five times greater than observed during the PDAF study in GP surgeries (5.3%) and concurred with the fraction of *'no-analysis'* $_{SL}$ECGs noted using the KMD in US nursing homes (26%) (Khan *et al.* 2020).

Albeit not documented for individual participants, the specific reasons underlying the poor-quality recordings were likely to agree with Khan *et al.* (2020) who postulated that the high prevalence of physical and cognitive impairments in this population were the primary cause of baseline artefact on $_{SL}$ECGs. In support of this hypothesis, during the present study one of the care home residents with Parkinson's disease could be screened using pulse palpation but not the KMD due to severe hand/arm tremor.

The poor quality of $_{SL}$ECG produced using the KMD translated into sub-optimal diagnostic sensitivity for AF, questioning the viability of this screening strategy in a care home setting. The sensitivity of the KMD algorithm (57.1%) was far below that reported during the PDAF study in GP surgeries (92.3%), other research in primary care (Lowres *et al.* 2014; Orchard *et al.* 2016; Lown *et al.* 2018; Himmelreich *et al.* 2019; Zaprutko *et al.* 2019) (87-100%), and even the equivalent study in US nursing homes (72.2%) (Khan *et al.* 2020). To our knowledge, this is the second lowest level of diagnostic sensitivity of the KMD algorithm reported in the literature, after the 37% ascertained in the secondary care cardiology setting (Desteghe *et al.* 2017). The KMD algorithm missed an alarming 3/7 (42.9%) of cardiologist-confirmed cases of AF compared to only 2/26 (7.7%) of false negatives during the PDAF study in GP surgeries. The diagnostic sensitivity of the other two index tests was even lower than that of the KMD algorithm (42.9%), and once more, substantially below the sensitivities reported during the PDAF study in GP surgeries (76.9% and 88.5% for pulse palpation and CP's interpretation of $_{SL}$ECG, respectively). Likewise, the sensitivity of $_{SL}$ECG interpretation by the CP was no match for the 77.0% reported by Lowres *et al.* (2014) in community pharmacies, whereas the sensitivity of pulse palpation did not compare to values presented by any previous studies in primary care (77-100%) (Sudlow *et al.* 1998a; Somerville *et al.* 2000; Morgan & Mant 2002; Hobbs *et al.* 2005; Lowres *et al.* 2014).

Despite slight differences in diagnostic sensitivity, the $_{SL}$ECG interpretation by the KMD algorithm or the CP displayed an identical 100% specificity, identifying all 45 true negatives without producing any false positive AF diagnoses. This encouraging finding was somewhat unexpected, although not far from the high specificity of KMD algorithm-based screening during the PDAF study in GP surgeries (97.4%) or the nursing home study by Khan *et al.* (2020) (94.7%), and similar to other research using the automated KMD algorithm in primary care (91-99%) (Lowres *et al.* 2014; Orchard *et al.* 2016; Lown *et al.* 2018; Himmelreich *et al.* 2019; Zaprutko *et al.* 2019). The specificity of $_{SL}$ECG interpretation by the CP exceeded that in GP surgeries (97.2%) and was above the 87.0% reported for community pharmacists (Lowres *et al.* 2014). Compared to the other two index tests, the specificity of pulse palpation was marginally lower (95.6%), yet still above the 92.2% during the PDAF study in GP

surgeries or the specificities reported by previous AF screening initiatives in various primary care settings (71-93%) (Sudlow *et al.* 1998a; Morgan & Mant 2002; Somerville *et al.* 2000; Hobbs *et al.* 2005; Lowres *et al.* 2014). As such, albeit not insignificant, the FDR of pulse palpation was down to 40% and resembled that of the other two index tests when screening in GP surgeries (39-41%), rather than the 59-92% range computed by previous primary care research (Sudlow *et al.* 1998a; Morgan & Mant 2002; Hobbs *et al.* 2005; Rhys *et al.* 2013; Quinn *et al.* 2018).

Unlike during the PDAF study in GP surgeries, the relatively minute differences in diagnostic accuracy of the three index tests discussed here did not reach statistical significance. The diagnostic classification by the cardiologist was also not statistically different from any of the three tests, although as noted during the PDAF screening in general practice, the KMD algorithm displayed the greatest inter-rater agreement with the reference standard (0.70), followed by the CP's interpretation of $_{SL}$ECG (0.57). Despite a much lower FPR than ascertained in GP surgeries (4.4% vs. 7.8%), the inter-rater agreement between the cardiologist and pulse palpation remained poor-to-moderate (0.44), suggesting that AF screening using the KMD in this setting is still likely to be more effective regardless of the poor-quality $_{SL}$ECG recordings. As proposed by Wiesel & Salomone (2017), an alternative AF screening option which may circumvent the issue of poor-quality $_{SL}$ECGs in a care home population includes using mBPMs, for instance those of the WatchBP® series. The direct comparisons of AF screening using the KMD and WatchBP® monitors to date suggest that the latter may display a superior diagnostic sensitivity (83-96% vs. 67-88%) at the expense of a slightly lower specificity (94-99% vs. 99-100%) (Chan *et al.* 2017a; Lown *et al.* 2018).

Similar to pulse palpation, the lower diagnostic specificity of mBPMs reflect their inability to distinguish between the benign heart rhythm abnormalities, such as AEBs or VEBs, and the continuous rhythm irregularity displayed by AF (Chan *et al.* 2017a; Lown *et al.* 2018). In contrast, as showcased during the PDAF study in GP surgeries, $_{SL}$ECG recordings produced by the KMD might help identify those with AF or other rhythm abnormalities, ultimately leading to diagnoses of non-AF disorders, such as BBBs. This is achieved through a relative "excess" of provisional 'Unclassified'/'Unreadable' diagnoses which, with the KMD algorithm varies from 8.4% to 17.0% (Orchard *et al.* 2016; Lown *et al.* 2018; Selder *et al.* 2019; Orchard *et al.* 2019b; Zaprutko *et al.* 2019; Cunha *et al.* 2020), and reached 13% during the PDAF screening in general practice. The 32.7% prevalence of 'Unclassified' diagnoses observed during this study in care homes may have reflected the high proportion of 'Poor'-quality $_{SL}$ECG recordings (27%) and would have produced unnecessary $_{12L}$ECG referrals in > 15% of care home residents. This number was nearly double the 8% of

unnecessary referrals with pulse palpation or CP's interpretation of $_{SL}$ECG, and the 7% observed with the KMD algorithm during the PDAF study in GP surgeries. Although additional 'Unclassified' diagnoses by the KMD algorithm or the CP's interpretation of $_{SL}$ECG would have helped identify the single care home resident with a 'new' AF, who would have otherwise been missed by pulse palpation, the value of such screening in light of disproportionate $_{12L}$ECG referrals, remains unclear.

Access to healthcare and follow-up

Apart from one 'new' case of AF, contrary to PDAF screening in GP surgeries, none of the care home residents during this study were diagnosed with a 'new' non-AF cardiovascular condition at follow-up. It is of course possible that the permanent or frequent presence of clinical staff in selected care homes facilitated a rapid diagnosis of cardiovascular conditions before the beginning of this study. For instance, the residents of some care homes may see their GP more than once a month and may be diagnosed with AF or another cardiovascular condition during these routine visits (Victor *et al.* 2018; Gordon *et al.* 2014). Nonetheless, residents of other care homes may only have contact with their GP or another HCP three or four times a year (Victor *et al.* 2018) compared to an average of six annual consultations in the general public (NHS Digital 2009). In support of these data, the review by the Care Quality Commission (2012) concluded that as many as 56% of all care homes in England may not receive regular GP visits. As such, home visits, including those to care homes, form only 4% of all yearly GP consultations in England (NHS Digital 2009), despite the fact that, as shown by the present and many other studies, these residents are often in most clinical need (Shah *et al.* 2011; Gordon *et al.* 2014).

During this study, 10/16 (62.5%) of care home residents referred for $_{12L}$ECG underwent the procedure compared to 66/87 (75.9%) after the PDAF screening in GP surgeries. More significantly, the average time to $_{12L}$ECG amongst care home residents reached 24.5 [15.5; 50.8] days and was substantially above the 16.0 [11.0; 24.0] days during the PDAF screening in GP surgeries. In one instance, a resident with a 'Possible AF' and a CHA_2DS_2-VASc score of six waited a total of 188 days (or more than six months) to undergo a $_{12L}$ECG, potentially exposing them to an annual 13.6% risk of ischaemic stroke, transient ischaemic attack or systemic embolism (Friberg *et al.* 2012). Considering this length of time, it is therefore unsurprising that, whilst the overall yield of 'new' AF during this study (1.9%) was above that of PDAF screening in GP surgeries (0.7%), the proportion of participants with 'unknown' AF who were ultimately diagnosed with the condition at follow-up was only 20% (1/5) compared to 38% (3/8) in general practice. In other words, aside from the one resident with suspected AF who did not respond to an invitation, 75% (3/4) of care home participants

with ‘unknown’ AF who did undergo a $_{12L}$ECG and may have presented with PAF at the time of screening (Kirchhof *et al.* 2016), were found to be in SR at follow-up. This was rather unexpected since the prevalence of PAF typically peaks in younger individuals, as opposed to older persons or those with associated comorbidities who tend to experience a more persistent or permanent disease (Zoni-Berisso *et al.* 2014). It is however possible that, due to longer follow-up times, even those care home residents with persistent AF may have reverted back into SR and were not identified as AF by the time of their $_{12L}$ECG.

The reasons underlying the generally low follow-up rate and the long procedure waiting times encountered during this study in care homes are likely multifactorial. Paradoxically, even though care home residents are often perceived as having limited access to healthcare (Care Quality Commission 2012; NHS England 2020b), there is little published information about the barriers to their healthcare access. The findings of a qualitative study by Robbins *et al.* (2013) suggested that the effective delivery of healthcare in care homes may be limited by an array of barriers from the unpredictable nature of residents’ illness, the delays in the transfer of clinical information and inadequate working relationships between the care home staff and GPs to confusion about professional responsibilities and the mismatch between the healthcare needs and the HCPs’ time. Some GPs interviewed by Robbins *et al.* (2013) also expressed their concerns about the true value of medical interventions in this group of patients, who may be at the end of their lifetime, and may experience more harm than benefit from certain treatments. Whilst this perception may certainly be applicable to some care home residents, it overall opposes the NHS drive towards the concept of person-centred care (NHS England 2019d). For example, as demonstrated by the present study, some high-risk care home residents with AF may display a lower risk of bleeding than patients encountered in GP surgeries and may wish to be considered for stroke prevention with an OAC on a case-by-case basis.

Similarly, the systematic review by Davies *et al.* (2011) proposed that the effectiveness of integrated working between the care homes and primary care services may be improved by placing a greater emphasis on the priorities of individual residents and the better utilisation of care home staff. The new EHCH model addresses both of these goals by tailoring the proactive services to the needs of individuals and by integrating the expertise of care home staff more closely with other primary care organisations, including the PCNs (NHS England 2020b). The inclusion of general practice-based CPs within this model of care (NHS England and BMA 2019c) offers an opportunity to improve the care home resident access to a package of healthcare services during routine visits. During this study, we have demonstrated that trained CPs can perform AF screening in care homes using a variety of

AF detection tools as part of seasonal influenza vaccination visits. Future studies may wish to explore the alternative models of AF screening in this setting, for instance by establishing the aforementioned integrated one-stop AF detection and anticoagulation clinics, which have been successfully implemented in community pharmacies (Care City 2019; Antoniou *et al.* 2019).

Cost-effectiveness of the intervention

In order to establish the cost-effectiveness profile of the CP-led AF screening intervention in care homes, the economic model constructed here compared it with the 'no-screening strategy' and the cost-effectiveness of the PDAF intervention in GP surgeries. Compared to the 'no-screening' scenario, the CP-led AF screening in care homes remained cost-effective despite the lower diagnostic sensitivity and a higher proportion of 'Unclassified'/'Unreadable' diagnoses than observed in GP surgeries. As a matter of fact, at base case the mean ICER for AF screening using the KMD algorithm in care homes (£6,223/QALY gained) was approximately 132% lower than that during the PDAF study in general practice (£14,460/QALY gained). The estimated ICER value of £6,223/QALY gained in care homes was close to the ICERs of £8,498 and £7,642/QALY gained which were computed by Welton *et al.* (2017) for systematic population and systematic opportunistic screening of AF using the automated $_{SL}$ECG devices in 80-year-old individuals, respectively. The base-case cost-effectiveness was also not far from the ICER of £4,292/QALY reported for intermittent AF screening using the Zenicor® $_{SL}$ECG device during the STROKESTOP study (Aronsson *et al.* 2015) or the £4,589/QALY gained with the HeartCheck® $_{SL}$ECG screening in Canadian community pharmacies (Tarride *et al.* 2017). It however fell short of the £1,932/QALY gained estimated by Lowres *et al.* (2014) for KMD-based AF screening in an Australian community pharmacy setting.

Likewise, at 89.3% the probability of base-case cost-effectiveness in care homes was about 18% above that estimated during the PDAF study in GP surgeries (71.8%) and higher than the 60-80% range reported by earlier pulse palpation-based AF screening studies (Hobbs *et al.* 2005; Moran *et al.* 2016). It was also comparable to the 91% likelihood of cost-effectiveness with $_{SL}$ECG-based AF screening delivered in Canadian community pharmacies (Tarride *et al.* 2017), nevertheless was no match to an almost guaranteed 99-100% probability of cost-effectiveness stated by either the STROKESTOP study (Aronsson *et al.* 2015) or the $_{SL}$ECG-based AF screening of ≥ 65s during the influenza vaccination clinics in the Netherlands (Jacobs *et al.* 2018). The INB per individual with AF was also in favour of AF screening in care homes compared to GP surgeries (£1,903 vs. £3,937), and

translated into the monetary benefit of approximately £39 million when applied to all care home residents with 'new', screening-detected AF across England and Wales.

The pronounced economic superiority of AF screening in a care home setting over GP surgeries was to an extent unexpected, considering the poorer diagnostic performance of the KMD algorithm as well as the higher mortality and OAC-related bleeding rates experienced by the overall older care home residents (Friberg *et al.* 2012; Office for National Statistics 2014; Office for National Statistics 2017a; Office for National Statistics 2017b). These effects were likely offset by significant differences in the prevalence of 'unknown' or previously undiagnosed AF, which as discussed above, was more than seven times greater in care homes compared to GP surgeries. As such, proportionally more care home residents than individuals in GP surgeries had an opportunity to benefit from OAC therapy, reducing the financial impact of stroke. The overall 10-year incremental cost per individual with AF in care homes was only £1,778 compared to £4,968 in GP surgeries. As anticipated, due to higher mortality, the incremental 10-year QALYs per individual with AF in care homes were slightly lower than with the younger population in GP surgeries (0.29 vs. 0.34), although this difference allowed for the overall more favourable ICERs in a care home group presented above. Similarly, in a review by Welton *et al.* (2017) the cost-effectiveness of the systematic population AF screening using the automated $_{SL}$ECG algorithm was greater at the age of 80 than at the cut off age of 65 years (ICERs of £8,498 and £12,100/QALY gained, respectively).

During the PSA, the cost-effectiveness advantage of AF screening in care homes compared to GP surgeries persisted throughout the adherence to OAC range. Other deviations from the base case produced similar trends to those observed for the PDAF study in GP surgeries. As discussed in section **3.4.6** and as described for KMD-based AF screening in primary care (Lowres *et al.* 2014), the cost-effectiveness of the intervention in care homes increased dramatically when shifting from 40% to 80% adherence to OAC therapy. Contrary to analyses by Lowres *et al.* (2014) and Jacobs *et al.* (2018), the model was once again largely insensitive to changes in fractions of AF patients receiving the VKA and DOAC therapies. Nonetheless, the move to the warfarin-dominated model had a more pronounced effect on improving the cost-effectiveness of the intervention in care homes than in GP surgeries (6.5% and 2.1% improvement in cost-effectiveness, respectively), possibly due to the greater proportion of participants with 'new' AF initiated on OAC or smaller absolute ICER values in care homes. Similar to the PDAF study in GP surgeries, the ICERs of the economic model in care homes fluctuated by approximately -38% or +68% when increasing or decreasing the participation in AF screening rates, thereby contradicting the findings by

Lowres *et al.* (2014) and Moran *et al.* (2016) who showed no such impact. Interestingly, reducing the prevalence of 'Unclassified'/'Unreadable' diagnoses from 32.7% to 16.4% in the care home model had a milder effect on the cost-effectiveness of the intervention than in GP surgeries (10% and 15% average reductions in ICERs, respectively). Whilst unnecessary $_{12L}$ECG appointments due to 'Unclassified'/'Unreadable' diagnoses in 32.7% and even 16.4% of care home residents are by no means insignificant, this suggested that their influence on the overall cost-effectiveness of AF screening is not even remotely comparable to the effect of greater AF prevalence in care homes versus the general public.

5.5.2 Strengths and limitations

This study benefitted from an established AF screening and follow-up protocol developed and tested during the PDAF study in GP surgeries (Veale *et al.* 2018). Similar to the main PDAF study, the recruitment strategy utilising the matching criteria for AF screening and seasonal influenza vaccinations in care homes (Kirchhof *et al.* 2016; Public Health England 2020a), helped identify residents with AF who were at risk of ischaemic stroke and thus might benefit from the OAC therapy. The convenient delivery of AF screening within the participants' homes may have also reduced the risk of selection bias due to the 'healthy volunteer effect' (Froom *et al.* 1999; Delgado-Rodriguez & Llorca 2004), which may otherwise occur with typical influenza vaccinations in a general practice setting. To our knowledge, this study was the first to conduct a structured AF screening programme in UK care homes. It therefore adds unique evidence to UK-based population studies (Shah *et al.* 2011; Gordon *et al.* 2014), showcasing the high level of undiagnosed AF in this at-risk group, which may potentially be similar to or above that reported in US or Portuguese care homes (Wiesel & Salomone 2017; Chaskes *et al.* 2018; Khan *et al.* 2020; Cunha *et al.* 2020).

Apart from epidemiological considerations, this research was the first to evaluate the diagnostic accuracy of both conventional pulse palpation and $_{SL}$ECG-based AF screening in a care home setting, contributing to the evidence of AF detection using these two ESC-recommended methods (Kirchhof *et al.* 2016) in other primary care settings (Sudlow *et al.* 1998a; Somerville *et al.* 2000; Morgan & Mant 2002; Hobbs *et al.* 2005; Lowres *et al.* 2014; Orchard *et al.* 2016; Lown *et al.* 2018; Himmelreich *et al.* 2019). Similarly, this study was the first to assess the cost-effectiveness of AF screening in this distinct group of individuals, most of whom were aged ≥ 85 years and were likely to display greater than average risk of all-cause death, ischaemic stroke and OAC-induced haemorrhage (Olesen *et al.* 2011; Friberg *et al.* 2012; Office for National Statistics 2014; Office for National Statistics 2017a; Office for National Statistics 2017b). The economic benefits of single time point AF

screening in a care home setting presented here provide a novel, first-hand perspective to the cost-effectiveness of AF screening amongst the ≥ 80s, previously estimated in a systematic review by Welton *et al.* (2017). Last but not least, this study appraised the feasibility of pharmacist-led AF screening in a care home environment, thereby adding evidence to the findings of the PDAF study in GP surgeries (Savickas *et al.* 2020b; Savickas *et al.* 2020c) or other studies which investigated AF detection in community pharmacies (section **1.3**).

Despite its novelty, the findings of this study should be interpreted with adequate caution, primarily due to the small sample size, which was significantly below the 101-245 participants recruited by equivalent studies in US nursing homes (Wiesel & Salomone 2017; Chaskes *et al.* 2018; Khan *et al.* 2020), and involved less than 50% of all available residents. The remainder of residents were excluded from the study based on severe physical and/or mental impairments. Considering the established relationships between AF and cognitive/physical impairments (Ball *et al.* 2013; Staerk *et al.* 2017), as well as between dementia, CVD and the risk of stroke (Olesen *et al.* 2011; Kuźma *et al.* 2018), it is possible that some of the excluded care home residents could have had AF and benefitted from appropriate stroke prevention. As discussed above, this often poses an ethical dilemma for clinicians considering the OAC therapy, since those care home residents with multiple physical or cognitive impairments or polypharmacy are also likely to have the shortest life expectancy (Shah *et al.* 2013) and some may experience an elevated risk of bleeding (Friberg *et al.* 2012). During this study, provisions were made to include those care home residents with a fluctuating mental capacity, however no such individuals were entered into the study following consultation between the assessing GP and a personal/nominated consultee. This was in consideration of the unfavourable risk versus benefit balance of treatment, should AF be detected.

Contrary to the PDAF study in GP surgeries, this project was also not adequately powered to detect statistically significant differences of diagnostic accuracy between any of the tests. The relatively small number of AF cases also meant that the diagnostic accuracy measures were much more sensitive to any discrepancies between the index tests and the reference standard, and hence may not be the true representation of each test's diagnostic performance in this setting. Besides the other limitations of the PDAF protocol acknowledged in **Chapters 2 and 3**, the diagnostic accuracy of each index test may also have been subject to a greater risk of misclassification bias due to the presence of a single CP in contrast to seven CPs during the PDAF study in GP surgeries (Schmidt & Factor 2013). Furthermore, compared to participants in GP surgeries, only one care home resident

with AF provided the details of their alcohol consumption, urging care when generalising the lower HAS-BLED scores of care home residents beyond this group of participants. Similar to the PDAF study in GP surgeries, the care home sample recruited during this study was also almost universally White British (98%), and hence is not representative of the diverse population of Kent or England and Wales (Office for National Statistics 2018c; Kent Public Health Observatory 2011). As postulated in **Chapter 3**, the generalisability of findings from PDAF studies in either care homes or GP surgeries may therefore be improved through targeted screening of individuals from ethnic minority groups, who may experience barriers to accessing conventional healthcare (NHS England 2018a).

The cost-effectiveness analysis conducted as part of this study was limited by the assumption that all individuals with 'unknown' AF who were identified by each index test would ultimately be offered stroke prevention. In reality only one out of five care home residents with 'unknown' AF were diagnosed with a 'new' AF and treated accordingly (20%), thus likely over-estimating the economic benefits discussed here. The economic model also did not take into account the additional costs, which may have incurred as a result of follow-up procedures between the care homes and GP surgeries. This may for instance have included the administrative costs of arranging the inter-setting follow-up appointments or the travel and staff costs associated with district nurse visits to care homes in order to perform the $_{12L}$ECGs. The lack of such considerations may have over-estimated the cost-effectiveness of AF screening in a care home setting presented here, and one should apply an appropriate caution when interpreting the economic superiority of AF screening within this environment compared to GP surgeries.

5.6 Conclusion

This chapter presented the findings of the CP-led AF screening programme in UK care homes during the influenza vaccination season. The evidence provided here suggested that the total prevalence of AF in UK care homes may be more than five-fold above the population average, and close to one in ten of all residents may have an undiagnosed AF. All care home residents with AF identified by this study qualified for stroke prevention with OAC therapy, and had an overall lower risk of bleeding than individuals recruited in GP surgeries. Moreover, based on the economic model, the AF screening intervention in care homes was highly cost-effective compared to either the no-screening scenario or the AF screening in general practice. Not only do these results highlight the proportion of AF patients who may benefit from treatment in a care home setting, but they also encourage clinicians to undertake a person- rather than demographic-centred assessment of risks and benefits when considering the initiation of OAC in this vulnerable group of individuals. The

feasibility of AF screening in a care home setting was somewhat compromised by the low diagnostic accuracy of all index tests compared to the level of accuracy recorded in GP surgeries, although the use of the automated KMD algorithm remained the most accurate means of AF detection. The feasibility of recruitment and AF screening in this population was also affected by the high prevalence of physical and cognitive impairments, which allowed for the recruitment of less than 50% of all residents, and may have been the cause of poor-quality $_{SL}$ECG recordings.

The results of this study concurred with pre-existing literature which emphasised the limited access to healthcare experienced by care home residents. Compared to patients in GP surgeries, 13% fewer care home residents had a $_{12L}$ECG follow-up appointment, and those who did, had to wait on average almost nine days longer. Whilst national efforts are already on the way to reduce this inequality, the results presented here suggest that a CP-led model of AF detection in care homes during the influenza vaccination season is likely to be both effective and cost-effective provided that appropriate AF detection tools are in place. This urges commissioners and policy makers to utilise the opportunity provided by the ongoing MOCH agenda and the CP integration within the PCNs to deliver AF detection as an add-on to existing pharmaceutical or cardiovascular services.

In addition to practice and policy implications, several research questions raised by this study remain unanswered. First of all, it is unclear whether or not the other AF detection tools may display a similar diagnostic accuracy in a care home setting to that reported for pulse palpation or the KMD algorithm here. The use of mBPMs, such as the WatchBP® series, may be of a particular interest due to their automated function, which may allow the testing of participants with physical or cognitive impairments – an element which limits the practicality of the KMD. Secondly, unlike the PDAF study in GP surgeries, this study also did not collect any stakeholder feedback to support the feasibility of the intervention. Whilst this may be difficult to achieve due to the high prevalence of cognitive impairment within this population, future studies may consider conducting surveys or qualitative investigations to ascertain the acceptability of AF screening in the care home setting from the perspectives of residents, care home staff, CPs and clinicians, particularly GPs, geriatricians and stroke consultants. The qualitative research element may explore the culture and attitudes of multiple stakeholders involved in the identification and treatment of care home residents with AF, which may help ascertain the specific facilitators and barriers underlying the effective follow-up processes as well as the initiation of the OAC therapy. The qualitative findings may also inform the development of a future, larger-scale AF screening programme within the care home setting, for example by determining whether or not it should routinely

include residents who lack the mental capacity to provide an informed consent (upon the advice of an appropriate consultee). Lastly, the pharmacist-specific aspects of feasibility require a further investigation to establish whether CPs would be able to assess the mental capacity of care home residents independently of the accompanying GP, and whether the proposed intervention could be successfully integrated within the umbrella of current CP-led services, for instance the medication reviews for patients with long-term conditions.

Chapter 6: Atrial Fibrillation Screening using Single-lead ECG within a South Asian Community

6.1 Introduction

As illustrated by the PDAF study, CP-led AF screening during the influenza vaccination season may be an effective and cost-effective means of identifying the previously undiagnosed AF in up to 1.3% of individuals aged ≥ 65 years visiting their GP surgeries (**Chapters 3 and 4**). According to the results of the PDAF screening extension in care homes (**Chapter 5**), an even greater prevalence of undiagnosed AF (9.6%) may be detected amongst the high-risk population of care home residents who may not have a regular access to GP services in primary care. Besides care home residents, barriers to engagement with healthcare services are experienced by several other population groups, for instance the housebound or individuals from the BAME groups (Szczepura 2005; Musich *et al.* 2015b). Those with limited access to healthcare may be less likely to participate in public health or research initiatives, and as such the under-representation of the BAME groups in clinical research is a well-documented phenomenon (Redwood & Gill 2013; Smart & Harrison 2017). The AF screening studies are not an exception, with White British participants forming over 93% of all individuals recruited by previous UK-based AF screening programmes (Hobbs *et al.* 2005; Halcox *et al.* 2017). Similarly, ≥ 97% of all individuals screened by PDAF studies in GP surgeries and care homes were of White British ethnicity, compromising the generalisability of their findings to the otherwise multi-ethnic population of England and Wales or Kent (Kent County Council 2011; Office for National Statistics 2018b).

The Asian/Asian British is the second largest ethnic group in England and Wales, and in Kent, constituting 7.5% and 3.3% of the total population, respectively (Kent County Council 2013; Office for National Statistics 2018c). Individuals of South Asian origin, primarily Indian, Bangladeshi and Pakistani, form most of this category (71%) (Office for National Statistics 2018c). The South Asians are subject to perhaps the greatest burden of CVD out of all UK ethnic groups (British Heart Foundation 2010; George *et al.* 2017), making them one of the priorities in the current national CVD agenda (Public Health England 2019c). Compared to the general population, South Asian people display a 10-year earlier presentation of CVD and up to 1.5-fold increased mortality due to IHD (IHD) or stroke (Wild & Mckeigue 1997; George *et al.* 2017). The phenomenon of increased CVD burden amongst the South Asians has been partially explained by the higher than average prevalence of conventional CVD risk factors, such as diabetes mellitus, dyslipidaemia and

obesity (Bhopal *et al.* 1999; Gunarathne *et al.* 2008; British Heart Foundation 2010; George *et al.* 2017), which have in turn been attributed to physiological or genetic predisposition, socioeconomic inequalities and lifestyle habits (Kuppuswamy & Gupta 2005; Palaniappan *et al.* 2018). Interestingly however, other clinical conditions which typically co-exist with IHD, such as hypertension or heart failure (Mahmood *et al.* 2014), may be less prevalent amongst individuals of South Asian ethnicity compared to either the British White or Black African Caribbean populations (Bhopal *et al.* 1999; British Heart Foundation 2010; Gill *et al.* 2011; Gillott *et al.* 2017; George *et al.* 2017). As could be expected from a strong association between the risk of AF and heart failure (Benjamin *et al.* 1994), the estimated prevalence of AF amongst South Asians is only 0.2-1.0%, or up to 13-fold below the general population and the White British average (Lip *et al.* 1998; Conway & Lip 2003; Gill *et al.* 2011; Mathur *et al.* 2013; Gillott *et al.* 2017; Public Health England 2017a).

The reasons underlying this discrepancy between the high prevalence of conventional CVD risk factors and the low prevalence of AF amongst South Asians may be physiological or anatomical (Amponsah *et al.* 2013; O'Neill & Tayebjee 2018). For instance, the smaller than average left atrium may protect this group against the development of AF by reducing the extent of atrial fibrosis (O'Neill *et al.* 2018b). Nevertheless, it is also possible that the low prevalence of AF in South Asians reported to date could be a product of their low engagement with healthcare and/or research. Most of the epidemiological studies in this group were conducted retrospectively using either the primary or secondary care registries (Conway & Lip 2003; Newton *et al.* 2005; Gunarathne *et al.* 2008; Mathur *et al.* 2013; Gillott *et al.* 2017; O'Neill *et al.* 2018a), whereas the prospective study by Gill *et al.* (2011) suffered from under-recruitment. In either case, South Asian individuals who did not actively engage with healthcare or clinical research yet suffered from undiagnosed AF may have not been captured.

Low engagement in research and/or healthcare observed amongst the BAME groups, including South Asians, may be influenced by socioeconomic, linguistic, cultural and educational factors (Szczepura 2005; Quay *et al.* 2017). For example, some South Asian individuals, particularly first-generation immigrants to the UK, perceive weight gain as a sign of good health whereas the development of type 2 diabetes is understood to be the will of God, potentially discouraging them from leading a healthier lifestyle and from seeking healthcare advice (Greenhalgh *et al.* 1998; Ludwig *et al.* 2011). Language barriers can influence the access to healthcare with more than one in 10 individuals from some South Asian communities unable to speak English (Office for National Statistics 2018a) and some struggling with written language (Palmer *et al.* 2015). The complexity of the UK healthcare

system may also play a part. According to recent NHS surveys, South Asian patients were the least likely of all ethnic groups in England to be satisfied when making an appointment to see their GP, and 18% were unable to schedule an appointment when needed (NHS England 2018a; NHS Digital 2019d). Socioeconomic deprivation completes this vicious cycle by limiting South Asian access to costly education (Ministry of Housing 2018), thus preventing an improvement of their health literacy, lifestyle habits and English language proficiency (Public Health England 2015; Emadian *et al.* 2017). The *'Improving access for all'* resource by NHS England pledged to tackle such inequalities by empowering primary care HCPs to work closer with local communities in order to address the barriers to healthcare access amongst specific patient groups (NHS England 2018a).

One of the approaches to facilitating both research and healthcare engagement of the BAME groups may be to bring any public health initiatives nearer to their communities, for instance by delivering such programmes in conjunction with local leaders, faith institutions or community events (Netto *et al.* 2010; Palmer *et al.* 2015). Early efforts within the South Asian communities in England reported improvements in healthy diet and weight loss following the targeted interventions by either members of the local community or a team of HCPs (Snowdon 1999; Williams & Sultan 1999). More recently, several studies in religious and community settings of UK and Canadian South Asian populations demonstrated the feasibility of mass CVD risk factor screening programmes, which in some cases helped optimise the management of dyslipidaemia and hypertension (Mathews *et al.* 2007; Patel *et al.* 2007; Rao *et al.* 2012; Jones *et al.* 2013). As shown by qualitative evaluations of these CVD risk screening programmes their delivery within the local venues, including the places of worship, may offer a convenient access to healthcare for communities who may not otherwise visit their GP, whilst providing an opportunity to educate them about the CVD and associated risks (Netto *et al.* 2007; Eastwood *et al.* 2013). The acceptability and efficiency of health screening programmes tailored to South Asian communities may be further improved by ensuring the consultation is delivered in their mother tongue, referred to as the *'language concordance'*, and by a person matching the individual's cultural or ethnic background, referred to as the *'ethnocultural concordance'* (Laveist & Nuru-Jeter 2002; Freeman *et al.* 2002; Netto *et al.* 2007; Eastwood *et al.* 2013; Jones *et al.* 2013; Ahmed *et al.* 2015; Waibel *et al.* 2018).

Despite the recent endeavours to improve the identification of South Asian individuals at risk of CVD within their local communities, none of the initiatives to date have incorporated the detection of AF. The recent KMD-based AF screening programme delivered in conjunction with the Aboriginal Community Controlled Health organisations in Australia

however suggested that a community-focused testing approach may be well-accepted and could help identify 'new' AF in up to 0.6% of this high-CVD risk population (Macniven *et al.* 2019; Gwynn *et al.* 2020). This chapter builds on the learning from PDAF studies in GP surgeries and care homes as well as the previous CVD screening initiatives in ethnic minority groups from the literature, and presents the quantitative evidence in support of the AF screening programme within a South Asian community setting (**Figure 6.1**). It hypothesises that the relatively low prevalence of AF within the UK South Asian population ascertained by previous epidemiological studies may be influenced by the low engagement with research and health services in primary care. Based on the comments from stakeholders during the PDAF study and the evidence of non-HCP-led AF screening (Orchard *et al.* 2014; Twigg *et al.* 2016; Zaprutko *et al.* 2019; Anderson *et al.* 2020), this research also tested a hypothesis of whether or not AF screening using $_{SL}$ECG devices might be successfully delivered by staff who were less clinically-qualified than CPs, such as trained pharmacy undergraduates.

With reference to evidence discussed above, in order to improve the uptake of the intervention, the study described in this chapter offered AF screening within the places of worship of a selected South Asian community and delivered it as part of the existing public health campaigns. Following the success of a public health campaign-driven AF screening by Antoniou *et al.* (2017), this study was delivered in conjunction with a PPO (AF Association). It was also led by a member of research team (SB) whose ethnic background and language proficiency identified with that of the target population. Similar to the parent PDAF study in GP surgeries, the feasibility of the AF screening intervention within a South Asian community setting was evaluated from the perspectives of recruitment, diagnostic accuracy, participant feedback and the economic impact. This study therefore mapped onto both the feasibility/piloting and evaluation elements of the MRC (2006) guidance for complex interventions outlined in section **2.2**. Considering the diagnostic superiority of $_{SL}$ECG devices over pulse palpation ascertained by the PDAF studies, this initiative excluded the latter test, and focused on the diagnostic accuracy of $_{SL}$ECG interpretation by the automated algorithm of the KMD.

The South Asian community are by no means a homogeneous ethnic group, and there may be variations in the prevalence of CVD and/or risk factors between those originating from different countries in the Indian sub-continent (Bhopal *et al.* 1999). Considering the feasibility focus of this study however, we targeted a single ethnic group of British Indian individuals, specifically those who attended the local Gurdwaras, the places of worship of the Sikh religious group (British Sikh Report 2017; Office for National Statistics 2018c).

Approximately 423,000 people identify themselves as Sikhs in England and Wales, an equivalent of 0.8% of the total population, making them the third largest ethnic minority religious community in England/Wales and in Kent following the Muslims and Hindus (Office for National Statistics 2012; Kent County Council 2013). According to the British Sikh Report (2017), 91.6% of all British Sikhs consider themselves to be British Indian with smaller numbers corresponding to those of other ethnic groups (4.8%), other Asian backgrounds (2.2%) or British Afghan (1.4%). It was anticipated that this feasibility study using an established AF screening protocol adapted to this relatively homogeneous community would provide the foundations for future large-scale AF screening programmes amongst this or other South Asian groups.

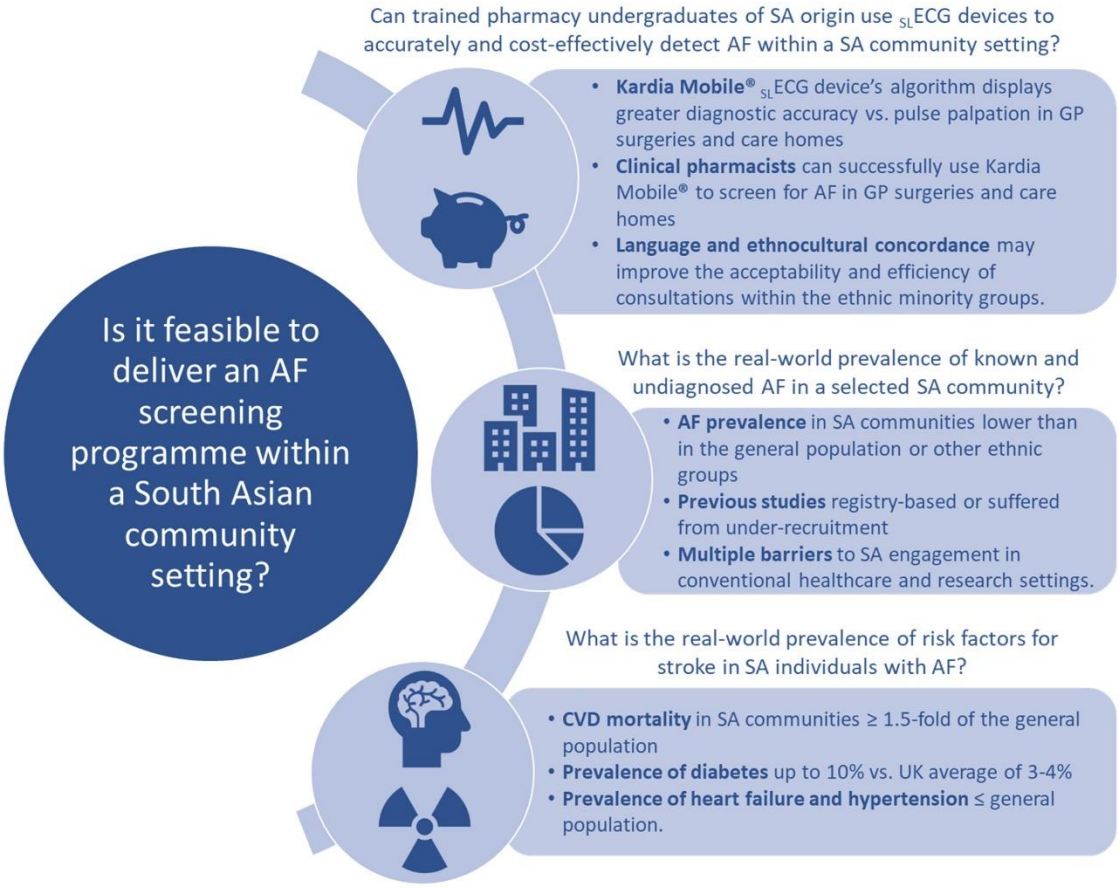


Figure 6.1 A summary of the study rationale and main questions

Data retrieved from Wild & Mckeigue (1997); Freeman et al. (2002); Laveist & Nuru-Jeter (2002); Conway & Lip (2003); Newton et al. (2005); Szczepura (2005); Gunarathne et al. (2008); British Heart Foundation (2010); Mathur et al. (2013); Ahmed et al. (2015); Gillott et al. (2017); Quay et al. (2017); O'Neill et al. (2018a); Waibel et al. (2018); Savickas et al. (2018). Abbreviations: AF – atrial fibrillation; CVD – cardiovascular; GP – general practitioner; SA – South Asian; SLECG – single-lead electrocardiogram.

6.2 Aim and objectives

Aim:

To assess the feasibility, accuracy and economic impact of AF screening using $_{SL}$ECG delivered by trained pharmacy undergraduates under the supervision of a CP at places of worship of a selected South Asian community.

Objectives:

1. To determine the recruitment rate amongst the community of South Asian individuals attending the places of worship, through a single time-point AF screening strategy using the protocol adapted from the PDAF study.
2. To measure the total prevalence of AF in the study sample as determined by the study cardiologist, including the prevalence of 'known' and 'unknown' AF cases, and the proportion of each that may qualify for OAC therapy.
3. To measure the prevalence of 'Unclassified' and 'Unreadable' provisional diagnoses in the study sample ascertained by the automated algorithm of the $_{SL}$ECG device compared to the study cardiologist.
4. To determine the differences in the prevalence of AF and non-AF comorbidities between the participants screened at places of worship in different geographical locations.
5. To determine the difference in the prevalence of AF between the participants aged < 65 and ≥ 65 years.
6. To determine the differences in the prevalence of non-AF comorbidities between the participants with and without the cardiologist-confirmed AF.
7. To determine the quality of $_{SL}$ECG recordings produced by trained pharmacy undergraduates.
8. To determine the accuracy of AF screening by the automated algorithm of the $_{SL}$ECG device compared to the study cardiologist.
9. To ascertain the proportion of screened individuals who were referred to the GP and were followed-up, including the yield of 'new' AF and non-AF diagnoses after an appropriate follow-up action.
10. To determine the feasibility of AF screening and the acceptability of the intervention proposed by obtaining feedback from study participants.
11. To estimate the financial impact of the AF screening strategy proposed for the healthcare system.

6.3 Methods

6.3.1 Study design

This was a prospective, cross-sectional diagnostic accuracy study (Thiese 2014), which evaluated the feasibility of the systematic population screening strategy of British Indian individuals aged ≥ 18 years attending a local Gurdwara during a public health campaign or event (Welton *et al.* 2017). Participants who were given an inconclusive test result or a provisional diagnosis of AF were given a referral letter and encouraged to see their GP. All were requested to inform the research team of the outcome of their GP review, however were not actively followed-up. The screening was conducted at a Gurdwara in Kent over a two-week period around the time of the Global AF Aware Week (November 2019), and then again at a Gurdwara in South Yorkshire during a one-day public health event in March 2020.

The study investigated the diagnostic accuracy of a single index test, which included the $_{SL}$ECG interpretation by the automated KMD algorithm, and was selected based on the results of the PDAF studies (this index test is appraised in section **2.6.1**). The accuracy of the index test was compared against the reference standard of $_{SL}$ECG interpretation by the cardiologist.

6.3.2 Study setting and sites

This study was conducted within the places of worship of a selected religious group, namely the Gurdwaras of Sikh communities of Kent and South Yorkshire. The AF screening programme in Kent was carried out at the Guru Nanak Darbar (Gravesend), which is thought to be one of the largest Gurdwaras in Europe, providing access to the population of approximately 7,743 Sikhs (7.6% of the total population of Gravesham borough) (Kent County Council 2013; Guru Nanak Darbar 2019). In order to enable a geographical comparison, the AF screening was also delivered in Sheffield (South Yorkshire) at the Shri Guru Gobind Singh Ji Sikh Temple, which is the only Gurdwara in the city serving the population of about 700 local Sikhs and those from the wider South Yorkshire region (Sheffield City Council 2011; Shri Guru Gobind Singh Ji Sikh Temple Sheffield 2020).

The two Gurdwaras were purposively chosen as locations for AF screening due to their close links with the MSOP through SB. The AF screening at the Gurdwara in Kent was also expected to provide a demographic comparison for the results of PDAF studies, which involved a predominantly White British population within the same region.

6.3.3 Selection and training of the research team

A group of 3rd and 4th year pharmacy undergraduate students enrolled onto the Master of Pharmacy (MPharm) programme at the MSOP were purposively sampled by the research team (Palys 2008) if they originated from a South Asian heritage (Office for National Statistics 2018c), and were able to communicate in either Hindi or Punjabi, which are the common languages of the British Sikh community (British Sikh Report 2019). All four pharmacy undergraduates who conducted AF screening at the Gurdwara in Kent were in their 4th (final) year of the MPharm degree whereas the two students who delivered the intervention in South Yorkshire where both 3rd years.

In preparation to conduct AF screening, all students underwent a two-hour mixed theory and practice training session with a CP who previously delivered AF screening during the PDAF studies in GP surgeries and care homes and was also a PhD researcher at the MSOP (VS). The training materials for this session were adapted from the PDAF study, and covered the fundamentals relating to AF diagnosis and treatment, the use of the KMD, the screening protocol/documentation and the principles of informed consent. During the practical component of the training session, VS was assisted by SB and another member of academic staff who were fluent in Punjabi and provided students with an opportunity to practise the screening process in this language. Similar to the PDAF study, pharmacy undergraduates were also given a chance to develop and consolidate their knowledge and skills during a two-hour 'mock' AF screening session with a group of South Asian volunteers, composed of students and staff from the MSOP, and the gatekeeper of the Gurdwara in Kent. Apart from mandatory training, pharmacy undergraduates were provided with regular feedback on their performance by VS and SB throughout the study.

During the screening process at each Gurdwara, students were supervised by CPs (VS, SC or SB) at a ratio of at least one CP per two students. The CPs ensured that students followed an appropriate study protocol and answered any questions the students or participants might have. In addition to supervisory responsibilities, SB provided students with support when recruiting eligible participants and when communicating in Punjabi or Hindi. The students and CPs conducting the screening at the Gurdwara in Kent were also assisted by the team of three additional members of academic staff from the MSOP, all of whom were introduced to the study and relevant documentation by the VS. Two members of staff were members of the Sikh community, were able to communicate in Punjabi and provided assistance with recruitment and translation where appropriate. The other member of staff helped with the technical aspects of the study, including the filing process and the printing of $_{SL}$ECG recordings.

6.3.4 Outcome measures

Primary outcome

The recruitment rate and sample size of all study participants and those of British Indian ethnicity, achieved by conducting a time-limited, single time point AF screening at the Gurdwaras in Kent and South Yorkshire.

Secondary outcomes

1. The total prevalence (%) of AF in the study sample, including the prevalence of 'known' and 'unknown' AF as determined by the reference standard.
2. The proportion (%) of individuals with 'known' and 'unknown' AF who may qualify for OAC therapy (defined as males with a CHA_2DS_2-VASc score of ≥ 1 or females with a score of ≥ 2 (NICE 2014a)).
3. The prevalence (%) of 'Unclassified' and 'Unreadable' diagnoses ascertained through $_{SL}$ECG interpretation by the KMD algorithm compared to the reference standard.
4. Statistically significant differences in the prevalence of AF and non-AF comorbidities between the participants screened in Kent and South Yorkshire.
5. Statistically significant difference in the prevalence of AF between the participants aged < 65 and ≥ 65 years.
6. Statistically significant differences in the prevalence of non-AF comorbidities between the participants with and without the reference standard-determined AF.
7. The quality of $_{SL}$ECG recordings produced by trained pharmacy undergraduates using the KMD, defined as proportions (%) of $_{SL}$ECG recordings classified by the CP as 'Excellent', 'Acceptable', 'Poor' or 'Unreadable'.
8. The diagnostic accuracy of pharmacy undergraduate-led AF screening using the automated KMD algorithm compared to the reference standard when screening all study participants and those aged ≥ 65 years. The diagnostic accuracy measures used for this outcome measure included: sensitivity, specificity, accuracy, PPV, FDR and FPR. The complete definitions of each measure are provided in section **2.7.2**.
9. The proportion (%) of screened individuals who were referred to the GP and were followed-up, including the yield of 'new' AF and non-AF diagnoses after the confirmation by $_{12L}$ECG.
10. The feasibility and acceptability of the AF screening strategy proposed, ascertained through feedback questionnaires from study participants.
11. The barriers to South Asian engagement in health screening initiatives, ascertained through feedback questionnaires from study participants.

12. The cost-effectiveness of the AF screening strategy proposed compared to the no-screening scenario. The cost-effectiveness of the intervention compared to no-screening was defined as an ICER < WTP of £20,000/QALY gained and a positive INB (NICE 2012a; Welton *et al.* 2017).

6.3.5 Sample size

In the absence of previous AF screening studies within the target setting or the target population, the desired sample size for this study was determined empirically using the guidance provided by the NIHR, which advised that a sample size between 24 and 50 individuals might be adequate for an initial feasibility study (NIHR Research Design Service London 2020). The recruitment rate and effect sizes obtained during this feasibility study were expected to inform the development of future larger-scale AF screening studies within a South Asian community setting (Blatch-Jones *et al.* 2018).

6.3.6 Eligibility criteria

Inclusion criteria

- Age ≥ 18 years.*

Exclusion criteria

- Age < 18 years
- Patients fitted with a pacemaker or defibrillator
- A lack of mental capacity to provide written informed consent with reference to the criteria outlined in the Mental Capacity Act 2005 (The National Archives 2005)
- Severe co-existing medical condition which a researcher considers to be the reason to exclude the patient from the study (e.g. terminal illness with life expectancy under 1 month).

**N.b.* participants of all ethnicities and religions were eligible to enter this study for ethical reasons. However, in order to maximise the generalisability of findings to a particular ethnic group, the data analysis presented below focused on participants of British Indian ethnicity, who formed the majority of the Sikh community (British Sikh Report 2017). Similarly, all adults aged ≥ 18 years were welcome to participate, although a separate sub-group analysis was carried out to compare the demographics of participants aged < 65 and those aged ≥ 65 who would qualify for opportunistic AF screening according to the ESC guidance (Kirchhof *et al.* 2016).

6.3.7 Translation of study materials

All study materials were adapted from those employed during the PDAF study in GP surgeries and the AF Association's materials used for the Global AF Aware Week campaigns with permission of each party. In order to increase the uptake of screening, the appropriate study materials, including the promotional poster/leaflet (**Appendix 46**)**,** text message invitation (**Appendix 47**), the study website (**Appendix 48**), PIL (**Appendix 49**), consent form (**Appendix 50**), CRF (**Appendix 51**), provisional diagnosis letter (**Appendix 52**), follow-up outcomes form (**Appendix 53**) and participant feedback questionnaire (**Appendix 54**) were translated in Punjabi and were made available to those participants who preferred to use this language instead of English. The translation of these documents was undertaken by an experienced translator within the MSOP who was fluent in both Punjabi and English. It was independently back-translated from Punjabi to English by an independent translator outside the MSOP to ensure the rigour and accuracy of translation (Chen & Boore 2010).

6.3.8 Recruitment and informed consent

Study participants were recruited using a convenience sampling approach, which involved consecutively recruiting all eligible individuals attending the participating Gurdwaras (Martínez-Mesa *et al.* 2016). Participant recruitment at the Gurdwara in Kent took place around the time of the Global AF Aware Week 2019 (18th-24th of November 2019), over a period of two weeks between the 12th and the 24th of November 2019. In order to increase the uptake of the intervention, the timing of the initiative in Kent was also aligned with the 550th birthday of Guru Nanak Devi Ji, the founder of Sikhism, which was celebrated on the 12th of November 2019. The recruitment and AF screening were conducted on eight days within a two-week period, lasted approximately 3-8 hours each day and offered prospective participants a variety of morning (9 am – 12 pm), afternoon (1 pm – 5 pm) and evening (5 – 8 pm) sessions for convenience purposes. Following the initial recruitment period, an additional opportunity to carry out AF screening arose at the Gurdwara in South Yorkshire, where recruitment took place at a one-day public health event facilitated by local HCPs on the 8th of March 2020 (between 10 am and 3 pm).

Individuals visiting either of the two Gurdwaras at the time of recruitment were approached and offered to take part by academic staff or pharmacy undergraduates (**Figure 6.2**).

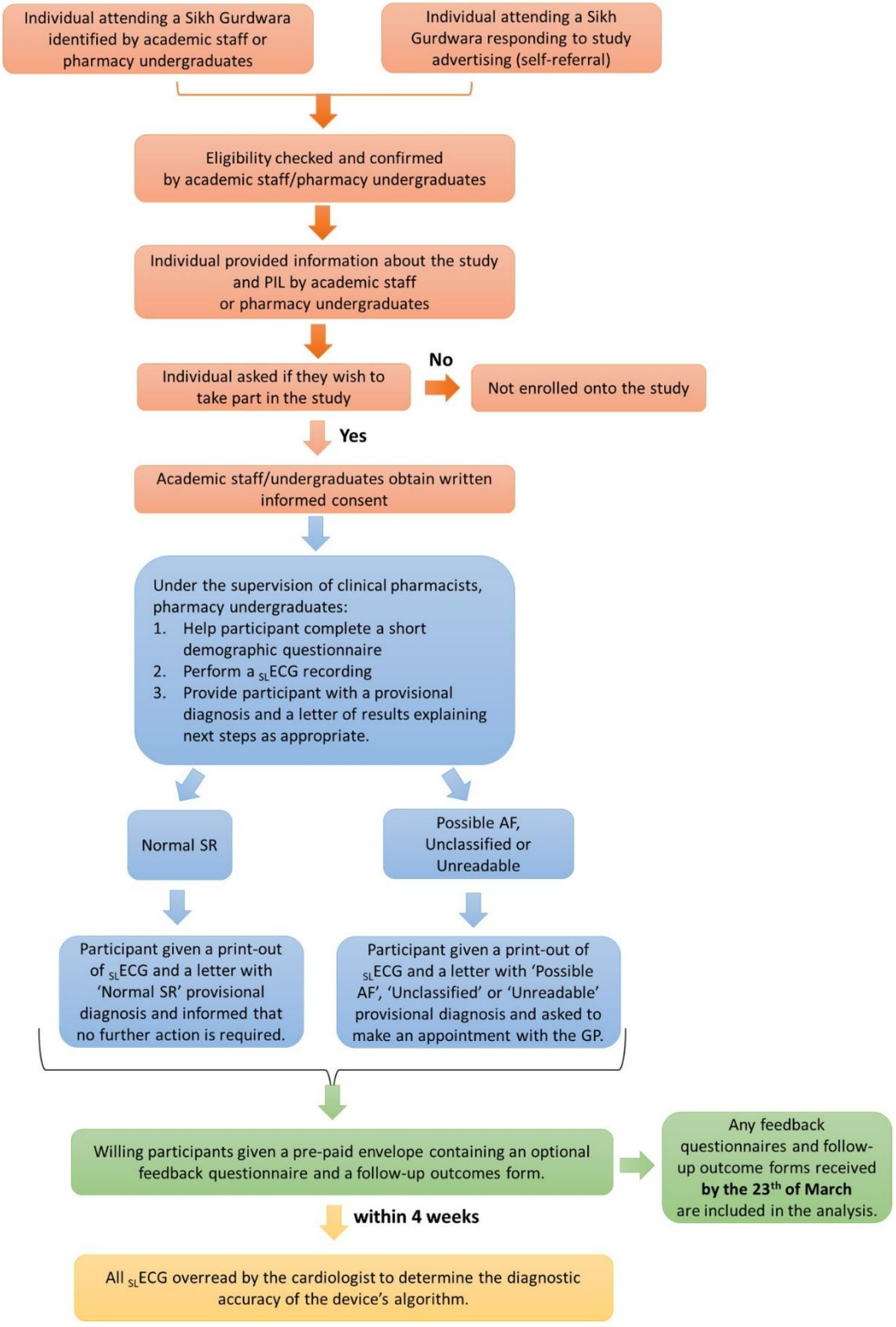


Figure 6.2 The flowchart of the study within the South Asian community setting

The figure includes the details of recruitment, informed consent, screening procedure and the post-appointment processes. Abbreviations: AF – atrial fibrillation; GP – general practitioner; PIL – participant information leaflet; $_{SL}$ECG – single-lead electrocardiogram; SR – sinus rhythm.

Alternatively, interested individuals were able to self-refer by responding to study advertisement, which included the display of physical promotional leaflets/posters at each Gurdwara (**Appendix 46**) and the study website (**Appendix 48**). In addition to these methods, during the recruitment in Kent, promotional leaflets/posters were displayed on the television screens and as a pull-up banner inside the Gurdwara. The gatekeeper of the Gurdwara in Kent also sent out the text message invitations (**Appendix 47**) via the Gurdwara Whatsapp® group on the 11th and the 18th of November 2019. The dates and times of AF screening scheduled to take place at the Gurdwara in Kent were displayed as a physical timetable alongside the promotional materials.

Prior to their enrolment onto the study, each prospective participant had their eligibility checked by members of the academic staff or pharmacy undergraduates who also provided them with a PIL in either English or Punjabi (**Appendix 49**). The PIL contained information about the study aims, the eligibility criteria, the AF screening and follow-up processes, the data management, the process of withdrawal, the funding details and relevant contact information. The academic staff or pharmacy undergraduates also provided prospective participants with a brief description of the study, the screening protocol and the management of their data with reference to the PIL in either English, Punjabi or Hindi. Participants were given as much time as they needed to make an informed decision as to whether or not to take part and were offered an opportunity to ask researchers any questions they might have. Those participants in Kent who were interested but were unable to participate on the day of recruitment could return and undergo AF screening at a more convenient time. A written informed consent was obtained from each participant by academic staff or pharmacy students immediately before the AF screening appointment, with one copy of the consent form (**Appendix 50**) retained by the participant and one by the research team.

6.3.9 Screening protocol and follow-up

Once informed consent was obtained, pharmacy undergraduates completed a short demographic questionnaire (**Appendix 51**)**.** They then proceeded to record a 30-second $_{SL}$ECG using a KMD and noted the provisional diagnosis by the device's algorithm on the CRF as either 'Normal SR', 'Possible AF', 'Unclassified' or 'Unreadable' as described for CPs in section **3.3.8**. These four diagnostic categories were the only possible classifications by the automated KMD algorithm at the time of the study design. The range of diagnostic classifications was however expanded to include 'Sinus Tachycardia' (HR ≥ 100 bpm) and 'Sinus Bradycardia' (HR ≤ 50 bpm) by the time the study was commenced in November

2019 (AliveCor 2019a). In order to account for these new diagnostic categories, where they occurred, pharmacy undergraduates were asked to manually record ‘Tachycardia’ or ‘Bradycardia’ in the comments section of the CRF, although participants who were issued either of these two provisional diagnoses followed the same protocol as those with ‘Unclassified’/’Unreadable’ diagnoses.

Following the $_{SL}$ECG recording, pharmacy undergraduates gave all participants a print-out of their $_{SL}$ECG and a letter containing the details of the provisional diagnosis by the KMD algorithm (**Appendix 52**). Participants who were issued a ‘Normal SR’ diagnosis by the KMD algorithm were advised that their heart rhythm was normal at that time, and that they did not require any further action. They were also advised that the KMD only provided a “snapshot” of their heart rhythm and did not account for the state of their heart or cardiovascular health as a whole. Participants who were given a ‘Possible AF’ diagnosis by the KMD were advised by students that there was a possibility they might have AF and that they should make an appointment to see their GP accordingly. They were also given further information about AF in a form of the (BHF 2014) booklet. Lastly, participants with provisional diagnoses of ‘Unclassified’/’Unreadable’ or ‘Sinus Tachycardia’/’Sinus Bradycardia’ were informed that, albeit their $_{SL}$ECG did not show AF, the test result was inconclusive and that they should make an appointment to see their GP. After the screening appointment, all participants, regardless of their provisional diagnosis, were asked to complete an optional anonymous feedback questionnaire (**Appendix 54**), which they were able to hand in to researchers on the day of screening or post back using a pre-paid envelope. Those participants who were referred to the GP were also given a follow-up outcomes form (**Appendix 53**), which they could return to the research team after their GP appointment using the same pre-paid envelope. Any feedback questionnaires and follow-up outcome forms received by the 23rd of March 2020 were included in the final data analysis.

All $_{SL}$ECG recordings produced during the study were pseudonymised and securely emailed by pharmacy undergraduates to a corporate, password-protected University of Kent email address. They were then securely downloaded and assessed for quality by VS using the principles outlined in section **3.3.8** as either ‘Excellent’, ‘Acceptable’, ‘Poor’ or ‘Unreadable’. All $_{SL}$ECGs were also shared via the secure NHS.net server with the study cardiologist who over-read them within four weeks to either confirm or reject the provisional diagnoses. The cardiologist’s diagnoses were used as a reference standard to estimate the diagnostic accuracy of the KMD algorithm and were not used to inform the follow-up actions by the GP as undertaken during the PDAF study in GP surgeries or care homes.

6.3.10 Participant feedback questionnaire

The acceptability of the AF screening intervention was assessed using a 17-item questionnaire which was offered to all study participants (**Appendix 54**). The aim of the questionnaire was to ascertain the participants' knowledge about AF, their experience during the test, any perceived barriers to South Asian engagement in health screening, and their views about the potential future health screening initiatives at the Gurdwara. The questionnaire consisted of 16 closed-ended questions, which included six three- or four-point Likert scale questions (from 'Very important', 'Very satisfied' or 'Very good' to 'Not important', 'Very dissatisfied' or 'Very Poor'), nine 'Yes' or 'No' answer questions and one multiple-answer question in relation to barriers affecting South Asian engagement in health screening. Participants were also able to add free-text responses to four of these questions relating to positive/negative aspects of the service, any future screening initiatives at the Gurdwara and barriers to South Asian engagement in health screening. Another open-ended item at the end of the questionnaire offered respondents an opportunity to provide further comments to help the research team improve the AF screening strategy proposed.

6.3.11 Quantitative data analysis

The quantitative data analysis followed the fundamental statistical considerations and assumptions outlined in section **2.7**. The data were overall analysed and presented as for the PDAF study in GP surgeries (section **3.4**). The CHA_2DS_2-VASc score of participants with 'Possible AF' was normally distributed and was expressed both as a mean ± standard deviation and as a median [interquartile range] to enable a comparison with data from the PDAF study. The data analysis of study outcomes focused on the homogeneous sample of participants who declared their ethnicity as British Indian in the pre-screening demographic questionnaire. Any associations between the geographical location of AF screening and the participants' responses to closed-ended questions of the feedback questionnaire were ascertained using the Pearson's Chi-square or Fisher's exact test with Freeman-Halton extension and a Bonferroni correction where appropriate as described in section **2.7.1**. According to the study cardiologist, none of the participants screened in South Yorkshire displayed a $_{SL}$ECG corresponding to 'Possible AF', therefore the analysis of screening outcomes, diagnostic accuracy, cost-effectiveness and follow-up outcomes focused on British Indian participants recruited in Kent ('the main cohort'). The sub-group analyses compared the demographic characteristics of study participants screened in Kent versus (vs.) those in South Yorkshire, and the characteristics of participants with and without the cardiologist-confirmed AF. The prevalence of AF amongst the sub-group of participants aged < 65 years was also compared with that amongst those aged ≥ 65 years who would benefit the most from AF detection (Kirchhof *et al.* 2016). The prevalence of non-AF

comorbidities amongst the participants recruited in Kent and South Yorkshire was age-adjusted using the age distribution of the British Indian population in England and Wales (GOV.UK 2018b) and a direct standardisation method adapted from Naing (2000) and Gillott et al. (2017). The diagnostic accuracy of the automated KMD algorithm for the detection of AF was compared between the entire sample and the participants aged ≥ 65 years.

6.3.12 Economic analysis

The economic analysis was constructed as a Markov cohort simulation and focused on the comparison of costs and utilities accrued by two hypothetical cohorts of individuals with AF aged ≥ 18, derived from the total population of British Indian individuals across England and Wales (a population of 1,412,958) (Office for National Statistics 2018c): the 'intervention cohort' or the 'screening strategy' (who underwent the screening) and the 'control cohort' or the 'no-screening strategy (who did not undergo the screening). The detailed rationale for this method and the breakdown of key model assumptions is provided in section **2.8.**

The baseline transition probabilities between the health states were ascertained from major OAC trials and were adjusted for the increased rates of ischaemic stroke and stroke mortality amongst individuals of South Asian ethnicity (Wild & Mckeigue 1997; Gunarathne *et al.* 2009; George *et al.* 2017). The baseline mortality rate was also corrected for the lower all-cause mortality rate observed in South Asian individuals born outside the UK (Bhopal *et al.* 2018) (**Appendix 55**). The assumptions of the base-case economic analysis utilised the study outcomes derived from the sample of British Indian participants screened in Kent, and in addition to general model assumptions (section **2.8.3**), included the following:

- The prevalence of total and 'unknown' AF of 1.0% as determined by the reference standard (*N.b.* none of the participants with 'Possible AF' declared that they had a diagnosis of AF at the time of screening).
- The rate of 'Unclassified'/'Unreadable'/'Sinus Tachycardia' diagnoses of 9.1% as determined by $_{SL}$ECG interpretation using the KMD algorithm.
- The sensitivity and specificity of the KMD algorithm with regards to the reference standard of 100% and 99.2%, respectively.
- That 60% of all participants with 'new' AF were eligible for OAC therapy (a CHA_2DS_2-VASc score of ≥ 2 for females, or ≥ 1 for males).

The general costs of the base-case model were as outlined in section **2.8.4** and **Appendix 55**, and included the purchasing cost of KMDs, the supervisory time of CPs (seven

minutes/appointment) (NHS Employers 2019), relevant medical interventions ($_{12L}$ECG/GP interpretation and GP/cardiologist appointments for 'new' AF) (NHS Improvement 2017; Welton *et al.* 2017), the cost of OAC therapy, ischaemic strokes/major bleeds (NICE 2014b) and false positive AF and 'Unclassified'/'Unreadable'/'Sinus Tachycardia' diagnoses by the KMD algorithm. The purchasing cost of the KMD included 806 devices with reference to the AHSN initiative in England, adjusted for the population size of British Indian individuals in England and Wales (The AHSN Network 2019a; AliveCor 2019c).

The PSA employed a Monte Carlo simulation generating 100,000 iterations of the economic model, and tested the major deviations from the base case investigated during the PDAF study in GP surgeries (sections **2.8.5** and **3.3.11**). An exception to this was the cost-effectiveness analysis of pulse palpation-based AF screening, which was replaced with that of the KMD-based screening in a sub-group of British Indian participants aged ≥ 65 years. Within this deviation, the key differences compared to the base-case model included:

- The all-cause mortality was age-adjusted for individuals aged ≥ 65 years (Office for National Statistics 2017b).
- The acquisition cost of KMD devices included the cost of 66 devices (adjusted for the British Indian population aged ≥ 65 years in England and Wales of 115,863 individuals) (Office for National Statistics 2018c).
- The prevalence of total and 'unknown' AF of 1.5% as determined by the reference standard.
- The rate of 'Unclassified'/'Unreadable'/'Tachycardia'/'Bradycardia' diagnoses of 6.7% as determined by $_{SL}$ECG interpretation using the KMD algorithm.
- The specificity of the KMD algorithm with regards to the reference standard of 98.4%.
- 100% of all participants with 'new' AF being eligible for OAC therapy.

The mean INBs were calculated per British Indian individual with AF and per all British Indian individuals with 'new', screening-detected AF across England and Wales (Office for National Statistics 2018c).

6.4 Results

6.4.1 Study participants

The pharmacy undergraduate-led AF screening took place on eight days between the 12th and the 24th of November 2019 at the Gurdwara in Kent and on the 8th of March 2020 at the Gurdwara in South Yorkshire. A total of 611 eligible participants took part in the initiative at the two Gurdwaras: 560/611 (91.7%) in Kent and 51/611 (8.3%) in South Yorkshire (**Figure 6.3**) Of these, 39/611 (6.4%) were excluded from data analysis either because they were not of British Indian ethnicity (5.9%, 36/611) or because their gender and age were both missing from pre-screening demographic questionnaires (0.5%, 3/611). Out of the 36 participants who did not declare their ethnicity as British Indian, 13/611 (2.1%) indicated no particular ethnicity whereas the rest considered themselves to be either White British or English (1.6%, 10/611), Afghan (1.1%, 7/611), Japanese (0.5%, 3/611), European, Portuguese Indian or Latvian (0.2%, 1/611 each). None of the participants excluded from the study had a cardiologist-confirmed AF.

A total of 572/611 of eligible participants (93.6%) were included in data analysis: 528/560 (94.3%) of participants from the main cohort screened in Kent and 44/51 (86.3%) of those screened in South Yorkshire. Compared to participants recruited in South Yorkshire, a greater proportion of those screened in Kent were males (47.2%, 249/528 vs. 36.4%, 16/44) and a smaller fraction were born in the UK (16.2%, 84/520 vs. 27.3%, 12/44), although these differences did not reach statistical significance (**Table 6.1**). Participants in Kent were also on average six years older (61.0 [48.0; 68.0] years vs. 55.0 (40.0; 65.8] years vs.; Mann-Whitney U test, $p = 0.023$), and had a significantly greater prevalence of hypertension (36.0%, 190/528 vs. 15.9%, 7/44; Chi-square test, $p = 0.007$). The significance of the latter difference was diminished upon age-adjustment (16.0% vs. 7.7% for age-adjusted prevalence of hypertension amongst participants in Kent and South Yorkshire, respectively; Chi-square test; $p = 0.082$).

None of the participants in either of the two cohorts reported a previous history of AF at the time of screening, and all five cases of cardiologist-confirmed AF were detected amongst individuals screened in Kent (1.0%, 5/528 vs. 0%, 0/44; Fisher's exact test, $p = 1.000$). Three of the five cardiologist-determined possible cases of AF occurred amongst those aged ≥ 65 years (1.5%, 3/195) and one was detected in < 65s (0.3%, 1/323; Fisher's exact test, $p = 0.152$; *N.b.* age was missing for 10 participants in Kent including one other participant with cardiologist-determined AF). Similar proportions of participants in both

cohorts considered themselves to be alcohol drinkers (25.0%, 131/524 vs. 20.5%, 9/44 for those in Kent and South Yorkshire, respectively) and only 2.3% in each case were current smokers. The average BMI in the two groups was comparable and above 25 kg/m^2.

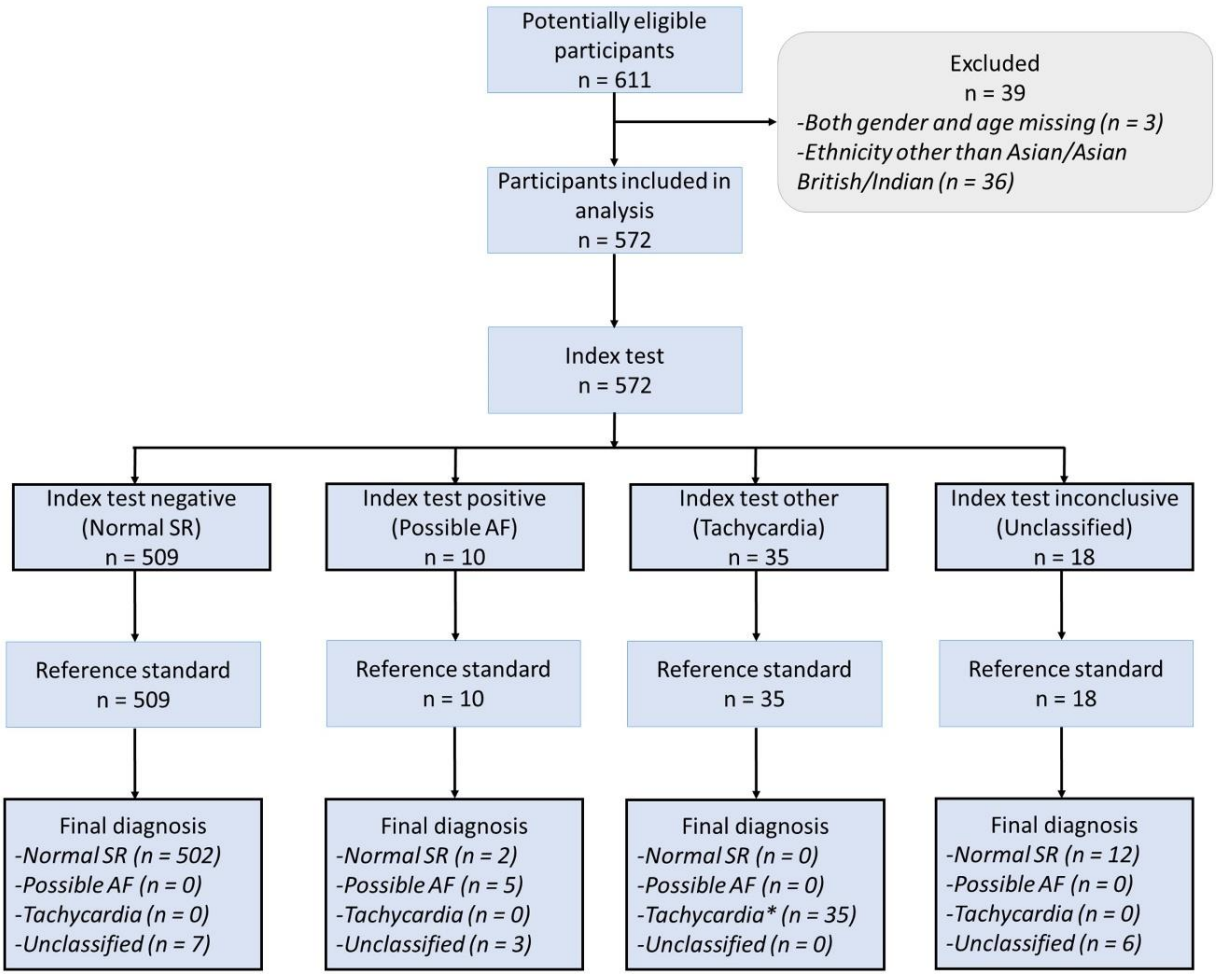


Figure 6.3 STARD flow diagram for the AF screening study within a South Asian community

*The figure was adapted from Cohen et al. (2016), and displays the inclusion/exclusion of study participants and the diagnostic classification by the index test, i.e. the algorithm of single-lead ECG device, and the reference standard, i.e. the cardiologist's interpretation of single-lead ECG. N.b. 'Tachycardia' refers to sinus tachycardia. *With or without other diagnoses. Abbreviations: AF – atrial fibrillation; SR – sinus rhythm; Standards for Reporting Diagnostic Accuracy Studies.*

Table 6.1 Demographic characteristics of participants in Kent and South Yorkshire

Continuous variables are expressed as a median [interquartile range]. Categorical variables are expressed as a number of participants (% total of the group). Between-group differences determined using a Mann-Whitney U test for numerical variables and a Pearson's Chi-square or Fisher's exact test with Freeman-Halton extension and Bonferroni correction as appropriate for categorical variables. Abbreviations: AF – atrial fibrillation; BMI – body mass index; bpm – beats per minute; DVT – deep vein thrombosis; IHD – ischaemic heart disease; PAD – peripheral arterial disease; PE – pulmonary embolism; TIA – transient ischaemic attack.

Characteristics	**Participants in Kent (n = 528)**	**Participants in South Yorkshire (n = 44)**	**P value (2-sided)**
Age, years	61.0 [48.0; 68.0] (n = 518)	55.0 (40.0; 65.8]	0.023
Male	249 (47.2)	16 (36.4)	0.168
Country of Birth	*n = 520*	*n = 44*	
India	394 (75.8)	31 (70.5)	0.432
UK	84 (16.2)	12 (27.3)	0.060
Kenya	25 (4.8)	0 (0.0)	0.137
Other	17 (3.3)	1 (2.3)	0.718
Language of consultation	*n = 515*	*n = 44*	
English	352 (68.3)	33 (75.0)	0.361
Punjabi	132 (25.6)	10 (22.7)	0.671
Mixed English & Punjabi	21 (4.1)	0 (0.0)	0.172
Hindi	10 (1.9)	1 (2.3)	0.879
Current alcohol drinker	131 (25.0) (n = 524)	9 (20.5)	0.502
Current smoker	12 (2.3) (n = 524)	1 (2.3)	1.000
Height, cm	165.1 [160.0; 172.7] (n = 524)	161.5 [156.3; 170.4]	0.090
Weight, kg	71.0 [64.0; 80.0] (n = 513)	74.7 [64.1; 83.0]	0.597
BMI, kg/m^2	25.8 [23.8; 28.5] (n = 510)	27.0 [23.9; 31.4]	0.102
Heart rate device, bpm	80 [72; 91]	78.5 [71.0; 87.0]	0.255
Comorbidities			
Hypertension	190 (36.0)	7 (15.9)	0.007
Hypercholesterolaemia	178 (33.7)	11 (25.0)	0.238
Diabetes mellitus	97 (18.4)	6 (13.6)	0.432
IHD	24 (4.5)	2 (4.5)	1.000
PAD	18 (3.4)	0 (0.0)	0.385
Stroke/TIA	12 (2.3)	0 (0.0)	0.613
DVT/PE/systemic embolism	11 (2.1)	0 (0.0)	1.000
Heart failure	4 (0.8)	0 (0.0)	1.000

Most consultations in both Kent and South Yorkshire were conducted in English (68.3%, 352/515 and 75.0%, 33/44, respectively), with a smaller number of participants choosing to communicate in Punjabi (25.6%, 132/515 and 22.7%, 10/44, respectively), mixed English and Punjabi (4.1%, 21/515 and 0%, 0/44) or Hindi (1.9%, 10/515 and 2.3%, 1/44). The median appointment time was 7.0 [6.0; 8.0] minutes during AF screening in Kent and 8.0 [6.0; 9.0] minutes when screening in South Yorkshire.

6.4.2 Screening outcomes

Participants with 'Possible AF'

Following AF screening at each Gurdwara, the study cardiologist was asked to retrospectively inspect all $_{SL}$ECG recordings and indicate both their suspected diagnosis, and where appropriate, a follow-up action based on their diagnosis, for instance, a referral for a $_{12L}$ECG. The cardiologist was able to interpret $_{SL}$ECG recordings of all 572 participants screened at the Gurdwaras in Kent and South Yorkshire (100%). None of the participants screened during a public health event in South Yorkshire displayed a 'Possible AF' on their $_{SL}$ECG recordings, therefore the analysis of screening outcomes focused on the results of participants recruited in Kent (**Figure 6.4**).

According to the study cardiologist, 5/528 of individuals who underwent AF screening in Kent exhibited the signs of 'Possible AF' on their $_{SL}$ECG and would have required a $_{12L}$ECG confirmation, giving rise to the total AF prevalence of 1.0% (95% CI, 0.3-2.2%). None of the participants declared that they had a medical history of AF at the time of the screening appointment, and as such, the prevalence of 'known' AF was assumed to be 0% whereas the prevalence of 'unknown' or undiagnosed AF matched that of the total prevalence.

As shown in **Table 6.2**, participants with cardiologist-confirmed 'Possible AF' had a median age of 82.0 [56.8; 84.8] years and were on average 21 years older than the rest of the study group (61.0 [48.0; 68.0] years; Mann-Whitney U test, p = 0.034). Four out of five participants with cardiologist-confirmed AF also spoke Punjabi during the consultation compared to only a quarter in the rest of the group (80.0%, 4/5 vs. 25.1%, 128/510; Fisher's exact test, p = 0.041) who were instead predominantly English speakers (68.8%, 351/510 vs. 20.0%, 1/5). There were no substantial differences in the prevalence of non-AF comorbidities or the average number of such comorbidities between those with cardiologist-confirmed AF and those with other diagnoses (1.0 [0.5; 2.0] and 1.0 [0.0; 2.0] comorbidities, respectively; Mann-Whitney U test, p = 0.493).

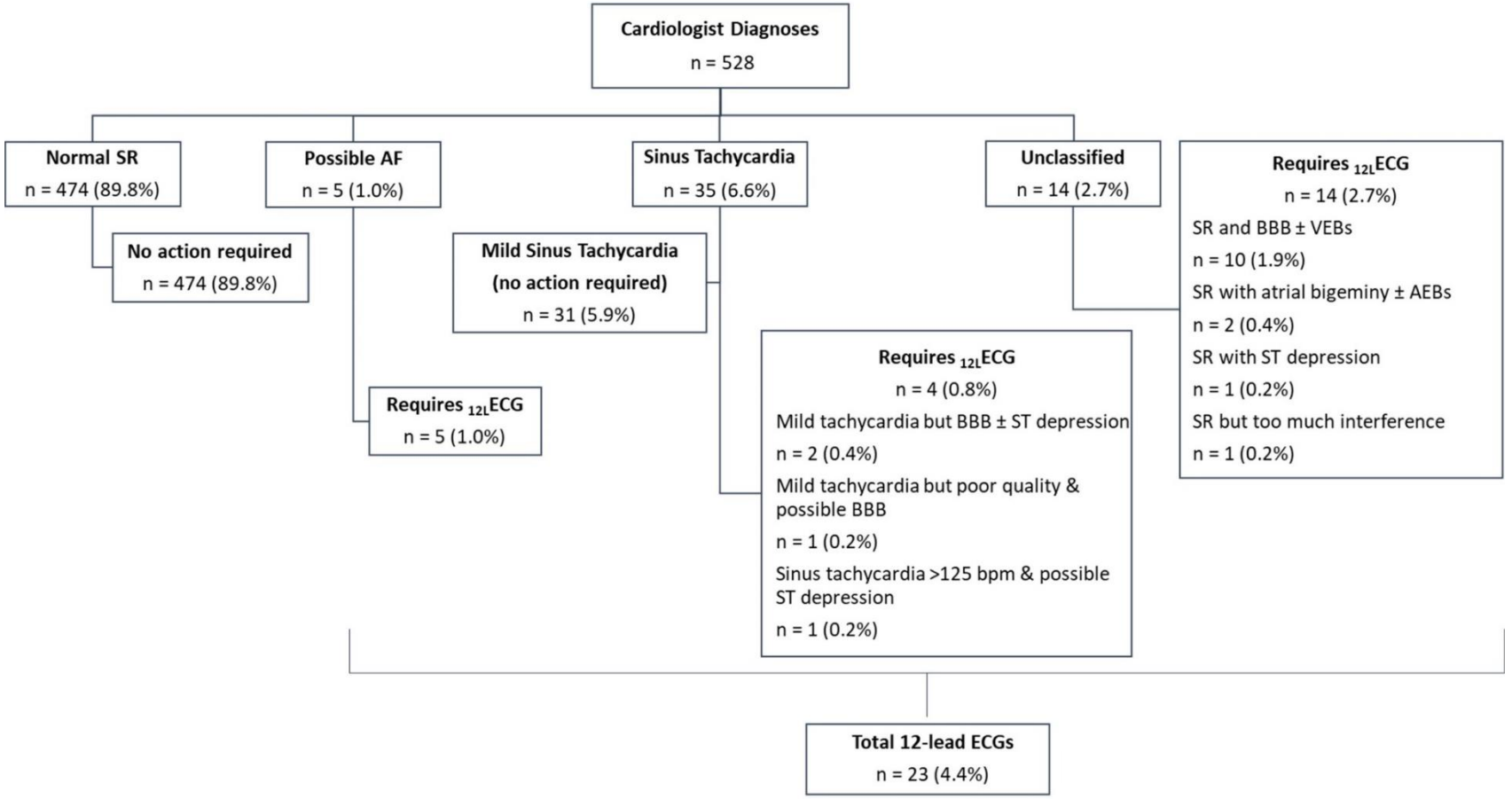


Figure 6.4 Cardiologist's diagnoses and recommended follow-up actions based on the interpretation of single-lead ECG recordings

All variables are expressed as a number of participants (% total). Abbreviations: Abbreviations: 12LECG – 12-lead electrocardiogram; AEBs – atrial ectopic beats; AF – atrial fibrillation; BBB – bundle branch block; bpm – beats per minute; SR – sinus rhythm, ST – ST segment of the ECG cycle; VEBs – ventricular ectopic beats.

Table 6.2 Demographic characteristics of participants with cardiologist-confirmed 'Possible AF' diagnoses

Continuous variables are expressed as a median [interquartile range]. Categorical variables are expressed as a number of participants (% total of the group). Between-group differences determined using a Mann-Whitney U test for numerical variables and a Pearson's Chi-square or Fisher's exact test with Freeman-Halton extension and Bonferroni correction as appropriate for categorical variables. Abbreviations: AF – atrial fibrillation; BMI – body mass index; bpm – beats per minute; DVT – deep vein thrombosis; IHD – ischaemic heart disease; PAD – peripheral arterial disease; PE – pulmonary embolism; TIA – transient ischaemic attack.

Characteristics	**Possible AF (n = 5)**	**Non-AF (n = 523)**	**P value (2-sided)**
Age, years	82.0 [56.8; 84.8] (n = 4)	61.0 [48.0; 68.0] (n = 514)	0.034
Male	1 (20.0)	248 (47.4)	0.377
Country of Birth	*n = 4*	*n = 516*	
India	3 (75.0)	391 (75.8)	0.971
UK	1 (25.0)	83 (16.1)	0.629
Kenya	0 (0.0)	25 (4.8)	0.652
Other	0 (0.0)	17 (3.3)	0.712
Language of consultation	*n = 5*	*n = 510*	
English	1 (20.0)	351 (68.8)	0.156
Punjabi	4 (80.0)	128 (25.1)	0.041
Mixed English & Punjabi	0 (0.0)	21 (4.1)	0.643
Hindi	0 (0.0)	10 (2.0)	0.752
Current alcohol drinker	1 (20.0)	130 (25.0) (n = 519)	1.000
Current smoker	0 (0.0)	12 (2.3) (n = 519)	1.000
Height, cm	162.6 [156.2; 163.9]	165.1 [160.0; 172.7] (n = 519)	0.128
Weight, kg	69.9 [67.0; 78.5]	71.0 [63.6; 80.0] (n = 508)	0.932
BMI, kg/m^2	26.4 [26.1; 30.6]	25.8 [23.8; 28.5] (n = 505)	0.203
Heart rate device, bpm	99 [67; 131]	80 [72; 90]	0.110
Comorbidities			
Hypertension	2 (40.0)	188 (35.9)	1.000
Hypercholesterolaemia	1 (20.0)	177 (33.8)	0.453
Diabetes mellitus	1 (20.0)	96 (18.4)	0.639
IHD	0 (0.0)	24 (4.6)	1.000
PAD	1 (20.0)	17 (3.3)	0.160
Stroke/TIA	1 (20.0)	11 (2.1)	0.109
DVT/PE/systemic embolism	0 (0.0)	11 (2.1)	1.000
Heart failure	0 (0.0)	4 (0.8)	1.000

The mean CHA_2DS_2VASc score amongst the four participants with cardiologist-determined 'Possible AF' and the full demographic data was 3.8 ± 2.5 (or a median of 3.5 [1.5; 6.3]). Three out of four were aged ≥ 80 years and had a CHA_2DS_2VASc ≥ 3 (0.6%, 3/528), thus potentially qualifying them for OAC therapy should AF have been formally diagnosed. One participant suffered from hypertension whereas one other participant reported a history of diabetes mellitus. The third participant who qualified for OAC therapy was a female with a medical history of hypertension, peripheral arterial disease and stroke, giving rise to a CHA_2DS_2VASc score of seven. The last participant with complete demographic data and a suspected AF was a 49-year-old female who had no other comorbidities. The female participant with 'Possible AF' who did not indicate her age on the demographic questionnaire suffered from hypercholesterolaemia and thyroid disease and took rivaroxaban for an unknown indication. None of the other four participants took OAC therapy at the time of screening.

Participants with non-AF diagnoses

Besides the five 'Possible AF' diagnoses, the cardiologist classified 474/528 (89.8%) of participants as displaying 'Normal SR', 35/528 (6.6%) – as 'Sinus Tachycardia' and 14/528 (2.7%) – as 'Unclassified'. According to the cardiologist, all participants with 'Normal SR' diagnoses and 31/528 (5.9%) of those with 'Sinus Tachycardia' who had a mildly elevated HR would not have required any further follow-up intervention. The remaining 4/528 (0.8%) participants with 'Sinus Tachycardia' would have needed a $_{12L}$ECG because they either had a BBB (0.4%, 2/528; *N.b.* one of these participants also displayed an ST-segment depression), a poor quality recording with a possible BBB (0.2%, 1/528) or a more pronounced sinus tachycardia with a HR > 125 bpm and a possible ST-segment depression (0.2%, 1/528).

All 14/528 participants with 'Unclassified' diagnoses (2.7%) would have also required a $_{12L}$ECG follow-up because they had a suspected a BBB (1.9%, 10/528; *N.b.* one of these participants displayed VEBs), SR with atrial bigeminy (0.4%, 2/528; *N.b.* one of these participants also displayed additional AEBs), SR with an ST-segment depression (0.2%, 1/528) or too much interference on their $_{SL}$ECG recording (0.2%, 1/528). In total, with reference to cardiologist's interpretation of $_{SL}$ECG, 23/528 (4.4%) of participants with 'Possible AF' diagnoses or other abnormalities should have been referred to the GP following AF screening at the Gurdwara in Kent.

6.4.3 Diagnostic accuracy

The KMD algorithm allocated 471/528 (89.2%) of participants screened in Kent a provisional diagnosis of 'Normal SR', 9/528 (1.7%) – a diagnosis of 'Possible AF', 35/528 (6.6%) – a diagnosis of 'Sinus Tachycardia' and 13/528 (2.5%) – an 'Unclassified' status (**Figure 6.5**). The device correctly classified all five participants with cardiologist-confirmed 'Possible AF' diagnoses resulting a perfect sensitivity of 100% (**Table 6.3**). However, it misclassified four participants without AF as 'Possible AF' giving rise to an FPR of 0.8% and an FDR of 44.4%. Out of the four false positive diagnoses by the KMD algorithm, one participant had a cardiologist-determined 'Normal SR' (0.2%, 1/528) and did not need any follow-up whereas the other three traces were deemed by the cardiologist to be 'Unclassified' (0.6%, 3/528) and required a $_{12L}$ECG either due to the presence of atrial bigeminy (0.4%, 2/528; *N.b.* one participant had AEBs) or too much interference on $_{SL}$ECG (0.2%, 1/528). Despite these misclassifications, the overall diagnostic accuracy of the KMD algorithm for AF was high at 99.2%, and it displayed a substantial inter-rater agreement with the cardiologist of 0.71 (McNemar's test for differences in diagnostic classification, p = 0.125).

In addition to one false positive AF diagnosis in a participant with a cardiologist-determined 'Normal SR', the use of KMD algorithm resulted in 31 unnecessary referrals amongst those with 'Sinus Tachycardia' who had a mildly elevated HR and did not require any follow-up action (5.9%, 31/528). It also produced eight false positive 'Unclassified' diagnoses in participants with cardiologist-confirmed 'Normal SR' (1.5%, 8/528). Where indicated by the cardiologist, this occurred due to the presence of VEBs or sinus arrhythmia (0.4%, 2/528 each).

Besides the unnecessary $_{12L}$ECG referrals in 40/528 (7.6%) participants, the KMD algorithm missed six participants with cardiologist-confirmed 'Unclassified' diagnoses who would have benefitted from a confirmatory $_{12L}$ECG because they had a suspected a BBB (1.0%, 5/528; *N.b.* one displayed VEBs) or SR with an ST-segment depression (0.2%, 1/528). All in all, the use of the KMD algorithm produced 57 referrals for $_{12L}$ECG (10.8%, 57/528), which included 34 additional referrals (6.4%, 34/528) compared to the study cardiologist.

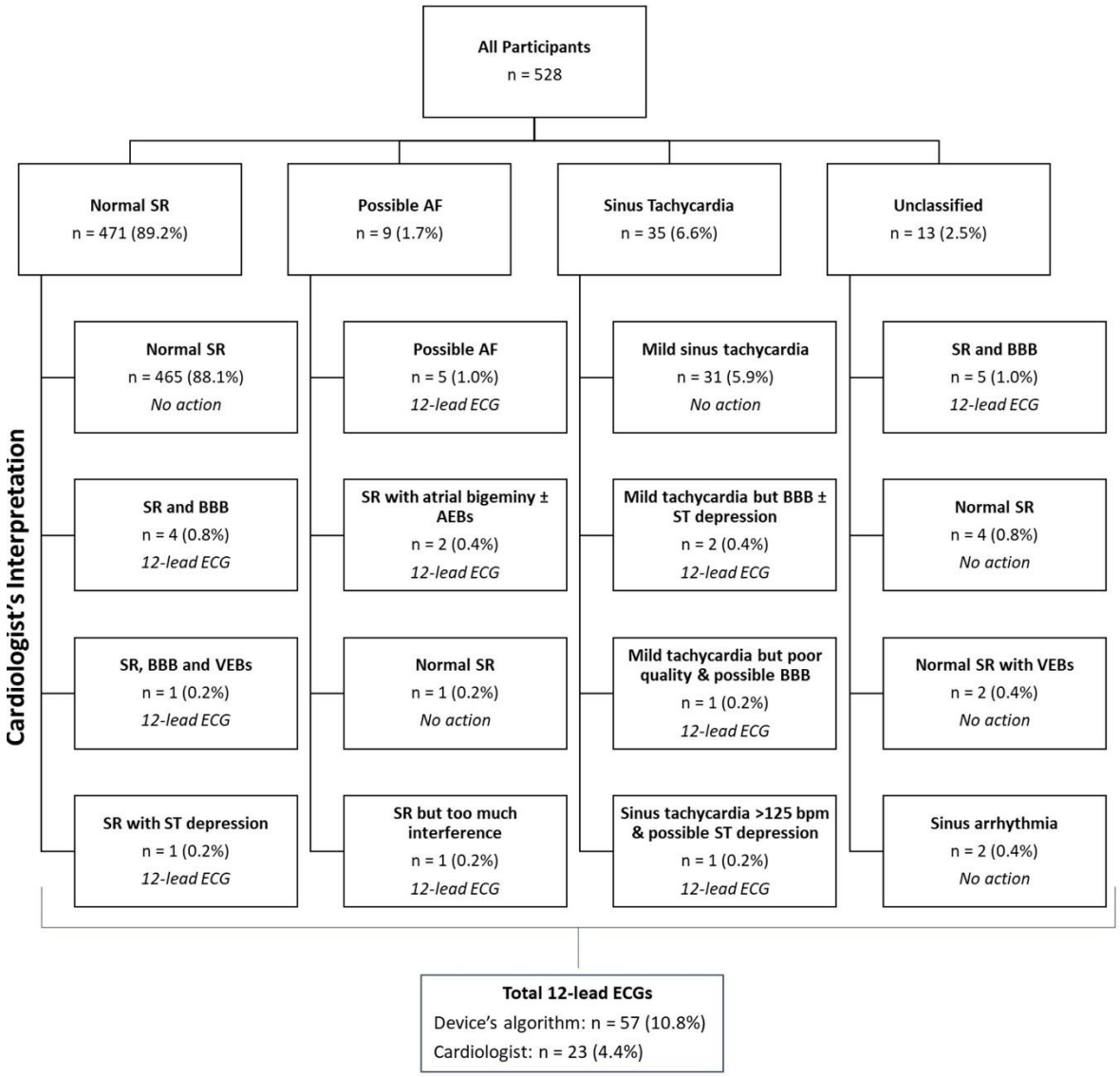


Figure 6.5 Diagnoses derived by the KMD algorithm compared to the cardiologist's interpretation of single-lead ECG recordings

The follow-up actions which would have been proposed by the cardiologist (e.g. 12-lead ECG) are indicated below each diagnostic category. All variables are expressed as a number of participants (% total). Abbreviations: AEBs – atrial ectopic beats; AF – atrial fibrillation; BBB – bundle branch block; bpm – beats per minute; ECG – electrocardiogram; KMD - Kardia Mobile® device; SR – sinus rhythm; ST – ST segment of the ECG cycle; VEBs – ventricular ectopic beats.

Table 6.3 Diagnostic accuracy of the KMD algorithm for the detection of 'Possible AF' in all participants compared to those aged 65 and above

The accuracy of $_{SL}$ECG interpretation by the KMD algorithm was estimated compared to the cardiologist's interpretation of $_{SL}$ECG (the reference standard). All measures are expressed as a mean (95% confidence intervals). Abbreviations: FDR – false discovery rate; FPR – false positive rate; GP – general practitioner; KMD - Kardia Mobile® device; PPV – positive predictive value; $_{SL}$ECG – single-lead electrocardiogram.

Diagnostic Accuracy Measures	**Study Groups**	
	All participants (n = 528)	*Participants aged ≥ 65 (n = 195)*
Sensitivity	100	100
Specificity	99.2 (98.1-99.8)	98.4 (95.5-99.7)
Accuracy	99.2 (98.1-99.8)	98.5 (95.6-99.7)
FPR	0.8 (0.2-1.9)	1.6 (0.3-4.5)
PPV	55.6 (21.2-86.3)	50.0 (11.8-88.2)
FDR	44.4 (13.7-78.8)	50.0 (11.8-88.2)
Cohen's Kappa	0.71 (0.44-0.98)	0.66 (0.30-1.02)

Apart from the diagnostic accuracy analysis within the main cohort, a further analysis explored the diagnostic performance of the KMD algorithm within the sub-group of individuals aged ≥ 65 years who might benefit the most from AF detection. The KMD algorithm maintained a 100% sensitivity for AF in this sub-group, identifying all three cases of cardiologist-confirmed AF. Due to three false-positive AF diagnoses, the specificity of the KMD algorithm within a smaller sample of ≥ 65s was marginally lower than that observed for all study participants (98.4% vs. 99.2%, respectively), with an FPR of 1.6% and an FDR of 50%. Reflecting this level of false positive diagnoses, the overall diagnostic accuracy and the Cohen's Kappa between the KMD and the cardiologist were slightly below the values noted for all study participants (98.5% vs. 99.2% and 0.66 vs. 0.71, respectively).

Following AF screening, in addition to cardiologist's interpretation, all $_{SL}$ECGs were also reviewed by one of the CPs to determine the quality of the recordings. The majority of participants screened in Kent only had one $_{SL}$ECG recording (94.9%, 501/528), although a second recording was performed in 5.1% (27/528) of cases due to poor quality of the original trace. According to the CP, close to 60% of participants screened in Kent displayed $_{SL}$ECG recordings of 'Excellent' quality (58.0%, 306/528) and more than a third – of 'Acceptable' quality (35.8%, 189/528). Less than 10% of $_{SL}$ECG traces were rated as either 'Poor' (5.9%, 31/528) or 'Unreadable' (0.4%, 2/528).

6.4.4 Follow-up outcomes

A total of 57/528 (10.8%) of participants who underwent AF screening using the KMD at the Gurdwara in Kent were referred to their GP for a further review and $_{12L}$ECG. Only 3/57 (5.3%) of participants returned the optional follow-up outcomes forms by post. All three participants were females. Two were < 65 years of age and were born in the UK whereas one was aged 73 and was born in India.

One of the younger patients aged 49 had a suspected AF diagnosis following her screening appointment, which was subsequently confirmed as 'Possible AF' by the study cardiologist. This lady underwent a 24-hour ECG accompanied by echocardiography and biochemical blood tests at her surgery, and was ultimately diagnosed with a single-episode of AF and iron-deficiency anaemia, resulting in a yield of 'new', screening-detected AF of 0.2% (1/528). As mentioned in section **6.4.2** above, she did not have any past medical history and was therefore not offered the OAC therapy (CHA_2DS_2VASc score of 1).

The other younger patient aged 57 was issued with a 'Sinus Tachycardia' diagnosis after the screening, which was thereafter confirmed as a mild sinus tachycardia by the overreading study cardiologist. This patient did not have a $_{12L}$ECG, but instead underwent unspecified blood tests and had a BP check. She had a pre-existing hypertension, hypercholesterolaemia and diabetes mellitus, and was not diagnosed with any new conditions or started on any new treatments.

The last patient was given an 'Unclassified' provisional diagnosis by the KMD algorithm but was then classified as displaying a sinus arrhythmia by the interpreting study cardiologist. This patient, who already suffered from hypertension and hypercholesterolaemia, underwent a $_{12L}$ECG at the GP practice and did not require any further interventions.

6.4.5 Participant feedback

A total of 299/560 (53.4%) of participants from the cohort screened in Kent completed the optional, anonymous participant feedback questionnaires. Out of these, 14/299 (4.7%) of participants completed the Punjabi version of the questionnaire, and the rest were completed in English (95.3%, 285/299). The feedback received was overwhelmingly positive with 99.3% (290/292) of respondents stating that they were either 'satisfied' or 'very satisfied' with the overall service received during the study (**Table 6.4**). Almost the same number (98.3%, 289/294) also agreed that they would be interested in getting tested again the following year should the service be offered to them.

Table 6.4 Responses to closed-ended questions of the feedback questionnaire from participants in Kent and South Yorkshire

Data presented as a number of responses/total number of respondents (% total). Between-group differences were determined using a Pearson's Chi-square or Fisher's exact test with Freeman-Halton extension and Bonferroni correction as appropriate. [a,b]*p < 0.001 for between group differences with regards to proportions of participants who were very dissatisfied (n = 2 in South Yorkshire vs. n = 0 in Kent in each case),* [c]*p = 0.005 for between group differences with regards to proportion of participants who were dissatisfied (n = 1 in South Yorkshire vs. n = 0 in Kent),* [d]*p = 0.032 for between group differences with regards to proportion of participants selecting the option. *N.b. not all respondents who selected this option provided a free-text (open-ended) response to support their choice.*

Question Item	Response	Participants in Kent	Participants in South Yorkshire
From your experience of it, how important was the screening for you?	Very important/important	289/295 (98.0)	24/25 (96.0)
Were you aware of this condition before you were screened?	Yes	106/297 (35.7)	10/23 (43.5)
Were you aware of any of the health risks associated with this condition, before you were screened?	Yes	96/298 (32.2)	12/24 (50.0)
How satisfied were you with the information provided before the appointment?	Very satisfied/satisfied	286/295 (97.0)[a]	22/25 (88.0)[a]
Did the researcher clearly explain what was involved in having an ECG?	Yes	293/297 (98.7)	25/25 (100)
Afterwards did the researcher clearly explain the results of the test to you?	Yes	296/296 (100)	23/24 (95.8)
How satisfied were you with the information provided after the appointment?	Very satisfied/satisfied	291/295 (98.6)[b]	22/25 (88.0)[b]
Please rate how well you thought the researcher carried out the tests	Very good/good	295/295 (100)	23/25 (92.0)
Did the researcher make you feel at ease?	Yes	283/286 (99.0)	24/24 (100)
How satisfied were you with the length of the appointment?	Very satisfied/satisfied	285/288 (99.0)[c]	23/25 (92.0)[c]
Overall how satisfied were you with the service that you received?	Very satisfied/satisfied	290/292 (99.3)	24/25 (96.0)
If the test was offered to you again next year, would you have it done?	Yes	289/294 (98.3)	25/25 (100)
Would you be happy for other screening tests to be delivered at the Gurdwara in the future?	Yes	267/271 (98.5)	24/24 (100)
In your opinion, what are the key barriers for individuals of South Asian origin to engage in health screening initiatives?			
Language	Ticked (selected)	152/246 (61.8)[d]	7/19 (36.8)[d]
Lack of health education	Ticked (selected)	125/246 (50.8)	9/19 (47.4)
Cultural norms	Ticked (selected)	51/246 (20.7)	6/19 (31.6)
Costs	Ticked (selected)	42/246 (17.1)	0/19 (0.0)
Religious beliefs	Ticked (selected)	30/246 (12.2)	1/19 (5.3)
*Other**	Ticked (selected)	49 (19.9)	2/19 (10.5)

The vast majority of respondents (98.0%, 289/295) considered AF screening to be either 'important' or 'very important'. However, more than 60% of all them were not aware of either AF as a medical condition (64.3%, 191/297) or the health risks associated with it (67.8%, 202/298). When asked about the quality of information provided during the study, most participants were satisfied both with information provided before and after their appointment (97.0%, 286/295 and 98.6%, 291/295, respectively). Nearly all respondents felt that pharmacy undergraduates conducting the screening clearly explained what was involved in having an ECG (98.7%, 293/297), and all participants (100%, 296/296) agreed that they had the results clearly explained to them after the test. In turn, $_{SL}$ECG tests carried out during the study were rated as only 'good' or 'very good' (100%, 295/295). Participants also generally thought that the researcher made them feel at ease (99.0%, 283/286) and were either 'satisfied' or 'very satisfied' with the length of the research appointment (99.0%, 285/288).

Fewer participants responded to questions concerning any other health screening initiatives or barriers to their engagement in such initiatives. Those who responded were mainly happy for other health screening tests to take place at the Gurdwara in the future (98.5%, 267/271). Twenty-two respondents (7.4%, 22/299) provided the details of potential health screening tests they would like to see being provided at the Gurdwara (*N.b.* some respondents indicated more than one test). The most popular choices included the checks for diabetes (59.1%, 13/22), cholesterol (27.3%, 6/22), hypertension (27.3%, 6/22) and eye conditions (9.1%, 2/22). Four participants (18.2%, 4/22) were happy to receive any blood tests or health checks.

Participant opinions diverged when they were asked to identify the key barriers to South Asian engagement in health screening initiatives. The primary barriers selected by over a half of all respondents included language (61.8%, 152/246) and the lack of health education (50.8%, 125/246). Around one in five respondents identified cultural norms (20.7%, 51/246) followed by costs (17.1%, 42/246) and religious beliefs (12.2%, 30/246). The free-text barriers to South Asian engagement in health screening were indicated by 40/299 (13.4%) of respondents who commonly referred to the lack of time (20.0%, 8/40), laziness (15.0%, 6/40), ignorance or poor health/service awareness (12.5%, 5/40), difficulties accessing conventional healthcare, such as making GP appointments (7.5%, 3/40), and not wanting to know they had the condition (5.0%, 2/40; *N.b.* some respondents specified more than one barrier). Interestingly, 14/40 (35.0%) of respondents stated that they did not think there were any barriers to South Asian engagement in health screening initiatives at all.

A total of 25/51 (49.0%) of participants attending the public health event in South Yorkshire also completed the feedback questionnaires (all in English). As displayed in **Table 6.4**, their responses to close-ended questions were overall comparable to those received from the cohort in Kent. As an exception, two respondents from South Yorkshire (8.0%, 2/25) were 'very dissatisfied' with both the information provided before and after their appointment (vs. 0%, 0/295 in the main cohort; Fisher's exact test, $p < 0.001$ for both) and one other respondent (4.0%, 1/25) was 'dissatisfied' with the length of the appointment (0%, 0/288 in the main cohort; Fisher's exact test, $p = 0.005$). Significantly fewer respondents from South Yorkshire also felt that language was a barrier to South Asian engagement in health screening initiatives (36.8%, 7/19 vs. 61.8%, 152/246 in Kent; Chi-square test, $p = 0.032$). Five participants from South Yorkshire (20.0%, 5/25) provided free-text answers regarding the barriers to South Asian engagement in health screening. Similar to the cohort in Kent, these included the lack of time, difficulties accessing appointments and poor health service awareness (20.0%, 1/5 each). Three participants (60.0%, 3/5) did not feel there were any barriers at present. As far as additional health screening was concerned, 7/25 (28%) of respondents from South Yorkshire provided free-text examples, which included checks for diabetes (71.4%, 5/7), eye conditions (28.6%, 2/7), cholesterol or hearing (14.3%, 1/7 each).

About 60% of respondents from the cohort in Kent (59.5%, 178/299) and over 70% of those from South Yorkshire (72.0%, 18/25) provided answers to open-ended questions concerning the positive or negative aspects of the service received and any potential improvements to the AF screening strategy proposed (**Figure 6.6**). Few notable differences were observed between the categories derived through content analysis of feedback from the two cohorts, and these are emphasised below where appropriate. Respondents from each group valued the screening carried out at the Gurdwara describing it as '*a perfect idea'* and *'a very good cause for the local community'* (1.7%, 3/178 in Kent; 16.7%, 3/18 in South Yorkshire), which was '*free', 'accessible', 'convenient' and 'time-saving'*, avoiding the need to make a GP appointment (16.9%, 30/178 in Kent; 38.9%, 7/18 in South Yorkshire). Several participants reflected on the other benefits of the research initiative, which offered the *'much needed knowledge'* relating to the South Asian ethnicity while contributing to primary CVD prevention and cost reduction (2.3%, 4/178 in Kent; 5.6%, 1/18 in South Yorkshire).

More than a quarter of respondents, almost all from Kent, appreciated the simplicity and the speed of the test (27.5%, 49/178 in Kent; 5.6%, 1/18 in South Yorkshire) while describing the equipment used as *'unique'* and *'non-invasive'* (2.8%, 5/178 in Kent). Participants also recognised the friendly and professional nature of researchers who were commonly described as *'helpful'*, *'approachable'*, *'caring'*, *'polite'*, *'patient'* and *'professional'* (19.1%, 34/178 in Kent; 77.8%, 14/18 in South Yorkshire). Some respondents praised the undergraduate students and/or academic staff for their knowledge and ability to provide a clear, detailed explanation which helped to educate the public and raise their awareness of AF (26.4%, 47/178 in Kent; 50.0%, 9/18 in South Yorkshire). The consultations were viewed as an opportunity to obtain reassurance about the health status (1.7%, 3/178 in Kent; 5.6%, 1/18 in South Yorkshire), with an option of communication in respondents' native language (2.3%, 4/178 in Kent; 5.6%, 1/18 in South Yorkshire). Besides the informative style of consultations, respondents mentioned the *'informal'*, *'personal'* and *'at ease'* environment of the appointment (6.7%, 12/178 in Kent; 16.7%, 3/18 in South Yorkshire). A small number of

Figure 6.6 A word-cloud representation of free-text responses to participant feedback questionnaires

Includes free-text responses concerning the positive/negative aspects of the service received and suggestions for the improvement of the AF screening strategy proposed (n = 178 for participants in Kent and n = 18 for participants in South Yorkshire).

participants from Kent also described the *'very well organised manner'* of research conduct (1.7%, 3/178) and acknowledged the benefit of convenience when timing such health screening initiatives with religious occasions, i.e. the 12th of November as the 550th birthday of Guru Nanak Devi Ji (1.1%, 2/178).

While none of the respondents reported any specific concerns or negative aspects of service provision, some participants had suggestions of how the AF screening strategy proposed could be improved or developed in the future (9.6%, 17/178 in Kent; 11.1%, 2/18 in South Yorkshire). Five respondents from Kent (2.8%, 5/178) wished for AF screening service to be expanded to other settings ranging from places of worship (mandirs, churches and mosques) to GP practices and other community locations, for example the *'fire service open day/events'*. Other participants appealed for more health-education-focused events (e.g. learning about the healthy diet) (1.7%, 3/178 in Kent), conducting more or diverse health screening (3.4%, 6/178 in Kent; 5.6%, 1/18 in South Yorkshire) or promoting the existing health services, particularly amongst the South Asian people (1.1%, 2/178 in Kent). One participant from each cohort also urged for AF screening to be repeated the following year provided it was '*affordable'* (0.6%, 1/178 in Kent; 5.6%, 1/18 in South Yorkshire).

6.4.6 Economic analysis

At base-case assumptions derived from the main participant cohort in Kent, the AF screening strategy targeting all British Indian participants was largely cost-effective compared to the no-screening scenario, producing a low ICER of £2,203 (95% CI, £1,412-£2,995;)/QALY gained (**Table 6.5**). The ICERs were kept below the WTP cost-effectiveness threshold of £20,000/QALY gained in 97.6% of the 100,000 Monte Carlo estimates (**Figure 6.7**). In turn, the 10-year INB of this AF screening strategy compared to no screening was a substantial £44,534 per individual with AF entering the model and an equivalent of £297,938,556 for all British Indian participants with 'new', screening-detected AF across England and Wales.

Table 6.5 Findings of the cost-effectiveness analysis of AF screening strategy within a South Asian community setting

*Incremental cost-effectiveness ratios (ICERs) are expressed as a mean (95% confidence intervals). Abbreviations: AF – atrial fibrillation; DOAC – direct-acting oral anticoagulant; VKA – vitamin K antagonist. N.b. *The percentage of AF patients eligible for anticoagulation were 60% and 100% for the base case and for those aged ≥ 65 years, respectively.*

Base Case Assumptions	**Level of Adherence to Oral Anticoagulant Therapy (%)**				
	40	**55 (base case)**	**60**	**70**	**80**
• 3-monthly AF screening cost/participant £261.54 • Prevalence of 'unknown' AF 1.0% • Rate of 'Sinus Tachycardia'/'Unclassified' diagnoses 9.1% • Participation in screening rate 50% • Test sensitivity 100% • Test specificity 99.2% • %Eligible patients on DOAC 56% • %Eligible patients on VKA 44%*	£2,508 (£1,580-£3,435)	£2,203 (£1,412-£2,995)	£2,106 (-£337-£4,549)	£1,926 (£809-£3,043)	£1,775 (£794-£2,756)
Deviations from Base Case					
• %Patients on DOAC 29% • %Patients on VKA 71%	£2,072 (-£61-£4,206)	£1,800 (-£2,631-£6,231)	£1,722 (-£2,253-£5,697)	£1,559 (-£4,034-£7,152)	£1,409 (£277-£2,541)
• Base-case assumptions • Screening participation rate 80%	£1,215 (-£6,816-£9,246)	£968 (£82-£1,852)	£891 (-£4,006-£5,788)	£736 (-£6,045-£7,516)	£599 (-£6,799-£7,998)
• Base-case assumptions • Screening participation rate 30%	£4,621 (-£3,800-£13,041)	£4,176 (-£10,423-£18,808)	£4,026 (-£4,054-£12,106)	£3,786 (£710-£6,862)	£3,568 (£32-£7,104)
• Rate of Tachycardia/Unclassified diagnoses 4.6%	£2,069 (£319-£3,820)	£1,805 (-£670-£4,281)	£1,709 (£538-£2,880)	£1,552 (-£3,867-£6,971)	£1,402 (-£7,739-£10,544)
• Aged ≥ 65 only (3-monthly cost/participant £223.52) • Prevalence of 'unknown' AF 1.5% • Rate of 'Sinus Tachycardia'/'Unclassified' diagnoses 6.7% • Test specificity 98.4%	£4,592 (-£1,026-£10,211)	£3,283 (-£11,435-£18,002)	£3,009 (-£3,870-£9,887)	£2,590 (£639-£4,542)	£2,273 (£82-£4,464)

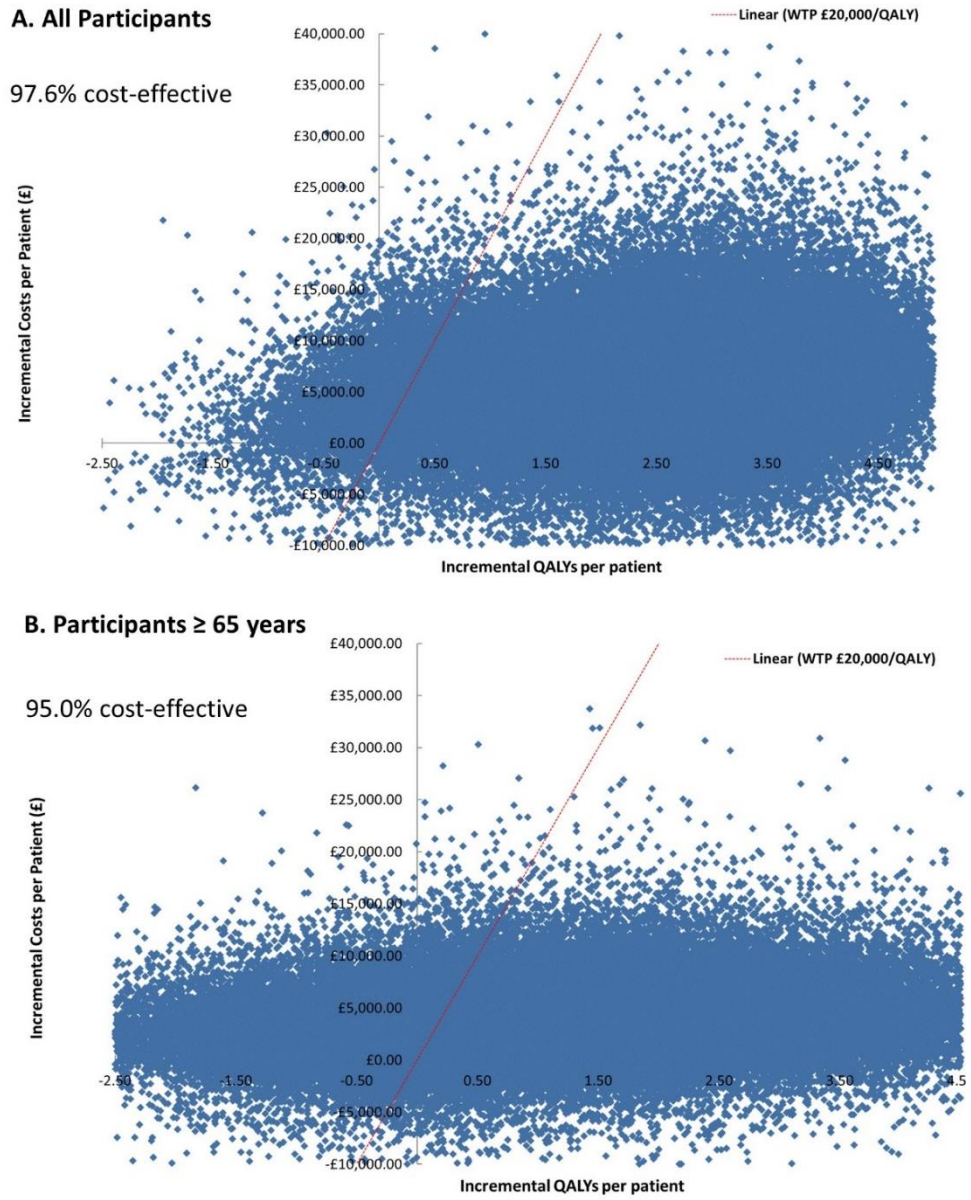


Figure 6.7 Incremental cost-effectiveness of AF screening within a South Asian community compared to no screening

Incremental cost-effectiveness planes show 100,000 pseudorandom Monte Carlo estimates of incremental costs and QALYs gained per British Indian individual with AF comparing: A. the base case of the AF screening strategy in all British Indian participants compared to no screening; B. the base case strategy in British Indian participants aged ≥ 65 years compared to no screening. Any points falling below the dotted line have an ICER < £20,000 per QALY gained. Abbreviations: AF – atrial fibrillation; ICER – incremental cost-effectiveness ratio; QALY – quality-adjusted life year; WTP – willingness to pay [threshold].

During the PSA, the cost-effectiveness of the intervention improved with increasing adherence to OAC therapy, from an ICER of £2,508 (95% CI, £1,580-£3,435)/QALY gained at 40% adherence to a 29.2% (£733) lower ICER of £1,775 (£794-£2,756)/QALY gained at 80% adherence. The ICERs were reduced by a further average of 18.7% (£391) across the OAC adherence range when adjusting the fractions of patients with AF receiving DOACs and VKAs from the 56:44 ratio observed during the PDAF study in GP surgeries to the NICE assumption of 29:71 (NICE 2014b). This deviation from the base case produced an ICER of £1,800 (95% CI, -£2,631-£6,231)/QALY gained at the 55% adherence to OAC therapy.

The cost-effectiveness model was particularly sensitive to the variability in AF screening participation rates. At the higher-end of the 80% AF screening uptake, the ICERs were on average 58.7% (£1,222) lower than in the base case scenario across the OAC adherence range, with a 55% adherence to OAC ICER below the £1,000/QALY gained: £968 (95% CI, £82-£1,852). On the other end of the spectrum for 30% screening uptake, the ICERs were on average nearly double the base case ones across the adherence to OAC range (92.5% or £1,932), with an ICER of £4,176 (-£10,423-£18,808)/QALY gained at 55% OAC adherence. Both deviations from the base case (especially the 30% participation rate) also presented a greater degree of uncertainty resulting in generally wider 95% CIs. Halving the proportion of device-detected 'Sinus Tachycardia' and 'Unclassified' diagnoses from 9.1% to 4.6% did not result in such a dramatic improvement of cost-effectiveness, even though ICERs declined by an average of 19.0% (£396) across the adherence to OAC range resembling the effect of a switch from the PDAF study to NICE distribution of OAC therapies: £1,805 (95% CI, -£670-£4,281)/QALY gained and £1,800 (95% CI, -£2,631-£6,231)/QALY gained at 55% OAC adherence rate for the two deviations, respectively.

Despite a lower three-monthly AF screening cost, the adjustment of base-case assumptions to British Indian individuals aged ≥ 65 years, produced on average 47.5% (£1,045) higher ICERs accompanied by wider 95% CIs compared to the main group of over ≥ 18-year-olds. At 55% OAC adherence rate, the difference between the cost-effectiveness of the intervention in the two sub-groups was close to 50%: £3,283 (-£11,435-£18,002)/QALY gained and £2,203 (£1,412-£2,995)/QALY gained for those aged ≥ 65 and ≥ 18 years, respectively. This pronounced difference was largely the result of markedly lower incremental QALYs gained per patient with AF in the ≥ 65 sub-group compared to the main cohort: 1.12 (95% CI, 1.11-1.13) and 2.50 (95% CI, 2.50-2.51) at 55% OAC adherence, respectively. The incremental costs per individual with AF on the other hand were greater amongst those aged ≥ 18 years than amongst the ≥ 65s: £5,514 (95% CI, £5,482-£5,546) and £3,682 (95% CI, £3,661-£3,702) at 55% OAC adherence, respectively. Albeit overall

less cost-effective than the AF screening strategy in the main cohort, the intervention remained highly economical in those aged ≥ 65 years with 95.0% of all ICERs below the WTP threshold of £20,000/QALY gained assuming the 55% OAC adherence rate. The INB per ≥ 65-year-old individual with AF was £18,746 and was expected to generate £16,706,933 for all British Indian participants aged ≥ 65 with 'new' AF in England and Wales over the coming 10 years.

6.5 Discussion

6.5.1 Comparison with existing literature

Recruitment and study participants

This study evaluated the feasibility of the AF screening programme delivered by trained pharmacy undergraduates under the supervision of a CP at places of worship of a particular South Asian community. Overall, a concentrated recruitment strategy over a period of nine days, provided this study with access to 611 eligible participants, and 572 individuals of British Indian ethnicity. The high recruitment efficiency observed here exceeded that reported by the multinational, awareness campaign-driven AF screening programme, which recruited > 2,700 individuals across 120 sites over a single month (da Costa *et al.* 2020). It was also above the recruitment efficiency of previous CVD risk factor screening initiatives held within the South Asian places of worship (Mathews *et al.* 2007; Rao *et al.* 2012; Jones *et al.* 2013), and certainly the PDAF study in GP surgeries which recruited 604 participants over a period of seven months (**Chapter 3**). In fact, the rate of recruitment noted here was not far from the 824 multi-ethnic individuals screened for CVD over 10 days by the *'Healthy Hearts Project'* in England, which was conducted in both community and primary care locations (Patel *et al.* 2007). Compared to other studies within the South Asian community settings, the more efficient recruitment during the present study may simply be a result of shorter appointment times due to the absence of other health checks, for instance the blood pressure measurements or capillary blood tests. Indeed, the AF screening appointments conducted here were on average only seven minutes long compared to 30-40-minute CVD risk factor screening reported by previous initiatives (Mathews *et al.* 2007; Rao *et al.* 2012). Likewise, some community pharmacies participating in the initiative by da Costa *et al.* (2020) offered AF screening as part of their routine services, for instance medication reviews or CVD risk factor clinics, thereby potentially reducing the recruitment efficiency.

The absence of pulse palpation during the present study may explain a two-to-four-minute shorter appointment times than the ones observed during the PDAF screening in care homes (**Chapter 5**) or GP surgeries (**Chapter 3**), respectively. Nevertheless, this minor time difference is unlikely to fully account for the difference in recruitment efficiency between the AF screening seen during the PDAF study in GP surgeries and a similar AF screening strategy at places of worship presented here. First of all, as shown by cumulative evidence (Laveist & Nuru-Jeter 2002; Freeman *et al.* 2002; Netto *et al.* 2007; Eastwood *et al.* 2013; Jones *et al.* 2013; Ahmed *et al.* 2015), the uptake and possibly efficiency of healthcare interventions within a South Asian community setting may be improved through language and ethnocultural concordance between the participants and researchers. Both of these measures were implemented during the present study and were positively appraised by respondents to participant feedback questionnaires. As mentioned by interviewees in the qualitative study by Eastwood *et al.* (2013), and some respondents to feedback questionnaires during this study, one other factor which may have encouraged people to attend AF screening at the Gurdwara was the accessibility of the health check within a comfortable, local environment without the need to make a GP appointment. Combining AF screening with community events, such as the public health event or the religious occasion, may have also increased the uptake or efficiency of screening due to the *'community spirit'* (Eastwood *et al.* 2013), which was acknowledged by a few respondents to feedback questionnaires. The presence of gatekeepers and academic or clinical staff from the same community at each Gurdwara may have played a role by encouraging the participation in AF screening, due to the *'community leader'* effect which has been utilised by a number of CVD screening initiatives (Rao *et al.* 2012; Jones *et al.* 2013; Eastwood *et al.* 2013). This leadership role may be somewhat similar to that of a *'champion'* referred to by previous AF screening programmes in primary care (Orchard *et al.* 2016; Orchard *et al.* 2019a; Orchard *et al.* 2019b; da Costa *et al.* 2020), and the qualitative evaluation of the PDAF study (**Chapter 4**), which emphasised the significance of GP support to maintain the uptake of AF screening. It is therefore likely that the recruitment success of future AF screening programmes targeting South Asian people will depend on the efforts of both community leaders and HCPs, and perhaps a mixed recruitment strategy in both community and healthcare settings observed during the *'Healthy Hearts Project'* (Patel *et al.* 2007).

Besides the lower recruitment rate, the PDAF initiatives in GP surgeries and care homes were limited by the lack of ethnic diversity, providing the rationale for the present study to target a selected South Asian ethnic minority group. As anticipated from the composition of local populations (Sheffield City Council 2011; Kent County Council 2013), AF screening at the Gurdwaras in Kent and in South Yorkshire mostly recruited individuals of British Indian

ethnicity providing a counterbalance to the ≥ 97% of the White British people screened by the PDAF studies. The demographic characteristics of the two British Indian cohorts were largely comparable, although it is perhaps interesting to note that those screened in Kent were somewhat older and hence suffered from a slightly greater burden of comorbidities, such as hypertension. Whilst the significance of these demographic differences may be limited by the small sample size or the slight differences in the recruitment strategy used in South Yorkshire (i.e. recruitment during a public health event), they may need to be considered when prioritising the resources to those communities who are in most need, such as the likely older and higher-CVD risk individuals in Kent (Olesen *et al.* 2011).

Prevalence of AF and risk factors for stroke

Since the prevalence of AF increases with age and the burden of comorbidities, such as hypertension (Benjamin *et al.* 1994; Ball *et al.* 2013), it was unsurprising that all five cardiologist-confirmed cases of AF (1.0%) were detected amongst the overall older and possibly more hypertensive participants screened at the Gurdwara in Kent. This level of AF matched the 1.0% prevalence reported for UK South Asians in secondary care (Conway & Lip 2003) but was slightly above the 0.2-0.7% range within the various UK South Asian communities in a primary care setting (Lip *et al.* 1998; Gill *et al.* 2011; Mathur *et al.* 2013; Gillott *et al.* 2017). It is however worth highlighting that the average age of the cohort screened in Kent (61.0 years) was somewhat above that of individuals in the studies by either Gill *et al.* (2011) (58.2 years; 0.7% prevalence) or Gillott *et al.* (2017) (39.4 years; 0.4% prevalence), thus potentially compromising the direct comparison.

The prevalence of AF was yet slightly greater amongst participants in Kent aged ≥ 65 years (1.5%) who, according to the ESC should be prioritised for opportunistic AF screening (Kirchhof *et al.* 2016). This on the other hand was still far from the 4.3% and 13.5% of the total AF prevalence amongst the predominantly White British ≥ 65s screened during the PDAF studies in GP surgeries and care homes, respectively, as well as the 3.7-11.0% prevalence reported by previous cross-sectional screening in primary care or community settings (Morgan & Mant 2002; Hobbs *et al.* 2005; Lowres *et al.* 2014; Kearley *et al.* 2014; Orchard *et al.* 2016; Kaasenbrood *et al.* 2016; Chan & Choy 2016). The ≥ 65-year-old prevalence of 1.5% was even below the 2.4% reported for the substantially younger group of White British individuals included in the retrospective, ethnicity-focused study by Gillott *et al.* (2017) (average age of 48.9 years), which reflected the 2.5% prevalence of AF observed amongst the general population of England (Public Health England 2017a). The findings of the present study therefore concur with the results of previous population-based studies, which concluded that the prevalence of AF amongst South Asian communities may

be substantially lower than in the general population or other ethnic groups (Newton *et al.* 2005; Conway & Lip 2003; Gill *et al.* 2011; Mathur *et al.* 2013; Khan *et al.* 2013; Gillott *et al.* 2017; O'Neill *et al.* 2018a). Since the measures put in place to improve South Asian access to AF screening by this study led to only a mildly greater prevalence of AF than previously reported, it appears that the lack of engagement with healthcare is unlikely to account for vast inter-ethnic variations of AF burden, which may instead be driven by physiological or anatomical factors (Amponsah *et al.* 2013; O'Neill & Tayebjee 2018; O'Neill *et al.* 2018b).

To our surprise, the conventional risk factors for AF, such as hypertension and diabetes (Benjamin *et al.* 1994), were substantially less prevalent during this study (36.0% and 18.4%, respectively) than in previous studies of South Asian ethnic groups (45.6-70.2% and 30.8-52.2%, respectively) (Gill *et al.* 2011; Mathur *et al.* 2013; Gillott *et al.* 2017). The prevalence of hypertension and diabetes were even comparable to those observed amongst participants with 'Normal SR' diagnoses during the PDAF study in GP surgeries (40.9% and 12.9%, respectively). This finding suggests that the paradox of low AF prevalence despite the high prevalence of its risk factors may not be apparent in all South Asian communities. The 'healthy volunteer' effect may also have played a part (Froom *et al.* 1999), leading to the recruitment of more participants with fewer comorbidities who proactively sought to be screened, in contrast to GP records-based studies which may have involved more individuals receiving routine care for multiple comorbidities (Gill *et al.* 2011; Mathur *et al.* 2013; Gillott *et al.* 2017).

Despite the low total prevalence of AF, none of the participants with cardiologist-confirmed 'Possible AF' diagnoses reported a history of this condition at the time of screening, suggesting that the prevalence of 'unknown' AF within this sample may be as high as 1.0% and 1.5% for those aged ≥ 18 and ≥ 65 years, respectively. If this was the case, the prevalence of previously undiagnosed AF amongst the ≥ 65s identified here would not be far from the 1.3% ascertained by the PDAF study in GP surgeries and would fall within the 0.8-2.4% range reported by most single time point AF screening studies in community and primary care settings (Morgan & Mant 2002; Hobbs *et al.* 2005; Kearley *et al.* 2014; Lowres *et al.* 2014; Lowres *et al.* 2013; Orchard *et al.* 2016; Kaasenbrood *et al.* 2016; Twigg *et al.* 2016; Chan & Choy 2016; Sandhu *et al.* 2016; Orchard *et al.* 2019b; Antoniou *et al.* 2019; Zaprutko *et al.* 2019; Anderson *et al.* 2020). Whilst this may suggest that the proportion of ≥ 65-year-old South Asians with undiagnosed AF identified by community-based screening is similar to the general population, the self-reported nature of medical history recorded during this study should be interpreted cautiously. To illustrate the magnitude of this

potential bias, only seven out of 18 patients with 'known' AF identified by the PDAF study in GP surgeries were fully aware of their condition at the time of screening. Perhaps as a reflection of this, only one of participant with 'Possible AF' was ultimately diagnosed with the condition during the present study, producing a low yield of 0.2%. Not only was this yield markedly below the prevalence of 'unknown' AF outlined above, but it was also lower than the $_{12L}$ECG yields reported by either the PDAF study in GP surgeries (0.7%), or by other cross-sectional AF screening initiatives of ≥ 65s in primary care or community settings (0.3-1.2%) (Hobbs *et al.* 2005; Rhys *et al.* 2013; Lowres *et al.* 2014; Kearley *et al.* 2014; Orchard *et al.* 2016; Sandhu *et al.* 2016; Quinn *et al.* 2018; Orchard *et al.* 2019b; Cunha *et al.* 2020).

The only participant diagnosed with a 'new' AF following the screening at the Gurdwara in Kent was a 49-year-old female who experienced a single episode of AF and did not require any further intervention or OAC therapy. The other three participants with a suspected AF and complete demographic data were however all aged ≥ 65 years, experienced a significantly greater risk of ischaemic stroke (CHA_2DS_2VASc scores ≥ 3) and as such would have all qualified for OAC therapy. In fact, the median CHA_2DS_2VASc score across all four participants with a 'Possible AF' (3.5 [1.5; 6.3]) was comparable to or slightly above the 3.0 [3.0; 4.3] observed during the PDAF study in GP surgeries, and even the 3.0 [3.0; 6.0] encountered in the high-risk sample of care home residents. This finding implied that, despite the relatively low prevalence or yield of AF within the South Asian population, those individuals who are identified as AF-positive during community-based screening may still benefit from an appropriate stroke prevention. It is also in line with pre-existing literature which points out the greater risk of ischaemic stroke and stroke-related death in South Asians with or without AF compared to other ethnic groups (Wild & Mckeigue 1997; Mathur *et al.* 2013; George *et al.* 2017).

Nonetheless, similar to the rest of the sample, South Asians with a 'Possible AF' during the current study displayed a lower self-reported prevalence of hypertension (40.0%) or diabetes (20.0%) compared to their GP and care home counterparts from the PDAF studies (hypertension 69.2% and 71.4%, respectively; diabetes 30.8% and 28.6%, respectively). Although the validity of this comparison may be complicated by the small number of AF cases, it is rather interesting that neither hypertension nor diabetes exhibited an association with AF during the present study, yet displayed such an association when comparing those with 'Possible AF' and those with 'Normal SR' in GP surgeries (section **3.4.2**). Despite discovering that hypertension was a strong predictor of AF diagnosis in both South Asian and White British cohorts, the study by Gillott *et al.* (2017) was similarly unable to demonstrate a relationship between diabetes and AF in South Asians, which was apparent

amongst the White British. The absence of this well-documented relationship (Sun & Hu 2010) may be partially attributed to smaller left atrial and left ventricular volumes of South Asian individuals compared to the White British population, which in turn protects them from AF (O'Neill *et al.* 2018b), perhaps even in the presence of hyperglycaemia. Since glucose intolerance has been linked with an increase in left ventricular mass (Rutter *et al.* 2003), it is also possible that the smaller myocardium of South Asian individuals is less susceptible to hyperglycaemia-driven cardiac remodelling, atrial fibrosis and hence the development of AF (Bell & Goncalves 2019).

Diagnostic accuracy

Contrary to PDAF studies in GP surgeries and care homes, the AF detection during this study within a community setting relied on the KMD algorithm and did not include either pulse palpation or $_{SL}$ECG interpretation by the operator of the device. In turn, the device was operated by trained pharmacy undergraduates rather than the fully qualified CPs who were utilised during the PDAF initiatives. Despite these variations, according to the supervising CP, the quality of most $_{SL}$ECGs recorded using the KMD during this study was either 'Excellent' or 'Acceptable' (93.8%), matching the 93.0% of 'Excellent'/'Acceptable' $_{SL}$ECGs produced by CPs during the PDAF screening in GP surgeries and far exceeding the proportion of high-quality recordings in care homes (73.1%). Similarly, the proportion of recordings corresponding to 'Poor' or 'Unreadable' quality (6.3%) was slightly lower than the 7.0% observed when screening in GP surgeries and markedly below the 26.9% noted in care homes. In line with high-quality of $_{SL}$ECGs, the over-reading cardiologist was able to interpret all of the recordings, which was not the case for approximately 1% of traces produced during the PDAF initiative or the KMD-based study by Lown *et al.* (2018) in GP surgeries. This was somewhat unexpected considering the public nature of AF screening at the Gurdwara, which may be associated with relatively high levels of noise, and hence an artefact on $_{SL}$ECG, compared to a generally quiet consultation room within a GP surgery. For example, as mentioned in section **3.5.1**, the $_{SL}$ECG-based AF screening study within a supermarket environment by Battipaglia *et al.* (2016) produced as much as 7% of 'Unreadable' recordings.

As observed during the PDAF study in GP surgeries, the high quality of $_{SL}$ECGs produced here translated into a high diagnostic accuracy of the KMD algorithm, which displayed a substantial inter-rater agreement with the cardiologist (0.71 and 0.66 for all participants and those aged ≥ 65 years vs. 0.72 in GP surgeries). The KMD algorithm exhibited a perfect diagnostic sensitivity (100%) and a near-perfect specificity (99.2%), which were

largely sustained in the sub-group of individuals aged ≥ 65 (100% and 98.4%, respectively). The high sensitivity and specificity of the KMD algorithm for AF detection were above those noted during the PDAF screening in GP surgeries (92.3% and 97.4%, respectively) and even the original validation study in a sample of cardiology patients (98.0% and 97.0%, respectively) (Lau *et al.* 2013). The sensitivity of the KMD algorithm was also higher than that noted during the PDAF study in care homes (57.1%), although at an expense of a marginally lower specificity (99.2% vs. 100%). Overall, the sensitivity and specificity of the KMD algorithm approached the upper end of the range for the two parameters reported by previous AF screening studies in primary care settings (sensitivity 87-100%; specificity 91-99%) (Lowres *et al.* 2014; Orchard *et al.* 2016; Lown *et al.* 2018; Himmelreich *et al.* 2019; Zaprutko *et al.* 2019) and was above the respective values for the community-based AF screening programme in Hong Kong by Chan & Choy (2016) (98.0% and 29.2%, respectively).

The four false positive AF diagnoses by the KMD algorithm (FPR 0.8%) meant that, compared to the cardiologist, it correctly classified 5/9 of those with AF positive diagnoses, giving rise to a PPV of 55.6% or the FDR or 44.4%. The false positive rate was yet higher for participants aged ≥ 65 years, in whose case the device produced three false positive diagnoses, correctly classifying 3/6 of those it considered to be AF positive (FDR of 50.0%). Whilst these numbers need to be interpreted carefully due to the small number of AF cases, the FDRs of the KMD algorithm in both those aged ≥ 18 and ≥ 65 years ascertained here were above the perfect FDR of 0% during the PDAF study in care homes and close to the 48.0% reported in American nursing homes (Khan *et al.* 2020). They were also somewhat greater than either the FDR of 38.5% when conducting the PDAF screening in GP surgeries or the 17-35% FDRs reported by other $_{SL}$ECG-based studies in primary care settings (Quinn *et al.* 2018; Himmelreich *et al.* 2019; Zaprutko *et al.* 2019). This paradox of excessive false discoveries in the presence of high diagnostic sensitivity/specificity may be the result of the low disease prevalence. As exemplified by Colquhoun (2014), a highly accurate test displaying a 95% specificity for a disease of 1% prevalence (i.e. matching the 1% prevalence of AF during the current study), may still have an FDR of 86%, meaning that only one or two participants out 10 who are given an AF positive diagnosis would actually have the disease.

Although the FDRs of 44-50% observed during the present study were not at all insignificant, they were superior to the FDR of 69% with pulse palpation during the PDAF screening in GP surgeries or the range of FDR values reported for pulse palpation by previous studies in primary care (59-92%) (Sudlow *et al.* 1998a; Morgan & Mant 2002;

Hobbs *et al.* 2005; Rhys *et al.* 2013; Quinn *et al.* 2018). These findings suggest that the use of the automated KMD algorithm may still be a more optimal method for AF screening within the community or religious setting of a selected South Asian community than the conventional pulse palpation. They also prove the hypothesis that staff other than HCPs (GPs, pharmacists or nurses) who had traditionally conducted AF screening (Sudlow *et al.* 1998a; Somerville *et al.* 2000; Morgan & Mant 2002; Hobbs *et al.* 2005; Lowres *et al.* 2014; Orchard *et al.* 2016; Sandhu *et al.* 2016; Orchard *et al.* 2019b), may be able to successfully operate the device without a major impact on the quality of $_{SL}$ECG recordings or the diagnostic accuracy. It is of course also plausible that the sustained high performance of KMD which in this instance was operated by less qualified personnel and in a public setting could be a product of the ongoing improvements to the automated KMD algorithm (AliveCor 2019a). This hypothesis may be partially supported by the recent study in community pharmacies, which utilised the student-operated KMDs, and despite a poorer $_{SL}$ECG quality (11% of 'Unreadable' recordings), ascertained the levels of sensitivity (100%) and specificity (98.7%) for AF similar to the ones reported here (100% and 99.2%, respectively) (Zaprutko *et al.* 2019).

Similar to the PDAF study in GP surgeries, the primary reason for false positive AF diagnoses identified by the KMD algorithm during the current study was the presence of ectopic beats (0.4% vs. 1.2% in GP surgeries). As before, ectopic beats were also a culprit of false positive 'Unclassified' diagnoses amongst those participants with cardiologist-determined 'Normal SR' (0.4%, vs. 1.7% in GP surgeries), although the proportion of these, as in fact the proportion of all 'Unclassified'/'Unreadable' diagnoses, was significantly lower than observed during the PDAF studies in GP surgeries (2.5% vs. 13.4%) and even more so in care homes (32.7%). The major reason for this pronounced difference may have been the relatively recent improvement of the KMD algorithm to identify some of the previously 'Unclassified' diagnoses as either 'Sinus Bradycardia' or 'Sinus Tachycardia' (AliveCor 2019a). During this study, a total of 35/528 (6.6%) participants screened at the Gurdwara in Kent were classified by the KMD device as displaying a 'Sinus Tachycardia' (SR with HR ≥ 100 bpm), and as such the total percentage of those with 'Sinus Tachycardia' or 'Unclassified' diagnoses (9.1%) was not too dissimilar from the proportion of 'Unclassified'/'Unreadable' diagnoses noted in GP surgeries (13.4%), falling within the 8-17% range reported by previous studies in primary care (Orchard *et al.* 2016; Lown *et al.* 2018; Selder *et al.* 2019; Orchard *et al.* 2019b; Zaprutko *et al.* 2019; Cunha *et al.* 2020). However, whilst difficult to stipulate due to variations in the device's algorithm, compared to the 6.6% of 'Sinus Tachycardias' during the current study, the equivalent proportions of those with 'Unclassified' diagnoses and a HR ≥ 100 bpm were lower during either the PDAF

studies in GP surgeries (2.2%) or care homes (5.8%). Furthermore, a greater proportion of participants without AF as a whole exhibited a HR ≥ 100 bpm during the current study (8.5%) than during either of the two PDAF initiatives (4.1% and 7.7% in GP surgeries and care homes, respectively). Reflecting these differences, the median HR of British Indian participants recruited in Kent was 80 [72; 91] bpm and above the 72 [65; 81] bpm in GP surgeries or the 76 [68; 82] bpm in care homes.

There may be several explanations for the higher prevalence of 'Sinus Tachycardia' amongst participants recruited during this study compared to the other two settings. First of all, the recruitment in Kent was timed with the major religious occasion. In addition to religious celebrations, the commemoration of the Guru's birthday incorporated a multitude of physical activities, such as pilgrim walks, which may have produced an elevated HR amongst the participants of this study. Secondly, intensive praying itself has been shown to activate the autonomic nervous system (Bernardi *et al.* 2001; Kurita *et al.* 2011), potentially leading to HR variations or a faster than expected HR. Last but not least, as demonstrated by O'Neill & Tayebjee (2018) and O'Neill *et al.* (2019), people of South Asian ethnicity may have an inherently higher resting HR compared to the White population. This faster HR may be induced by their higher than average sympathetic drive and a lower than average vagal stimulation (Bathula *et al.* 2010). Whilst this "autonomic dysfunction" may be a compensatory mechanism for a smaller than average myocardium, it could also be associated with insulin resistance and the consequent hyperglycaemia (Bernardi *et al.* 1992; Muntzel *et al.* 1995), which as discussed above are abundant in this ethnic group. Furthermore, the increase in parasympathetic activity may precede the development of AF (Chen & Tan 2007), and it is possible that the lower vagal activity in South Asians could protect them from AF yet at the expense of sinus tachycardia.

The reasons underlying the differences in the proportions of non-tachycardic 'Unclassified' diagnoses between this study (2.5%) and the two PDAF initiatives (10.2% and 26.9% in GP surgeries and care homes, respectively) are somewhat less clear. In case of care homes, this may be a result of the significantly poorer quality of $_{SL}$ECG recordings whereas the additional 'Unclassified diagnoses in GP surgeries, may be linked with 'Unclassified' $_{SL}$ECGs containing AEBs/VEBs (2.3% vs. 0.6% in the current study), excessive interference (1% vs. 0.2% in the current study) or inconsistent/unidentifiable p waves (2.6% vs. 0% in the current study). Indeed, the study by O'Neill *et al.* (2019) demonstrated that AEBs may be significantly less common amongst South Asian individuals than their White British counterparts. Although it may or may not be related to the dysfunction of the autonomic system (Xi & Cheng 2015), the occurrence of frequent AEBs predict the

development of AF (Chong *et al.* 2011; Himmelreich *et al.* 2018), potentially providing another explanation for the lower than average prevalence of AF amongst the South Asian community.

According to the study cardiologist, the vast majority of participants who were issued a 'Sinus Tachycardia' diagnoses following the screening at the Gurdwara in Kent had a mildly elevated HR, which did not warrant any further action (5.9%, 31/529). The high number of $_{12L}$ECG referrals due to 'Sinus Tachycardia' appeared to be counter balanced by the low proportion of false positive AF and 'Unclassified' referrals, meaning that the total rate of unnecessary referrals (7.6%) was still not far from the 6.8% noted during the PDAF study in GP surgeries and lower than the 15.4% observed in care homes. Interestingly however, during this study the KMD algorithm failed to identify six participants with cardiologist-determined 'Unclassified' status due to the presence of a BBB or an ST-segment depression (1.1%), which overall meant that the use of the KMD algorithm instead of the cardiologist generated additional referrals in 6.4% rather than 7.8% of all study participants. The phenomenon of such false negative 'Unclassified' diagnoses with the KMD was not previously documented and may hence be attributed to recent changes in the KMD algorithm (AliveCor 2019a). In turn, the clinical significance of a BBB and/or ST-segment depression might be limited, although in some cases a BBB may be associated with heart failure or hypertension (Jeong *et al.* 2004; Ponikowski *et al.* 2016) whereas an ST-segment depression could also indicate the presence of hypokalaemia or cardiac ischaemia (Pollehn *et al.* 2002; Levis 2012).

Unless trained and experienced in reading ECGs, a non-medical HCP, for instance a CP or a nurse, may not necessarily be able to decipher such abnormalities or make an appropriate referral. However, both CPs and nurses should be able to recognise a relatively benign sinus tachycardia, which during this study, may have helped reduce the number of unnecessary $_{12L}$ECG referrals by up to 6%. One may therefore hypothesise that a model where less qualified staff, such as pharmacy undergraduates, perform AF screening and HCPs, such as CPs, over-read $_{SL}$ECGs of participants with 'Sinus Tachycardia' (and possibly 'Unclassified') diagnoses may produce even more favourable results than reported here. Not only may such a model help avoid the unnecessary patient anxiety which may be associated with false positive referrals (Hafslund *et al.* 2012) but it may also decrease their burden on the healthcare system (Lafata *et al.* 2004). In some ways this approach would be similar to that by Orchard *et al.* (2014) or Zaprutko *et al.* (2019)/Anderson *et al.* (2020) who utilised general practice receptionists or pharmacy students, respectively to record a $_{SL}$ECG using the KMD, although in this instance GPs or

cardiologists would only have to overread those $_{SL}$ECGs with 'Possible AF' or 'Unclassified' diagnoses uninterpretable by CPs. Of course the use of pharmacy undergraduates to conduct AF screening is only one of an array of options, and as trialled by Twigg *et al.* (2016), may instead include other pharmacy professionals, for instance pharmacy technicians who have recently become more involved in the delivery of primary care clinical services (Boughen *et al.* 2017).

Acceptability of the intervention and barriers to engagement

The significance of an effective explanation and provision of information for individuals undergoing AF screening was supported by evidence from participant feedback questionnaires. As previously reflected in feedback collected during the PDAF study in GP surgeries (**Chapters 3 and 4**), respondents from Kent and South Yorkshire appreciated the informative nature of the consultation, which was seen as an opportunity to obtain reassurance about their health status and become more aware of AF. This concurred with the findings by Jones *et al.* (2013) who demonstrated that one in three South Asians attending CVD risk assessment at places of worship sought reassurance about their health whereas one in five were motivated to engage by the desire to learn more about cardiovascular health as a whole. Indeed, CVD-focused educational interventions within this high-risk population may be beneficial, since as shown by our findings, only 30-50% of individuals attending AF screening at each Gurdwara were aware of the condition or its risks prior to their appointment. On the other hand, this figure was not far from the 47% AF awareness ascertained from participant feedback questionnaires during the PDAF study in GP surgeries (section **3.4.5**) or the 56% AF awareness amongst those with pre-existing AF in community pharmacies (Lowres *et al.* 2014). Whilst this confirms that poor public awareness of AF is not limited to a single population group, educational interventions targeting each of these groups, and certainly those from different cultural backgrounds, such as South Asian individuals, should likely be tailored to their specific needs. Conventional multi-faceted educational programmes may help improve patients' knowledge of AF and even their treatment outcomes (Clarkesmith *et al.* 2013; Vinereanu *et al.* 2017; Guo *et al.* 2017), however additional measures, such as targeting the false perceptions about CVD (Greenhalgh *et al.* 1998; Ludwig *et al.* 2011), may be required to ensure the success of such programmes within the South Asian groups. As shown by the current study and previous CVD screening initiatives in religious settings of South Asian communities (Netto *et al.* 2007; Eastwood *et al.* 2013), AF screening programmes may serve as an opportunity to deliver such targeted educational interventions facilitated by pharmacists or pharmacy staff.

Although grateful for the information and education received, the participants of this study did not overall differentiate between the contact with less qualified pharmacy undergraduates and clinically trained CPs, commending both for their professionalism, knowledge and ability to provide appropriate information in a language of their choice. As highlighted by themes from the PDAF focus groups (section **4.4**) as well as the pre-existing literature (Gidman *et al.* 2012; Kelly *et al.* 2014; Lowres *et al.* 2015), such inability to differentiate between the CPs and the less qualified staff may be a product of poor public awareness of pharmacists' roles in general. The routine utilisation of pharmacists from local South Asian communities to facilitate CVD screening within the religious or community settings, which was undertaken by this and several previous studies (Rao *et al.* 2012; Jones *et al.* 2013), may ultimately help raise their profile both as community leaders and reputable HCPs. Up to one in five of UK-registered pharmacists are British Indian (General Pharmaceutical Council 2019), providing an excellent opportunity for ethnocultural concordance-facilitated AF-CVD screening and awareness campaigns within the British Indian communities.

Despite the relatively poor knowledge of AF and possibly the roles of CPs in the screening process, the overwhelming majority of respondents screened at either of the two Gurdwaras agreed that AF screening was important and were satisfied with the service they received. In line with the *'community spirit'* referred to above (Eastwood *et al.* 2013), respondents considered AF screening to be a great cause for their local community, which broadened the options for healthcare access whilst contributing to primary CVD prevention and clinical research. Some respondents, mostly those screened in Kent, were also impressed with the quick nature and the non-invasiveness of the $_{SL}$ECG test, thus echoing the findings of the feedback from the PDAF study as well as other AF screening initiatives in primary care (Orchard *et al.* 2014; Lowres *et al.* 2015; Orchard *et al.* 2016; Halcox *et al.* 2017). Even more importantly and similar to data from PDAF questionnaires in GP surgeries, respondents of the current study almost unanimously agreed to take part in repeated AF screening the following year. They were also happy to participate in other health screening initiatives delivered at the Gurdwara, mostly the tests for diabetes, hypercholesterolaemia and hypertension. Not only did this reflect the range of potential tests and the concept of CVD 'MOT' mentioned by participants of the PDAF study, but it possibly also showcased how important cardiovascular health may be to this widely regarded high-risk group of individuals (British Heart Foundation 2010; George *et al.* 2017) who are at the centre of the Government's CVD plan (Public Health England 2019c).

Besides a couple of respondents from South Yorkshire who were dissatisfied with either the information received or the length of the appointment, most respondents did not express any negative views about the intervention. Some of the participants screened in Kent proposed expanding the AF screening service to other settings, such as the places of worship of other ethnic/religious communities. Whilst this specific theme was not ascertained by qualitative studies of previous CVD risk factor screening programmes in South Asian groups, participants interviewed by Netto *et al.* (2007) expressed an increased willingness to raise the awareness of the service and make CVD screening programme more accessible to others within their community. The community leader- or champion-led multidisciplinary collaboration mentioned above may help achieve this goal (Rao *et al.* 2012; Jones *et al.* 2013; Eastwood *et al.* 2013; Orchard *et al.* 2019a), although the implementation of routine AF screening within this setting may be hindered by several barriers (Szczepura 2005; Netto *et al.* 2010; NHS England 2018a).

The primary barriers to South Asian engagement in health testing identified by respondents to feedback questionnaires were the language, the lack of health education and cultural norms, with the first one being more important for the older and possibly more Punjabi-spoken participants screened in Kent (61.8% in Kent vs. 36.8% in South Yorkshire). The popularity of these barriers was largely anticipated from the findings of previous ethnic minority-focused reviews (Szczepura 2005; Netto *et al.* 2010; Quay *et al.* 2017) as well as the qualitative CVD risk assessment studies in South Asian community settings (Netto *et al.* 2007; Eastwood *et al.* 2013), urging our study to implement the measures of language or ethnocultural concordance referred to above (Waibel *et al.* 2018). The option to communicate in Punjabi, Hindi or a mixture of English and Punjabi was taken up by 25% and 32% of participants in South Yorkshire and Kent, respectively making AF screening accessible to more than 30% of all British Indian participants who may have otherwise not engaged with the initiative. Crucially, four out of five participants with a 'Possible AF' diagnosis chose to communicate in Punjabi instead of English, emphasising just how important the language concordance might be when attempting to reach South Asian individuals in most need. The difficulty accessing GP appointments was mentioned by several respondents as a free-text barrier to healthcare access and may be tightly linked with the linguistic barrier (Netto *et al.* 2007). It could also indicate the lack of primary care capacity (The King's Fund 2019a; NHS England 2019e), which was highlighted by participants of the PDAF focus groups, and may in the future be partially addressed through multidisciplinary PCNs, including pharmacy teams amongst other staff (NHS England and BMA 2019b).

Costs were indicated as a barrier to engagement by 17% of respondents screened in Kent, suggesting that socioeconomic factors continue to play a role in South Asian engagement with healthcare (Gill *et al.* 2011; Orbell *et al.* 2017). Indeed, in 2011 more than 50% of Bangladeshi and Pakistani communities lived in the most deprived 20% of areas in England, and due to a close relationship between the socioeconomic deprivation and CVD, experienced a significantly greater CVD mortality compared to the general population (Public Health England 2017c). Socioeconomic health inequalities may also affect the recent immigrants to the UK who struggle to register with a GP surgery (NHS England 2018a) or may not be fully entitled to free NHS services (Public Health England 2020b). Bringing the health testing initiatives, such as the one presented here, closer to such communities by conducting them within local venues, or the hubs of services, may therefore not only target those in most need (NHS England 2018a) but may also reduce the healthcare or travel costs, which could otherwise deter people from seeking health services (Netto *et al.* 2010). Over 80% of British Indian participants screened by the present study were born outside the UK, and whist the majority undoubtedly had a permanent resident's status, others may not have been fully exempt from all NHS charges (Public Health England 2020b), thus benefitting from a free and locally delivered health screening intervention. Interestingly, a small group of respondents from both cohorts screened in Kent and South Yorkshire, did not think that there were any barriers to South Asian engagement in health testing. This finding may point to the variations in healthcare access within the community itself and should be considered for inclusion as a pre-defined option for questions about the barriers of healthcare access in future questionnaires.

Cost-effectiveness of the intervention

The economic impact of AF screening within the selected South Asian community was assessed by comparing its cost-effectiveness with the no-screening strategy in the entire study sample screened in Kent and in the sub-group of individuals aged ≥ 65 years. Similar to PDAF studies in GP surgeries and care homes, the AF screening intervention at the Gurdwara in Kent was cost-effective despite an almost 8% rate of unnecessary referrals for $_{12L}$ECG procedures. Compared to the no-screening strategy, the use of the KMD algorithm to detect AF in the entire sample of British Indian participants (aged ≥ 18 years) was highly cost-effective generating an ICER of £2,203/QALY gained at base-case assumptions. Whilst accompanied by on average 47.5% higher ICERs across the adherence to OAC range, the AF screening intervention also remained cost-effective in individuals aged ≥ 65 years (ICER of £3,283/QALY gained at 55% adherence to OAC therapy). The ICERs of AF screening in both those aged ≥ 18 and those aged ≥ 65 years were below the NICE WTP of £20,000/QALY gained (NICE 2012a) in over 90% of 100,000

iterations (97.6% and 95.0%, respectively). As such the intervention was expected to generate the 10-year INBs of £44,543 and £18,746 per individual with AF aged ≥ 18 and ≥ 65 years, respectively, leading to substantial benefits of £298 and £17 million, respectively when extrapolated to all British Indian participants of respective age groups with 'new' AF across England and Wales.

The anomaly of greater cost-effectiveness of AF screening amongst the entire sample than those aged ≥ 65 years, who were the most likely to benefit from the intervention (Kirchhof *et al.* 2016; Freedman *et al.* 2017), was unpredicted considering that the cost-effectiveness of AF detection typically increases with age (Welton *et al.* 2017). However, in light of previous population-based studies (Norberg *et al.* 2013; Public Health England 2017a), the cost-effectiveness analysis by Welton *et al.* (2017) assumed that the prevalence of AF increased with age from approximately 2% at the age of 50-54 to nearly 24% at the age of ≥ 85 years. Although this may be the case for individuals of all ethnicities, the gradient of increase may be to an extent lower amongst the South Asians than their White British age-matches (Mathur *et al.* 2013; Gillott *et al.* 2017). For instance, the data by Mathur *et al.* (2013) showed that the prevalence of AF amongst the White British individuals rose from approximately 0.2% at the ages of 18-49 to 14.0% in ≥ 80s (a 70-fold increase) whereas the equivalent figures in South Asian individuals of the same age groups were 0.1% and 4.0%, respectively (a 40-fold increase). A similar effect was noted during the present study where the prevalence of AF rose by only a fraction from 1.0% in the entire sample to 1.5% at the age of ≥ 65. This small increase in the prevalence of AF, and hence the proportion of patients who may benefit from AF detection, was not sufficient to offset the effect of higher mortality rate amongst the ≥ 65s compared to the entire sample of ≥ 18s, denoted by lower incremental QALYs (1.12 and 2.5 QALYs, respectively). Therefore, the base-case ICER of AF screening in ≥ 65s exceeded that of the entire sample irrespective of the lower incremental cost (£3,682 vs. £5,514 in ≥ 18s).

Despite the difference in economic benefits between the two age groups, the AF screening intervention with this South Asian community setting held an overall favourable cost-effectiveness profile in the context of pre-existing literature. The ICERs of £2,203/QALY gained and £3,283/QALY gained were not far from the £1,932/QALY gained reported for KMD-based cross-sectional AF screening of ≥ 65s in community pharmacies (Lowres *et al.* 2014) and were below the £4,292/QALY gained with intermittent AF screening of 75-76-year-olds using the Zenicor® $_{SL}$ECG device during the STROKESTOP study (Aronsson *et al.* 2015). The substantial ≥ 95% probability of cost-effectiveness also approached the 99-100% probabilities reported by Aronsson *et al.* (2015) or the MyDiagnostick® $_{SL}$ECG-

based AF screening of ≥ 65-year-olds in the Netherlands (Jacobs *et al.* 2018), and was significantly above the 60-80% probabilities of cost-effectiveness with pulse palpation-driven screening programmes (Hobbs *et al.* 2005; Moran *et al.* 2016). Moreover, the level of cost-effectiveness discovered by the current study was superior to the economic benefits of ≥ 65-year-old screening during either the PDAF study in GP surgeries (ICER £14,460/QALY gained; 71.8% cost-effective) or care homes (£6,223/QALY gained; 89.3% cost-effective).

There may be several explanations for this economic superiority of the adapted AF screening intervention within a South Asian community setting compared to parent studies in general practice or care homes. First and foremost, the AF screening strategies in GP surgeries and care homes accrued only 0.34 and 0.29 QALYs compared to the 1.12 QALYs with the screening of ≥ 65-year-old British Indian participants here. The key factor influencing this gap of incremental utility may have been the greater risk of ischaemic stroke and stroke mortality amongst South Asian individuals compared to the White British-dominated PDAF samples (Wild & Mckeigue 1997; Gunarathne *et al.* 2009; George *et al.* 2017), meaning that the former were more likely to benefit from the AF screening intervention. The difference in the probabilities of ischaemic stroke between the AF screening and no-screening scenarios was 3.4×10^{-3} for ≥ 65-year-old British Indians entering the model of this study, but only 7.0×10^{-4} for the PDAF sample in GP surgeries and 1.9×10^{-3} in care homes. Similarly, the difference in the probabilities of stroke mortality between the screening and no-screening was 1.75×10^{-2} for British Indian individuals compared to 4×10^{-3} for those during the PDAF study in GP surgeries and 1.14×10^{-2} in care homes. Furthermore, the generally greater diagnostic accuracy and the lower rate of 'Unclassified'/'Sinus Tachycardia' diagnoses (discussed above) meant that the incremental costs of AF screening amongst the ≥ 65s within the South Asian community were also lower than those in GP surgeries (£3,682 vs. £4,968), which overall translated into a more favourable ICER. In case of care home residents, the high proportion of individuals with previously undiagnosed AF who might benefit from AF screening (9.6% vs. 1.5% of ≥ 65-year-old British Indian participants) led to a low incremental cost of £1,778, however this was counterbalanced by the aforementioned low incremental QALYs, overall resulting in a less favourable ICER than those noted for British Indian participants.

Apart from age considerations, the remaining trends of the PSA conducted for the economic model of the present study were largely comparable to those observed during the PDAF studies. As discussed for KMD-based AF screening in GP surgeries and care homes, the cost-effectiveness of the intervention within a South Asian community was

preserved regardless of the variations in OAC adherence. Similar to the study by Lowres *et al.* (2014), the cost-effectiveness of the intervention was improved by about 29% with increasing level of OAC adherence, although this effect was less pronounced than the 50% change when transitioning from 40% to 80% adherence noted in GP surgeries and care homes. The ICER of the base case model was also reduced by almost 19% upon a shift to a warfarin-dominated scenario, indicating that the model was potentially more sensitive to changes in DOAC:VKA ratio than observed in GP surgeries (2.1%) or care homes (6.5%). This level of sensitivity was still far from the 57.4% improvement in cost-effectiveness when moving to a VKA-dominated model reported by Lowres *et al.* (2014), and may purely reflect the overall smaller absolute values of ICERs compared to PDAF studies. As in GP surgeries or care homes, the cost-effectiveness of the AF screening model presented here was particularly sensitive to changes in the screening participation rate, resulting in an almost 59% reduction of base-case ICERs with a screening uptake of 80% (38.4% in GP surgeries; 37.8% in care homes), however producing a 93% higher ICER with the uptake of 30% (69.3% in GP surgeries, 67.5% in care homes). Interestingly, halving the number of 'Unclassified'/'Sinus Tachycardia' diagnoses to 4.6% had a similar effect on improving the cost-effectiveness of the intervention as a switch from the DOAC- to VKA-dominated model (19%). That was not noticed in GP surgeries or care homes where halving the proportion of 'Unclassified'/'Unreadable' diagnoses resulted in 10% and 15% reductions of the base-case ICERs, respectively – far from the 2.1% and 6.5% reductions upon transitioning from the DOAC- to warfarin-based economic models. This phenomenon may be explained by differences in the proportions of 'Unclassified'/'Sinus Tachycardia' diagnoses, whereby their lower prevalence within a South Asian community setting (9.1% vs. 13.4% and 32.7% in GP surgeries and care homes respectively) made the model proportionally less sensitive to changes in this parameter.

6.5.2 Strengths and limitations

The primary strength of this study was its recruitment strategy, which included the delivery of AF screening within the local community setting of a selected South Asian group, assisted by language and ethnocultural concordance between the participants and the research team. As acknowledged by study participants in their feedback questionnaires, and as indicated by the use of non-English languages in > 30% of all consultations, this approach may have helped recruit those participants who may otherwise have not engaged in routine health testing delivered at GP surgeries due to linguistic, cultural or other common barriers (Netto *et al.* 2010; Palmer *et al.* 2015). It also helped identify patients who were suspected to have a previously undiagnosed AF, most of whom carried a high risk of ischaemic stroke (CHA_2DS_2VASc scores ≥ 3), possibly greater than that of

the PDAF study participants screened during the influenza vaccination season in GP surgeries or care homes.

To our knowledge, this study was the first to deliver an AF screening programme targeting a particular UK ethnic minority group and the first to implement the screening within a religious setting. The results of this feasibility study therefore complement the findings of the PDAF studies and other UK-based AF screening initiatives in primary care, which primarily recruited individuals of White British ethnicity (Hobbs *et al.* 2005; Halcox *et al.* 2017). They also add to the findings of previous epidemiological studies which investigated the prevalence of AF in South Asian ethnic groups (Conway & Lip 2003; Newton *et al.* 2005; Gunarathne *et al.* 2008; Gill *et al.* 2011; Mathur *et al.* 2013; Gillott *et al.* 2017; O'Neill *et al.* 2018a) by providing the real-world evidence in relation to both the prevalence of AF and the risk factors for ischaemic stroke within a community setting of a relatively homogeneous British Indian population. Similarly, the feasibility element of this study contributes to the results of previous CVD risk factor assessment programmes within the South Asian community or religious settings (Mathews *et al.* 2007; Netto *et al.* 2007; Patel *et al.* 2007; Rao *et al.* 2012; Jones *et al.* 2013; Eastwood *et al.* 2013). The feasibility of trained pharmacy undergraduates to deliver AF screening when supervised by CPs without a real-time input from the cardiologist adds to the results of other pharmacist-led AF screening programmes (section **1.3.3**) and may provide the foundations for a pharmacy team-focused AF screening model in primary care or community settings. Last but not least, the feasibility of the AF screening programme within a specific South Asian community discussed here was supported by the economic analysis which contributes to findings of previous general population-orientated cost-effectiveness studies (Hobbs *et al.* 2005; Lowres *et al.* 2014; Moran *et al.* 2016; Welton *et al.* 2017; Jacobs *et al.* 2018; Tarride *et al.* 2017).

As either of the two PDAF studies, this AF screening initiative was limited by its cross-sectional study design, which is critiqued in section **2.4.1**, and may have overlooked some of the individuals with AF due to the prevalence-incidence bias (Delgado-Rodriguez & Llorca 2004). Unlike during the PDAF studies in GP surgeries or care homes, the medical history of study participants screened by this study relied on self-reporting and was not validated with their GP records. Therefore, it is possible that the prevalence of AF or the risk factors for ischaemic stroke reported here were subject to a recall or reporting biases (Raphael 1987; Delgado-Rodriguez & Llorca 2004) and may not be an accurate estimate. The same effect may have also applied to the self-reported consumption of alcohol or

cigarette smoking, both of which may have been under-reported due to a related stigma in certain South Asian communities (Lee *et al.* 2008; Hrywna *et al.* 2016).

The absence of a pro-active, structured follow-up by the research team during this study may have affected the yield of 'new' AF diagnoses which was substantially below those reported for PDAF initiatives in GP surgeries or care homes. This deficiency of study design may have also prevented a well-rounded assessment of the feasibility associated with AF screening within this community setting, which in a real-world scenario would have included an established follow-up protocol, perhaps similar to the one-stop community pharmacy clinic described by Antoniou *et al.* (2019). Furthermore, owing to the feasibility design (NIHR Research Design Service London 2020), no sample size calculation was undertaken during this study, and as such it may have been underpowered to detect any statistically significant inferences in relation to either participant demographics or diagnostic accuracy. This study also focused on a single ethnic group of British Indian individuals recruited within a religious setting of a Sikh community. Whilst the findings presented here may be largely generalisable to individuals of a similar ethnic background, they may not be applicable to other South Asian ethnic or religious groups (Office for National Statistics 2012; Office for National Statistics 2018c). Finally, in the absence of study-derived data, the cost-effectiveness analyses conducted during this study assumed that the prevalence of 'unknown' AF was that reported by participants at the time of screening whereas the follow-up rate for $_{12L}$ECG procedures was adapted from the PDAF study in GP surgeries. The level of cost-effectiveness reported here may have therefore over-estimated the true economic impact of the AF screening intervention within this South Asian community setting.

6.6 Conclusion

This chapter presented the findings of the AF screening programme within a South Asian community setting, and evaluated its feasibility from the perspectives of recruitment, diagnostic accuracy, user acceptability and cost-effectiveness. The evidence outlined here supports the delivery of a systematic population screening of AF within this setting by trained pharmacy undergraduates using $_{SL}$ECG devices under the supervision of a CP. The convenience-focused recruitment strategy targeting individuals at local places of worship and delivering the consultations in their native language helped recruit a large and relevant sample of British Indian participants over a short period of time. The total prevalence of AF observed within this sample was marginally above the range of previous epidemiological studies in primary care, although concurred with the hypothesis that individuals of South Asian ethnicity may have a significantly lower prevalence of the

condition compared to the general population. The prevalence of previously undiagnosed AF amongst those aged ≥ 65 years (1.5%) was however comparable to the PDAF sample in GP surgeries (1.3%), and all ≥ 65s with AF and full demographic data qualified for OAC therapy, implying that the AF screening intervention within this community may still be largely beneficial.

In line with this finding, the automated algorithm of the KMD operated by pharmacy undergraduates displayed a high diagnostic accuracy for the detection of AF, which was similar to or above those observed during the PDAF studies in GP surgeries or care homes. Together with an elevated risk of ischaemic stroke within this ethnic group, the high diagnostic accuracy resulted in a favourable cost-effectiveness profile of the AF screening programme regardless of the participants' age group, possibly delivering greater economic benefits than the PDAF initiatives. The potential benefits of this community-based intervention were also apparent from its high acceptability amongst the study participants who praised the quick, informative and convenient AF screening within the stress-free environment, and expressed the willingness to engage with similar initiatives in the future. The encouraging findings of this study come at a time, when despite the overall improvement of CVD mortality, individuals from the BAME groups, particularly those of South Asian origin, continue to face an increased burden of IHD and stroke compared to the general population (Public Health England 2017c). The evidence presented here shows that conducting AF screening within a community or religious setting of South Asian ethnic groups may help reduce such health inequalities by providing a convenient access to healthcare and identifying those individuals with AF who are at a high risk of ischaemic stroke in a timely manner. The template of this intervention may help inform the development of future AF and/or CVD screening programmes within the BAME community settings to help achieve the targets set out in the Government's CVD agenda (Public Health England 2019c).

A number of questions were raised by the findings of this study and may form the basis of future research. First of all, respondents to feedback questionnaires highlighted several barriers to the implementation of health testing within South Asian communities, which may be further explored as part of a future qualitative evaluation. Qualitative research forms a crucial part of developing a complex intervention (MRC 2006), and similar to focus groups conducted during the PDAF study in GP surgeries (**Chapter 4**), may also help refine the screening protocol or roles of pharmacy professionals who may facilitate AF screening within this community setting in the future. Secondly, the lack of a structured follow-up and communication between the research team and GPs during this study makes it unclear as

to how such community-based AF screening programmes may operate outside the clinical research setting. Previous AF detection and CVD risk assessment studies conducted outside the general practice environment reported concerns about the effectiveness of follow-up care (Eastwood *et al.* 2013; Lowres *et al.* 2015; Sandhu *et al.* 2016; Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020), suggesting that a clearly defined GP referral pathway may be a priority for the successful implementation of future AF screening initiatives within community or religious settings. In order to ensure the sustainability of routine AF screening in this environment, future researchers and commissioners should also consider the appropriate models of funding or reimbursement, which would likely involve its branding as an enhanced service within an appropriate NHS contract (NHS England and BMA 2019a; Department of Health and Social Care 2019). Lastly, future feasibility studies may wish to explore the implementation of AF screening intervention proposed here amongst the other UK BAME groups, such as the African Caribbean communities, who may experience a similar paradox of high CVD risk-low AF prevalence reported for individuals of South Asian origin (Conway & Lip 2003; Mathur *et al.* 2013).

Chapter 7: General practitioners' perspectives on UK atrial fibrillation screening programme: a qualitative study

7.1 Introduction

The qualitative component of the PDAF study (**Chapter 4**) revealed the key facilitators and barriers to CP-led AF screening in GP surgeries from the perspectives of service users (patients), service providers (CPs) and GPS. None of the GPs from participating practices within the PDAF study were available to attend these focus groups. However, they did evaluate the AF screening intervention by completing a short questionnaire (**Chapter 3**). Although responding GPs were overall pleased with the PDAF initiative, the use of KMDs to detect AF and the idea of CP-led AF screening, several of them identified potential barriers to future implementation, such as the lack of funding, which may require a further exploration.

As the leads of service commissioning and delivery in primary care, GPs have traditionally been at the centre of service development and implementation (Woodrow *et al.* 2006; Pickles *et al.* 2016; NHS Providers and NHS Clinical Commissioners 2018; NHS England 2019d). The deepening workforce crisis in general practice means that it is perhaps now more crucial than ever to consult GPs alongside other stakeholders when developing or evaluating a new service (Gibson *et al.* 2017; The King's Fund 2019a; NHS Digital 2019b). This may be particularly important for a widespread implementation of a relatively controversial public health service, such as the national AF screening programme (Lown *et al.* 2017a), which is not currently endorsed by the UK NSC (2019) due to the lack of direct evidence pertaining to clinical outcomes. Nevertheless, according to a recent UK-based survey (Taggar *et al.* 2016b), over 90% of GPs and practice-based nurses follow the international consensus by conducting routine opportunistic pulse checks (Kirchhof *et al.* 2016; Freedman *et al.* 2017). Whilst this may be driven by professional responsibility to identify those with undiagnosed AF and to offer a timely treatment, it is also likely incentivised by the inclusion of AF-related quality indicators in the QOF (NHS England and BMA 2019a). The achievement of targets set out in the QOF has been made easier by the recent AHSN's AF screening initiative in England (The AHSN Network 2019a). It is therefore unsurprising that GP surgeries in England achieve over 97% of the QOF scores available for maintaining a register of patients with AF and for assessing a stroke risk in those with a CHA_2DS_2-VASc score of ≥ 2 (NHS Digital 2019c).

The reality of conducting opportunistic AF detection in order to meet the QOF demands and the Government's CVD targets (Public Health England 2019c; NHS England and BMA 2019a) within the pressured general practice environment may however be somewhat less bright. The survey by Taggar *et al.* (2016b) suggested that healthcare professionals (HCPs) who may be ultimately responsible for the delivery of the national AF screening programme, including GPs, nurses or HCAs, were all affected by common barriers such as the need for further training, excessive workload and the lack of funding. GPs who typically lead the diagnosis and management of AF in particular appealed for extra resources to facilitate the national AF screening programme and raised concerns about being *'overstretched with work and conflicting demands'* (Taggar *et al.* 2016b). The findings of qualitative AF screening evaluations in Australian GP surgeries echoed some of these themes, emphasising the funding and time considerations, especially where screening was delivered in conjunction with other time-pressured services, such as seasonal influenza vaccinations (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019a). As observed during the qualitative evaluation of the PDAF study (**Chapter 4**), some of the interviewees involved in these initiatives stressed the importance of GP leadership to champion the programme, and that of established protocols to facilitate the follow-up and management of individuals with AF (Orchard *et al.* 2016; Orchard *et al.* 2019a).

Despite the fact that qualitative research plays an essential role in the refinement and evaluation of a complex intervention prior to its implementation (MRC 2006), few UK-based studies to date have taken an opportunity to consult their stakeholders about the facilitators and barriers to AF screening (Lown *et al.* 2020; Savickas *et al.* 2020c). In turn, to our knowledge and pending the results of the SAFER study (ISRCTN Registry 2019), none of the UK-based primary care research to date had interviewed GPs about their views towards routine AF screening interventions or programmes (Sudlow *et al.* 1998a; Somerville *et al.* 2000; Morgan & Mant 2002; Hobbs *et al.* 2005; Rhys *et al.* 2013; Kearley *et al.* 2014; Twigg *et al.* 2016; Halcox *et al.* 2017; Lown *et al.* 2018; Antoniou *et al.* 2019; Lown *et al.* 2020). As shown by the results presented by Taggar *et al.* (2016b) and studies in Australian primary care (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019a), several aspects of the prospective AF screening programme may be subject to a further qualitative exploration. Besides the facilitators and barriers to AF screening outlined above, one may for instance wish to explore the success of any local or regional AF screening initiatives. The recent independent evaluation of the AHSN programme reported a mixed reception from GPs who were happy to use $_{SL}$ECG devices to help detect AF, yet were confused about their added value to conventional pulse palpation, and were more likely than any other user groups to drop out of the initiative (Wessex AHSN 2019). Similar to their

Australian counterparts (Orchard *et al.* 2014; Orchard *et al.* 2019b), some of the GPs interviewed by the AHSN evaluation struggled with the technological aspects of using the KMD or reported issues with the device's reliability (Wessex AHSN 2019). A further qualitative investigation may help explore these barriers, and may ascertain whether or not they apply to other modern AF detection tools, such as the other $_{SL}$ECG devices, mBPMs or PPG-capable technology, which typically display a favourable diagnostic accuracy, cost-effectiveness and user-acceptability (Taggar *et al.* 2016a; Halcox *et al.* 2017; Welton *et al.* 2017; Lown *et al.* 2018; Duarte *et al.* 2019; Lown *et al.* 2020).

Another consideration in the development of the national AF screening programme may be a selection of appropriate staff to conduct the screening. As shown by evidence presented in **Chapters 3-6** and previous primary care-based initiatives (Orchard *et al.* 2014; Lowres *et al.* 2014; Lowres *et al.* 2015; Orchard *et al.* 2016; Twigg *et al.* 2016; Zaprutko *et al.* 2019; Wessex AHSN 2019; da Costa *et al.* 2020), AF screening responsibilities may extend beyond GPs or nurses to pharmacists, pharmacy technicians/assistants, clinical support/administrative staff, and even pharmacy students. Following a degree of success when conducting AF screening programmes in care homes (**Chapter 5**) (Wiesel & Salomone 2017; Khan *et al.* 2020), community pharmacies (Lowres *et al.* 2014; Twigg *et al.* 2016; Sandhu *et al.* 2016; Zaprutko *et al.* 2019; Bacchini *et al.* 2019; Antoniou *et al.* 2019; da Costa *et al.* 2020) and other public or community locations (**Chapter 6**) (Doliwa *et al.* 2009; Battipaglia *et al.* 2016), the developers of the future AF screening programme may also need to consider the most optimal target group(s) and setting(s) for its effective and efficient delivery. Last but not least, as discussed in section **1.2.3**, the effectiveness and cost-effectiveness of AF screening may vary with the selection of an appropriate screening strategy, such as opportunistic vs. population-based or targeted approaches, and single time point vs. intermittent screening.

This chapter presents the findings of a qualitative study with GPs in England, which aimed to ascertain their perspectives in relation to AF detection and the UK national AF screening programme by exploring the aspects of its design and delivery outlined above. It builds on multi-stakeholder feedback received during the PDAF study in GP surgeries (**Chapters 3 and 4**), the findings of the cross-sectional survey by Taggar *et al.* (2016b) and themes from previous qualitative studies with GPs (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019a; Wessex AHSN 2019) to determine how the concepts identified by these studies may apply to UK-based clinicians. Using the method of individual, semi-structured interviews and the TDF approach adapted from the PDAF qualitative evaluation (**Chapter 4**) (Atkins *et al.* 2017; Savickas *et al.* 2020c) this study focused on the facilitators and

barriers to the development and implementation of widespread AF screening. The qualitative themes derived through this study were expected to contribute to the development of future UK-based, centralised AF screening initiatives, and to act as a source and theory triangulation (Patton 1999) for qualitative themes from interviews with non-GP stakeholders presented in **Chapter 4**. This chapter therefore maps onto both the development and evaluation elements of the MRC (2006) guidance for complex interventions.

7.2 Aim and objectives

Aim:

To explore the perspectives of UK-based GPs in relation to the national AF screening programme, focusing on the facilitators and barriers to its development and implementation.

Objectives:

1. To ascertain the views of GPs with regards to the perceived importance of AF screening, and patient or public awareness of AF.
2. To explore the current GP involvement in any AF screening initiatives locally, regionally or nationally, including any facilitators and barriers to their development and implementation.
3. To ascertain the views and opinions of GPs with regards to the most optimal AF screening strategy, setting/environment and staff responsibilities.
4. To investigate the key strengths and limitations of different AF screening methods or tools (pulse palpation, $_{SL}$ECG devices, mBPMs, PPG-capable technology) from the perspectives of GPs.
5. To derive the key facilitators and barriers to the development and implementation of the national AF screening programme from the perspectives of GPs.
6. To map the key facilitators and barriers onto the TDF in order to determine the primary areas of concern to be addressed in the development and implementation of future AF screening initiatives, including the national AF screening programme.

7.3. Methods

7.3.1 Study design

This qualitative research project was designed and delivered in a sequential manner following the PDAF study (Giddings & Grant 2006; Tariq & Woodman 2013), using the TDF

methodology adapted from Islam *et al.* (2012) and Atkins *et al.* (2017), and the parent study in GP surgeries (**Chapter 4**) (Savickas *et al.* 2020c). The use of the TDF in health services research and its application to qualitative evaluations included in this enquiry are discussed in section **2.4.2**. During this study, the TDF domains and component constructs were consulted when designing the topic guide and when analysing the qualitative data. In order to facilitate the engagement of time-pressured GPs, this study utilised a convenient data collection method of individual semi-structured interviews (Breen 2006; Adams 2015; DeJonckheere & Vaughn 2019), which have been commonly used to explore the views of GPs by previous AF screening programmes (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019a). Individual interviews also offer an opportunity to focus on private and relatively uninfluenced experiences or perspectives of participants, which was desired by this study considering its local/regional recruitment strategy and hence the possible interviewee relationships that may otherwise affect the findings (Adams 2015; DeJonckheere & Vaughn 2019).

7.3.2 Design of topic guide

A flexible, semi-structured interview topic guide was designed by VS using the themes of previous qualitative evaluations of AF screening programmes in primary care (Orchard *et al.* 2014; Lowres *et al.* 2014; Orchard *et al.* 2016; Sabater-Hernandez *et al.* 2018), and the multi-stakeholder feedback obtained during the PDAF study in GP surgeries (**Chapters 3 and 4**). The development of the topic guide also took into account the themes reported in the evaluation of the AHSN initiative (Wessex AHSN 2019), the cross-sectional AF screening survey by Taggar *et al.* (2016b) and the systematic review of AF screening strategies by Welton *et al.* (2017). The structure of the topic guide, the questions and follow-up probes were further refined using the domains and component constructs of the TDF (Cane *et al.* 2012), and the questioning route for semi-structured interviews proposed by DeJonckheere & Vaughn (2019). The topic guide (**Appendix 56**) consisted of an introduction followed by nine open-ended questions to explore the importance of AF screening as a whole, the GP involvement in any previous or ongoing AF screening initiatives, the design aspects of a potential AF screening programme (strategy, target group, environment, staff selection, screening tools) and the patient or public awareness of the condition. The planned prompts or follow-up questions, which accompanied the main questions, were designed to probe into participants' answers and the emerging themes (DeJonckheere & Vaughn 2019).

The draft of the topic guide was piloted by VS during semi-structured interviews with a convenience sample of four GPs from Kent, UK (Saumure & Given 2008a). Although no

formal changes to the topic guide were introduced following the pilot, several emerging themes, for instance the increase in service demand due to public health campaigns, were further explored during the subsequent interviews. The data from pilot interviews were included in data analysis. The final version of the topic guide was reviewed and approved by VS and SC, who was the PI for the study.

7.3.3 Recruitment and informed consent

A convenience sampling method was employed to recruit GPs based in Kent, using a list of contacts with local GP surgeries and CCGs, which was maintained by members of the PDAF research team (Saumure & Given 2008a). The list encompassed organisations from five out of eight CCG areas of Kent (Medway, Canterbury and Coastal, Ashford, Thanet and West Kent), and included all four GP surgeries based in the Canterbury and Coastal CCG area that were involved in the PDAF study (Kent County Council 2020). All prospective participants who were registered as a GP with the General Medical Council (GMC) were eligible to take part in the study unless they had a lack of mental capacity to provide an informed consent. With reference to previous qualitative studies involving GPs in the UK or elsewhere, the preliminary sample size required to reach data saturation (Atkins *et al.* 2017) was estimated to lie between three and 38 participants (Woodrow *et al.* 2006; Bösner *et al.* 2014; Orchard *et al.* 2014; Orchard *et al.* 2016; Croxson *et al.* 2017; Wessex AHSN 2019).

In October 2019, VS sent out email invitations (**Appendix 57**) with an enclosed PIL (**Appendix 58**) and a consent form (**Appendix 59**) to gatekeepers of each GP surgery or CCG asking them to circulate the email to any GPs within their respective organisations. The email invited eligible GPs to take part in a short telephone interview with a researcher aimed at exploring their perspectives on AF screening initiatives, which may ultimately contribute to the development of a future national AF screening programme. Those who were interested in participating were asked to reply to the email and provide the further details of their name/surname, the GMC registration number, the preferred contact details and the convenient date/time for the interview. Following the example set by previous UK-based qualitative studies with GPs (Woodrow *et al.* 2006; Croxson *et al.* 2017), each participant was incentivised to take part by reimbursing their time with a £50 Amazon voucher.

All consecutive GPs who replied to the email invitation were enrolled onto the study and were contacted by VS to arrange a telephone interview. Prior to commencing each interview, VS explained the purpose of the study, the structure of the interview and the data management referring to the PIL as necessary. Each prospective participant was also given

an opportunity to ask VS any questions they may have. A written informed consent was then obtained from each participant by physically or electronically signing a consent form in line with the ethical approval, with one copy retained by the participant and one by the research team. Data saturation was considered following the interviews with all GPs who responded to the initial round of email invitations. Since no new information about the facilitators and barriers to the national AF screening programme emerged following the interview with the eighth participant (Atkins *et al.* 2017), the consensus of VS and SC was that data saturation was reached, and no further invitations to take part were distributed.

7.3.4 Facilitation and data collection

All interviews were conducted at a time and location convenient for each participant. In order to minimise the risk to their confidentiality, each participant was advised to avoid any public places during the conduct of the telephone interview and were informed that remaining in their office at the GP surgery may carry a small risk of being overheard by colleagues or patients. In turn, during the conduct of each interview, the facilitator stayed in a quiet enclosed office at the MSOP, which was expected to maximise the quality of audio recordings and reduce the risk of being unintentionally overheard or interrupted by other members of staff or students (DeJonckheere & Vaughn 2019).

All interviews were facilitated by VS who had previously conducted several focus groups as part of the PDAF study evaluation (**Chapter 4**). In preparation for the study, VS reviewed the principles of semi-structured individual interviewing outlined by Adams (2015) and DeJonckheere & Vaughn (2019), placing a particular emphasis on the interviewing technique. The layout of the interview followed that of the flexible topic guide, which was in turn structured around the questioning technique described by DeJonckheere & Vaughn (2019). After introducing each participant to the study and obtaining informed consent, VS began the interview with a general question about the importance of AF screening. This was followed by seven core questions to explore the various aspects of AF detection and AF screening initiatives, and a closing question asking the participant whether or not they had any further comments or thoughts. Each of the questions were accompanied by planned and unplanned follow-up questions or prompts to ascertain more information about the participants' responses. For instance, some of the follow-up questions explored the participants' concerns about the new tools for AF detection*, 'What are the key limitations of* $_{SL}$*ECG devices in your opinion?'* or the AF awareness campaigns, *'What are your concerns about raising AF awareness through public health campaigns?'*.

The interviews were audio-recorded using Olympus® recorders provided by the MSOP. In addition, VS maintained a diary of notes or memos recorded in the comments section of the topic guide for each interview, which acted as a supplementary source of information for data analysis (Patton 1999; DeJonckheere & Vaughn 2019). The audio recordings were transcribed verbatim by VS, with the accuracy of transcription confirmed by SC.

7.3.5 Data coding and analysis

The coding and data analysis were carried out by VS using the deductive-inductive TDF approach adapted from Atkins *et al.* (2017), Islam *et al.* (2012) and the PDAF qualitative evaluation (Savickas *et al.* 2020c) as outlined in section **2.9**. The memos noted down by VS during the interviews were consulted after the preliminary analysis to support the identification of key facilitators and barriers (Lincoln & Guba 1985b; Forero *et al.* 2018). The coding of transcripts and data analysis were independently reviewed and verified by SC. The main themes and subthemes derived during the analysis were also subject to a further analyst and theory triangulation (Patton 1999) by ensuring they were reviewed by another researcher with extensive qualitative research experience (SB) and by two additional members of the research team who provided the less specialist views (EV and AM).

7.3.6 Reflexivity

VS and SC were both registered pharmacists and were heavily involved in the design and delivery of the PDAF study (**Chapters 3-5**). As such they maintained a reflexive account to acknowledge the potential of their personal bias or the influence of their professional background on the findings of the study (Stewart *et al.* 2007; Hiller & Vears 2016). For instance, as a CP who conducted AF screening during the PDAF study, VS may have been more subconsciously inclined to explore the AF screening models which focus on the role of primary care pharmacists during the semi-structured interviews. SC who led the qualitative component of the PDAF study may have inadvertently looked for themes voiced by participants of the focus groups, including the facilitators that may enable the delivery of AF screening in GP surgeries. In turn, due to the conduct of the PDAF study and the close proximity of the MSOP to GP surgeries in the region, some of the participants interviewed during this project may have had a previous contact with VS or worked at GP surgeries participating in the PDAF initiative. As such, some of them may have been more biased or inclined to tailor their answers to the expectations of VS rather than reflect their true views (Korstjens & Moser 2018).

7.4 Results

7.4.1 Study participants

A total of ten GPs from six different CCG areas of Kent took part in 20-40-minute semi-structured telephone interviews between November and December 2019 (**Table 7.1**). Three of the four GPs from the area of Canterbury and Coastal CCG worked at GP surgeries which had participated in the PDAF study (GP01, GP05, GP07). One other GP (GP10) practised at the surgery which had taken part in the AHSN's *'Detect, Protect and Perfect'* initiative for AF detection.

The level of medical experience amongst participants ranged from nine to 34 years whereas the number of years as a registered GP varied from two to 13 years (*N.b.* although the GMC register was established in 1858, the GP section of the register was created only in 2006 (GMC 2020a; GMC 2020b)). One of the participants (GP01) was a GP with an extended role (GPwER) in cardiology.

Table 7.1 Demographic characteristics of study participants

Abbreviations: CCG – clinical commissioning group; GMC – General Medical Council; GP – general practitioner.

Characteristics		**N = 10**
Gender	Male	4
	Female	6
CCG Area	Canterbury and Coastal	4
	Ashford	2
	Medway	1
	West Kent	1
	South Kent Coast	1
	Thanet	1
Years on GMC Register	9-12	4
	13-24	5
	34	1
Years on GP Register	2-4	2
	6-8	3
	10-13	5

7.4.2 Key findings mapped onto the TDF

The coding and analysis of qualitative data from semi-structured interviews identified five key TDF domains which were expected to influence the development and implementation of the future national AF screening programme. The bulk of facilitators and barriers were derived from two or more of these. Where a factor was associated with multiple domains it was presented under the domain perceived to be most relevant (**Table 7.2**). For example, the facilitator 'Obtaining evidence to support screening' was originally mapped onto both 'Goals' and 'Knowledge' domains but was presented under the latter to reflect the close relationship between clinical knowledge and research-generated evidence.

The domain of **'Environmental context and resources'** prevailed in conversations with all 10 GPs who expressed their concerns about the additional costs and human resources required to facilitate new services at the time of an ongoing GP workforce crisis. In most instances however AF detection was perceived as a long-term investment due to the cost-effective prevention of its deleterious consequences, for example, cardioembolic stroke. The majority of interviewees agreed that the use of resources could also be optimised by carefully planning the screening of individuals at risk of AF and/or stroke in multiple care settings and by the consistent use of cheap yet effective detection methods, such as conventional pulse palpation or $_{SL}$ECG devices.

The other key **'Goals'** for the development and implementation of the national AF screening programme included improved leadership by regional or national bodies, engagement of local champions and appropriate service design within the existing infrastructure to capture at-risk individuals. Besides the resource and design considerations, participants focused on the **'Social or professional role and identity'** of themselves and other clinical or non-clinical staff within the possible AF screening initiatives. Most GPs were confident about their current practice which incorporated opportunistic *ad hoc* AF detection amongst at-risk or symptomatic patients. Nevertheless, they appreciated that the ever-increasing demand on GP services meant some of these responsibilities would need to be allocated to the MDT, if a national AF screening service would be viable in the future. Participants also felt that a simultaneous shift in the mindset of GPs with regards to the necessity for routine AF detection was essential to implement a consistent service across the board.

'**Knowledge'** was the primary TDF domain perceived to affect the patient engagement in AF screening services. GPs identified the lack of public awareness in relation to AF and its risks highlighting the importance of measured and well-organised public health campaigns. Some interviewees appealed for more clinical evidence to support routine AF screening

whilst the vast majority recognised the need for further staff education and training. Conversations relating to professional confidence and inaccuracies of current AF detection methods dominated the **'Beliefs about capabilities'** domain, and a number of participants perceived the inability to keep up with new technology as a possible barrier to patient and HCP engagement.

The final inter-domain analysis enabled the organisation of facilitators and barriers from the five TDF domains into three overarching themes: prioritisation of resources, service organisation and integration, and knowledge and capabilities. Each of the themes with underlying subthemes, including the facilitators and barriers, is discussed below.

7.4.3 Prioritisation of resources

Workload and funding

All participants expressed a degree of concern that the introduction of formal AF screening service would lead to extra workload at the time when primary care was already facing immense pressure and struggled to ensure the fundamental safety of existing services. Apart from time taken to conduct the screening, GPs pointed out the resource-demanding nature of follow-up tasks and disease management, such as biochemical test results, patient consultations and anticoagulation monitoring, which might divert staff from undertaking other key professional tasks, for example the delivery of vaccinations or care for patients with long-term illnesses:

'One of the reasons our vaccination rates have dropped among children is because it's difficult accessing appointments. So I think the last thing we want to do is add in another appointment-heavy system that's gonna slow down the rest of general practice … I think that we're at the point where GP surgeries simply can't take on any more work and carry on offering a safe service.' [GP03]

Nine out of ten GPs thought that additional staff capacity required to facilitate a future AF screening programme could be created through appropriate regional or national funding streams and financial incentives. Two GPs doubted the effectiveness of current incentives, for instance the QOF reward scheme:

'I think QOF is pushing it but not to an extent that we would like it to be pushed.' [GP04]

Table 7.2 Key facilitators and barriers to the development and implementation of the future national AF screening programme mapped against the most relevant TDF domains

Abbreviations: AF – atrial fibrillation; GP – general practitioner, TDF – Theoretical Domains Framework.

TDF Domain(s)	Facilitators	Barriers
Environmental context and resources	Targeting individuals in multiple settings	Additional workload for insufficient workforce
	Appropriate AF detection tools	Service costs and limited funding
	Positive resource implications of AF detection	Variable healthcare resources
Goals	Prioritisation of target group(s)	Difficulties capturing at-risk individuals
	Optimal service organisation and leadership	Inadequate central organisation
	Integrating AF detection into existing services	Challenges of service integration
	Appropriate self-detection by patients	Health anxiety of self-detection
Social or professional role and identity	Utilisation of multidisciplinary team	Competing professional priorities
	Professional responsibility for AF detection	Disconnection from decision-makers
	Organisational commitment of surgeries	Short-term thinking or ignorance
		Competition between GP surgeries and community pharmacies
Knowledge	Knowledge and awareness	Health anxiety fuelled by public awareness
		Limited GP knowledge of novel technology
	Obtaining evidence to support screening	Knowledge of anticoagulation-related risks
		Poor public understanding of AF and risks
Beliefs about capabilities	Confidence in detection and management of AF	Limitations of current detection methods
	Preventing the consequences of AF	Educational needs of staff
		Challenges of using novel technology

Another interviewee suggested that introducing AF screening as an enhanced service within the GMS contract may be an effective alternative. This proposal was disputed by a different GP who pointed out the flaws in the logistics of the reimbursement system linked to the GMS contract:

'As you know the GP contract is a 'block' contract and so none of the work generated from a screening programme is funded … £80-£85 is how much we're paid to look after a patient the entire year no matter how many times they see us … So I think this whole funding system has got serious problems anyway.' [GP05]

Despite acknowledging the financial impact of new service development and implementation, most GPs viewed AF detection as a positive investment towards stroke prevention, which may ultimately lead to a reduction in treatment costs, improved use of human resources as well as enhanced patient care, QOL and productivity:

'It makes sense on many fronts: it makes sense in terms of the quality of life of patients, it makes sense economically, if you see the cost associated with say a dense hemiplegia and then the care and everything else … but obviously there's always this challenge to pay up front for that.' [GP01]

Tools for AF detection

Six interviewees from five different CCG areas reported having used handheld $_{SL}$ECG devices to either detect or monitor AF. This included two GPs from surgeries involved in the PDAF initiative and the GP whose surgery participated in the AHSN project. Four GPs used such devices selectively to detect AF in symptomatic patients either in a clinic setting or by asking patients to self-monitor at home. The other two GPs used the device for either opportunistic detection of AF in a clinic or to guide the management of PAF:

'I've got a couple of patients who have got AF which is paroxysmal and they have got this device, and whenever they feel their palpitation, they check.' [GP09]

Several GPs who used $_{SL}$ECG devices routinely praised their favourable cost-effectiveness profile and the simplicity of operation that enabled AF detection by patients or support staff, such as HCAs. Remote interpretation of $_{SL}$ECG or $_{6L}$ECG was suggested as an innovative option to address primary care workforce issues for services, such as AF screening:

'So the ECG doesn't have to be interpreted by them there, it can then go to someone for interpretation and who can then decide if someone needs a full ECG … And we need to adopt these new ways of working with our workforce problem.' [GP01]

However, not all GPs were positive about the introduction of new tools for AF detection. Half of all participants, including some of those who used modern technology for AF detection, highlighted the added costs of devices, education and human resources especially where devices were to be handed out to patients or previously untrained staff. Others were discouraged from using novel technology routinely due to additional time required and inconvenience caused when finding or setting up the devices, or by privacy concerns where devices were to be connected to their personal mobile phones:
'To me that's just a whole new element of time and you're gonna have to get a phone out and do that. I don't wanna use my own phone to do that.' [GP07]

A few interviewees shared their experience of inability to capture PAF and the inconsistent diagnostic accuracy or poor ECG quality associated with $_{SL}$ECG devices, which might lead to time- and resource-consuming false positive diagnoses. This included the GPwER in cardiology who, despite praising $_{SL}$ECG technology, admitted that a confirmatory $_{12L}$ECG check was typically required to diagnose the patient with AF before considering treatment:
'I know some of the tracings are very clear, but my own preference is to actually then confirm with a $_{12L}$ECG *… It's a big big thing to go on an anticoagulant for life and take on the risk of bleeding.'* [GP01]

Most GPs were also sceptical about the potential of other currently available novel technologies used to detect AF, such as the mBPMs and smart watches or mobile phone applications utilising PPG. Similar to $_{SL}$ECG devices, the questionable accuracy and self-monitoring nature of this technology was linked to an increase in health anxiety and the influx of false positive diagnoses leading to unplanned costs and workload:
'We have patients who have pulse oximeters and things, they look at their pulse. The people who buy them by large are the worried-well and cause an enormous amount of additional work … And that is costing system huge amount.' [GP10]

Novel technology was perceived to be a barrier not just for GPs, but also for service users. Several participants were concerned that routine use of more advanced technology (e.g. mobile phone applications) might prevent the engagement of older, at-risk individuals who were not *'tech-savvy'* or had physical comorbidities:
'By putting it in front the sort of really high-tech solution you're appealing to the 40- or 50-year-olds who are not going to be eligible for anticoagulation anyway. You've got to find something that's actually suitable for the people who may find it difficult to see, you know, trying to read when you got cataracts, is not easy. Trying to use devices where your hands

are full of arthritis is not easy … You've got to find something that is going to appeal to the age group which is most gonna benefit.' [GP05]

Instead of using novel technologies to detect AF, three participants advocated for conventional pulse palpation, which was perceived as a cheap, quick and convenient alternative:

'So the screening as I believe it has to be quick and easy, simple and cheap and acceptable for everybody. And you know of course if you have a preference to do a $_{SL}$ECG*, it's fine but it's still not as easy as feeling the pulse.'* [GP06]

This view was challenged by several GPs who thought that the sole use of pulse palpation may be as inaccurate as other means of AF detection due to the frequent occurrence of ectopic beats. One proposed the combined use of pulse palpation and $_{SL}$ECG to reduce the risk of false positive diagnoses:

'I think if you were just doing a pulse check, then that would be a risk. I think if you do pulse check plus then you had some way of taking $_{SL}$ECG *you'll get some false positives but not as many.'* [GP07]

Prioritisation of target group(s)

All participants agreed that, in order to be cost-effective, any future national AF screening initiative should target a clearly defined group of individuals. Some GPs focused on the detection of AF in symptomatic individuals, the group of patients which, according to one of the participants, carried the most clinical evidence to support the management of newly detected AF:

'We know about what happens with AF in symptomatic people but actually what we don't know is these people that don't have symptoms what the outcome of that might have been … So we do have AliveCor® devices within the practice that we generally use for screening symptomatic people. So not screening but for sort of assessing symptomatic people.' [GP10]

Apart from clinical assessment of symptomatic patients, the majority of GPs highlighted older patients with or without the comorbidities or risk factors for AF and stroke, such as diabetes, hypertension and IHD:

'I can support the idea of screening those at increased risk. Now whether sort of over 65 as being the only criteria is the best way of going about it, I hesitate to give a definite opinion on. I suspect there's probably a more nuanced way of stratifying patients that would perhaps be more effective, and I'm in the back of my mind thinking of the QRISK tool … it has

multiple independent risk factors, that it aggregates together to give an overall score.' [GP02]

The age of 65 appeared to be the common threshold for the pursuit of AF detection or screening and half of all interviewees conducted opportunistic pulse palpation amongst the older asymptomatic individuals. Three GPs suggested targeting slightly younger patients, particularly if they had or were likely to develop any of the aforementioned risk factors for stroke, which may qualify them for OAC therapy:

'We are seeing quite a few strokes in the younger population as well. And, I mean we had a few in around 55-58. So I think 62 to 65 is not right … It should be 50 and above in my understanding.' [GP04]

7.4.4 Service organisation and integration

Design and integration

Four GPs, two of whom were involved in the PDAF initiative, identified seasonal influenza vaccination clinics as a suitable companion service for AF screening interventions because of the shared age group of those eligible for this service. Several participants recalled the past or current opportunistic AF detection during the influenza vaccination clinics, but these initiatives were rarely formal or implemented consistently:

'The nurses will always check the pulse when they do a blood pressure so there is a lot of opportunistic screening that goes on at the flu clinics but not in a kind of formal way.' [GP07]

Other GPs considered the hectic and *'rapid-firing'* nature of influenza vaccination clinics to be a barrier to AF screening, making it nearly impossible to combine these clinics effectively with any intervention that lasts more than a few minutes. This limitation pointed back at the capped workforce and funding, which would need to be expanded in order to enable such an extensive service:

'Flu clinics are very very busy, very pressured. If you want to do screening with flu clinics together I think it's very good idea, however that really needs funding because giving a flu vaccine is about 10 seconds, giving a pulse check is another 10 seconds so you really slow down the flu clinics.' [GP06]

Three participants reflected on the possible competition between GP practices and community pharmacies which has resulted in an unpredictable uptake of seasonal influenza vaccinations and might in turn affect the effectiveness of the combined AF screening service. These GPs felt that the rate of 'new' AF detection may be further compromised by

the fact that individuals attending seasonal influenza vaccinations tended to be the pro-active, healthy group which participated in the service on an annual basis:
'You have that engaged group of patients so they will be getting screened every year. But I think you have others who don't take up flu. There's also those who actually don't have flu with the GP, they'll go and see a pharmacy.' [GP01]

In order to circumvent this issue and capture the at-risk population, half of all GPs considered opportunistic AF screening of patients with long-term conditions attending their annual (QOF) reviews (e.g. during a BP check) as an alternative to the combination with seasonal influenza vaccinations:
'If somebody is coming for say diabetes, hypertension, stroke, ischaemic heart disease, what else I think, peripheral artery disease. All the patients coming for the annual QOF review, their pulse is being checked manually. That's standard protocol in our practice.' [GP09]

One participant was also in support of conducting more formal AF screening during the NHS Health Check appointments:
'*That's why the NHS Health Check sort of comes to mind in that you are already doing blood pressure, cholesterol, maybe HbA1c [glycated haemoglobin], you're getting an age-defined population.'* [GP02]

This view was challenged by the rest of the cohort who felt that such appointments typically involved younger patients that were unlikely to benefit from AF detection and OAC therapy should AF be discovered. A few interviewees pointed out the fact that, similar to seasonal influenza vaccinations, individuals attending NHS Health Checks might also be the worried-well who are concerned about their health rather than the at-risk group that does not visit the GP:
'I look at people for example who turn up to NHS Health Checks, they're not the higher-risk people that you would want to be looking at. So I think that we need to think much more about how we make sure we get the right people coming forward.' [GP10]

Two participants from the same CCG area shared their experience of how pre-programmed prompts on electronic medical records may help capture the at-risk group as part of *ad hoc* opportunistic AF detection:
'We use Emis software system and it automatically brings a pop-up on the right lower corner to say, 'Pulse check needed.' So we automatically do the screening whenever we see a patient I think it's over 65.' [GP06]

One interviewee combined the thoughts of targeted and opportunistic AF screening to improve the coverage of at-risk group by proposing a system of annual AF detection as part of seasonal influenza vaccination clinics and opportunistic AF detection during routine appointments:

'But I think that would be only a one-off screening anyway and as you know you can go in and out of rhythm so that might need more opportunities to do it. I think it needs to be probably a combination of opportunistic and a sort of yearly-opportunistic, so flu jab.' [GP05]

As a deviation from the group consensus, one GP felt that the time pressure of routine appointments, for example medication reviews, meant AF screening was better suited to be a standalone intervention instead of becoming integrated within the service bundle:

'A medication review on its own is complicated enough without necessarily sort of having to add on something that's not directly related … I think ideally a screening effort probably ought to be a standalone thing in that it may be complicated enough as it is.' [GP02]

Despite the availability of novel technology, the majority of GPs did not support routine self-detection of AF by patients at home due to the aforementioned concerns about health anxiety. They were instead supportive of self-detection within a safe healthcare environment, for instance the community pharmacies or GP surgeries. More than half of all interviewees felt that stationary devices, such as those incorporating $_{SL}$ECG, could be made available in the waiting areas of healthcare institutions for patients to self-test in a similar way to BP machines. This would be followed by the referral to a HCP should any abnormalities be detected:

'Maybe if there is a device next to the check-in screen at the GP practice, 'Please put your thumb or finger on this device and it will tell whether your pulse is regular or whether you have AF. If it comes up with a red warning, please book an appointment with your GP.' [GP06]

Environmental considerations

Seven out of 10 GPs supported the development of AF screening programmes in a general practice setting. Interviewees talked about the established general practice infrastructure, access to universal health records, and its status as a hub of resources and clinical services which regularly engaged the prospective target group:

'General practice would be ideally placed, and this is for a couple of reasons. One is that it holds the care record for that patient and therefore is probably best placed to risk-stratify and identify the highest-risk patients and the ones that are most suitable for screening …

And the other one is that general practice is one of the few healthcare areas that does cover or is intended to cover the entire population.' [GP02]

Such arguments revealed the key limitations of conducing AF screening outside the general practice environment, including community pharmacies or public locations, for instance supermarkets. A number of GPs discussed the incomplete access to full-scale patient records and the lack of universal coverage compared to general practice:
'If you're doing it somewhere like a supermarket … I think it has to be somehow the practice doing it really because then they can potentially take details. I suppose you're gonna get patients from out of area that are not registered … We've got the governance in place to make sure that their GP is informed.' [GP07]

Several GPs also mentioned other community pharmacy-specific barriers, including their concerns surrounding patient confidentiality, competing professional priorities when providing essential supply-related services and the duplication of general practice workload leading to possible patient confusion:
'Or maybe the pharmacists, I know they are again very busy and they don't invite the patients behind the counter a lot of times so it could be technically a little bit awkward to feel the pulse over the counter.' [GP06]
'When we look at where health checks have been done in community pharmacies, you end up with an enormous amount of confusion when you're looking at people coming between services … And then some duplication really both for the patients and for the services involved.' [GP10]

Despite the infrastructural and logistical barriers, the majority of GPs agreed that offering AF screening in community pharmacies or at the *'pop-up clinics'* in public locations may improve patient's access to the service and may capture a different group of at-risk individuals during the time when scheduling appointments at the GP surgery was particularly challenging:
'I think community pharmacies are excellent, access is excellent. That would be quite a good idea because they are often more accessible than surgeries particularly at the moment with recruitment being hard and appointments being difficult.' [GP03]

Three GPs also welcomed the model of collaborative one-stop AF screening and management clinics in community pharmacies, which were perceived to improve patient convenience and help reduce general practice workload. Nevertheless, interviewees

requested that any models of AF detection in community pharmacies or public settings are centrally funded and have an established referral pathway to general practice:
'I think that would certainly take the pressure off the GP surgeries and may well increase an uptake because it takes away that having to call your surgery, having to make an appointment, if it's then centralised and set, like the breast screening.' [GP03]

Four GPs spoke positively about the outreach AF detection services for high-risk individuals with limited access to traditional healthcare, including the housebound patients, those residing in care homes or those attending day centres:
'Obviously go out into the community, with the Age Concern [Age UK] … Those sort of places, you know, day centres.' [GP05]
'In most of the nursing homes, care homes, the senior carer is there so that's a health professional in their own capacity. In nursing home, there are qualified nurses so they just do that and check that. And that can be communicated back to the practice's GPs.' [GP09]

Considering the variety of possibilities, some interviewees proposed a system where individuals were given a freedom to choose the most convenient setting to engage in AF screening, thereby expanding the coverage and likely the cost-effectiveness of the programme:
'If you've got the resources to do it in a variety of places, then I think doing a mixture, almost saying, 'Look, everybody should have this done, but you can go to your pharmacy, you can go to a general practice, there's gonna be these days when we're doing it at the supermarket.' In an ideal world that would be better cause you would get more people.' [GP07]

Organisation and leadership

All but one of the GPs agreed that greater involvement and commitment of regional and/or national organisations ranging from CCGs and PCNs to Public Health England and the Department of Health and Social Care, was required for any future AF screening programme to be successful. Whilst appreciating the AHSN initiative, participants felt disconnected from decision-makers and reported a regional disparity in the approach or attitude towards AF detection, the inconsistent recording of pulse palpation results, and the varied distribution of $_{SL}$ECG devices, which led to ineffective use of resources. The latter process appeared to be further complicated by the large amount of bureaucracy which discouraged GPs from engaging with the initiative:
'Like any successful screening programme that has to be done nationally … There was some funding for those AliveCor® devices. I think they were allocated to us but unfortunately

the amount of bureaucracy that was tied into that in terms of how much form filling had to be done put the staff off and surgery off from doing that.'' [GP01]

Together with central leadership, some of the possible solutions to this chaotic and haphazard effort included the preparedness for the level of uptake and output of the screening programme and the implementation of a clear, universal pathway/protocol for AF detection that may tie in with pre-existing guidelines and policies. This was considered to be especially important for any future self-testing service and for the timely initiation of OAC therapy:

'*I think you just need a clear pathway, 'if you've got an abnormal result on your phone, this is what you do next' so that you don't end up flooding GP appointments.'* [GP07]

More than half of GPs emphasised the catalytic significance of local clinical specialist and senior manager engagement in service development and implementation. The leadership of GPswER in cardiology and cardiology/stroke consultants was deemed to be particularly important due to their positive impact on AF awareness/education, attraction of resources and leadership towards AF detection and/or management:

'We have a GP with a specialist interest in cardiology so we are quite spoilt from that point of view in our practice. And the stroke consultant in the Trust, they are very very proactive. They speak out far, wide and loud about AF and they teach us and they travel around the country to make presentations and lead us on AF.' [GP06]

7.4.5 Knowledge and capabilities

Professional knowledge and capabilities

GPs generally considered themselves to be accountable for AF detection and admitted that general practice could be doing more to identify patients with undiagnosed AF, thus preventing the detrimental consequences of stroke for patients and the healthcare economy:

'I think we still know that there is a significant number of patients out there who are as yet undiagnosed. It's something that is in the consciousness of GPs to a certain extent.' [GP02]

The culture of ignorance and short-term thinking amongst some GPs was identified as a barrier to the more widespread implementation of AF screening. Interviewees felt that some colleagues perceived AF detection as a *'nuisance'* and a distraction from supposedly more essential tasks. Others mentioned the poor appreciation of AF-related consequences and the excessive fear of OAC-related risks:

'I suspect like anything it's funding and it's short-term thinking. Also I think in some places, it wasn't that long ago that we were just chucking a bit of aspirin at these people and hoping for the best. There is still that perception that it's not a dangerous disease.' [GP05]
'But that is what the misconception is … They feel that, 'Oh well, anticoagulation with warfarin is very risky… With all those treatments there is always a risk and benefits and we have to see which is overweighing the other one.' [GP09]

Some of these participants were proud of the progress achieved within their practice, reflecting on the organisational commitment that has led to established service specifications and a process for AF detection:
'We do regular manual pulse checks. If we do see an AF we give them an urgent requirement to be seen within a week to talk about AF implications and the treatment in terms of anticoagulation if it is appropriate … We have got clinical leads, everyone is aware of that.' [GP09]

A few other GPs felt particularly confident about AF detection and management provided there was a process in place. Patient assessment using pulse palpation was perceived as intrinsic to the GP skillset:
'It's so easy, it's not mentally challenging to feel somebody's pulse. It's a clear policy what you need to follow like an ECG or whatever. So it's not something that really should be a burden on any GPs.' [GP06]

One interviewee was less confident about the management of patients on OACs and requested more support from specialist hospital outpatient clinics:
'I'm all for that, but I think obviously a lot of anticoag [anticoagulation] is now done within the GP surgery … There should be a dedicated secondary care clinic for those AF patients where we were struggling with getting their anticoagulation up to where you want them to be.' [GP04]

Utilisation of MDT

All interviewees agreed that AF screening was better suited for the skillset of either nurses or HCAs than the GPs themselves. According to participants, these staff already performed pulse checks as part of other professional commitments and were perceived as superior to GPs at following the protocols:
'ECGs are perfectly able to be done by a HCA. I think it would be something that probably it's gonna be largely HCAs or in smaller practices that don't have HCAs, the practice nurse.' [GP02]

'I would expect our nurses to do a blood pressure and pulse check and to notice if the pulse is irregular, and therefore go on and do more.' [GP07]

General practice- or community-based pharmacists were considered as an alternative group of HCPs to conduct the screening. Most interviewees placed their faith in the clinical qualifications of pharmacists to deliver the screening and to help GPs manage the ever-increasing service pressures. Two GPs were more sceptical and struggled to justify the addition of AF screening onto the medicines-focused identity of pharmacists:

'You've got a device that has a low rate of false positives or a pharmacist that's trained in clinical assessment ... Then great because your false positive rate is likely to be low and therefore the GP doesn't have to be bothered.' [GP03]

'The pharmacists are highly trained people but again they are busy and normally they work at the back of the pharmacy … So it could cause some disruption for them.' [GP06]

A couple of participants mentioned a possibility of paramedic or social worker/carer-led AF detection. One interviewee was even more open-minded agreeing that AF screening could be facilitated by administrative staff, such as general practice receptionists. Some GPs were indifferent to the choice of staff to conduct the screening as long as they were appropriately trained:

'If you're talking about a national screening programme a bit like, you know, the smear screening programme, then I'd say you probably have more kind of people that were trained specifically to do that. And they don't necessarily need to be at the level of a nurse or a doctor. If you're talking more about increased opportunistic screening, then I'd say anyone that deals with patients clinically.' [GP07]

Most GPs concurred on the necessity to provide all staff involved in the delivery of AF screening with additional education and training to meet the service demands. This included the background knowledge of AF and anticoagulation, and competence in performing AF detection:

'One of the barriers to that is having staff who are used to taking pulses. And certainly some of our HCAs might only be trained in phlebotomy and not used to examining a pulse.' [GP03]

'If somebody quite nervous about anticoagulants for stroke picks something up that you then don't have the confidence to treat … I don't think on a personal level, that would be a barrier for me, but I think it might be for some people.' [GP07]

Knowledge and awareness

The majority of participants considered adequate staff awareness of AF and its risks to be a key enabler alongside targeted education. When asked, three participants themselves admitted to have never heard of the AHSN *'Detect, Protect and Perfect'* initiative and one was unaware of the presence of $_{SL}$ECG devices which may facilitate AF detection. Several GPs turned to the importance of centrally managed AF awareness campaigns for HCPs and non-clinical staff:

'The more you read and hear about how AF affects people and how easy it is to detect, I hope more people will come on board and start to think before it becomes a formal thing.' [GP08]

The group was split when it came to the consideration of clinical evidence in support of AF screening programmes. Two GPs were confident about the presence of favourable evidence, particularly the benefits of OAC therapy for stroke prevention. The rest of the cohort were either less confident or unconvinced, and warranted further clinical studies to show a direct positive impact of AF screening on patient outcomes and health economy before the national programme was implemented. One very experienced interviewee (qualified for 34 years) highlighted the need to generate more convincing evidence in relation to patients with asymptomatic AF:

'When something is nationally led, you then get the evidence to back it up … Because if there isn't a reduction in strokes and/or a reduction in morbidity, and actually what you do has caused a whole lot more GI [gastrointestinal] bleeds, then what's the point of doing the screening?' [GP03]

'Actually I'm worried that we start to even talk about it before we have the evidence … We're extrapolating from a sicker, often older group of patients and the sort of prognostic outcomes in that group of patients and inferring that the same would be true in an asymptomatic group.' [GP10]

This GP and another colleague also thought that further clinical evidence was required to inform the definition of the target group for AF screening:

'If we screen everyone, that would just be cost-ineffective … I think the people who decide that are the ones, who come up exactly with the evidence base and say, 'Look if we target this age group, then we'll get this sort of return.' [GP01]

The appropriate dissemination of AF knowledge and awareness amongst patients was considered to be just as crucial. Most participants thought that patients and the public were largely unaware of AF and associated risks, either due to its asymptomatic nature or the

lay-unfriendly medical term. As a result of this poor awareness, patients may have perceived AF as less a dangerous condition potentially limiting the uptake of any future screening services and affecting the continuing adherence to OAC therapy:
'I think it's all very well setting up a cancer screening programme because everyone knows what cancer is and people care about it. But setting up something for a condition that most people cannot pronounce let alone have heard of, I think trying to get some uptake might be hard … My experience with patients is that they don't like being treated for conditions that don't give them any symptoms.' [GP03]

As with AF detection, GPs generally felt responsible for educating the patients and raising their awareness of the condition. A few GPs shared the experience of how effective consultations might help patients understand the risks of AF and encourage their adherence to treatment:
'But equally if you counsel them wisely enough about the risk of stroke, then a lot of people have got friends or relatives that have had strokes, and are scared of that condition and therefore if you sell it out well enough then I haven't had too many people refuse to be treated for it.' [GP03]

Others reported challenges of convincing patients to take OACs or the need to re-educate them following their discharge from hospital where patients were initiated on a new medicine:
'But to put that in context of, if now increased your risk by X percent, then people are more likely to take it seriously. But even some people when I've explained to them those risks, choose not to be anticoagulated because of the fear of the drugs.' [GP05]
'Hospital would put a patient on some medication, they haven't quite explained what it is for, why they need to take it … then you have to invest the time to explain why that needs to happen.' [GP01]

In addition to their own initiative, participants considered central public health campaigns within the surgery or in community settings as a possible solution to raising patient and public awareness/knowledge of AF and its devastating consequences:
'Surgeries often have screens or posters. TV adverts I think work quite well … I think some sort of national public health campaign would be needed. I think equally we've had the FAST [face, arms, speech, time] campaign and what have you for stroke, and I think that's worked quite well.' [GP03]

Whilst this was perceived as one of the means to increasing the uptake of the future AF screening programme, multiple GPs were also worried about the health anxiety associated with poorly planned public health or awareness campaigns. As with self-screening, such awareness initiatives were predicted to flood the surgeries with the worried-well rather than the at-risk group of individuals, all while reducing the practice capacity to perform other vital functions:

'Before any of those sort of campaigns are run people need to look at the impact on services that are already extremely thinly stretched. Every time there's an advert on back of a bus about a cough, we end up with surgeries full of people with coughs, then maybe one or two people who have symptoms that relate to that.' [GP10]

One of the GPs thought that an alternative to such *'blanket'* public health campaigns might be a more targeted approach whereby at-risk individuals are invited for an informal event and are given positive messages to prevent any health anxiety (e.g. lifestyle advice) whilst also offering them an opportunity to get screened:

'You combine targeted information with a positive message, 'Let's talk about which will also give information about or the healthy groups that you can join in the surgery' … I think it should be targeted opportunities for people, 'Come along on this morning, and we'll check your blood pressure and do an AF screening.' [GP05]

7.5 Discussion

7.5.1 Comparison with existing literature

This study employed a TDF approach and a method of individual semi-structured interviews to explore the perspectives of UK-based GPs about the facilitators and barriers to the national AF screening programme. A total of 10 GPs from six out of eight CCG areas of Kent participated in the study, providing an opportunity to capture the views of clinicians working with distinct patient populations and having a varying degree of involvement in local or national AF screening initiatives (Kent County Council 2020). Interestingly, this included one GP practising within a CCG area which was not originally sent the invitations to take part in the study, suggesting that a degree of unintentional snowball sampling occurred during the recruitment process (Morgan 2008). The qualitative data analysis revealed five TDF domains which were the most likely to influence the development and implementation of widespread AF screening initiatives in the future. Interestingly, four of the five domains identified during this process matched the key domains amongst the PDAF study stakeholders (section **4.4.2**), suggesting that some of the factors perceived to influence the

development and/or implementation of AF screening services, such as the environmental considerations, may be shared between the patients, GPS, CPs and GPs. 'Social influences', which was the key domain amongst both patients and GPS interviewed during the PDAF study, was however replaced by 'Beliefs about capabilities' amongst the GPs interviewed here. This may reflect the more critical mindset of GPs as the clinical and commissioning leads in primary care (NHS Providers and NHS Clinical Commissioners 2018), which similar to previous reports led them onto the conversations about the reliability of novel AF detection tools (Wessex AHSN 2019; Orchard *et al.* 2019a) or the varying abilities of staff to detect and manage AF. As shown by the PDAF study, GPS, particularly the administrative staff, instead focused on becoming more engaged in new services and on improving communication between them and the frontline HCPs. This finding once again highlighted the gap between the priorities of the *'frontline'* and the *'back office'* staff, which may possibly be addressed through appropriate leadership from GPs and/or the practice managers (Orchard *et al.* 2016; Levesque *et al.* 2017). Similar to the AHSN evaluation (Wessex AHSN 2019), patients interviewed during the PDAF study were also less keen on appraising the performance of new technology or staff providing AF screening than the GPs interviewed here, and instead placed their attention on shared social experiences, such as the inaccessibility of GP surgeries. The latter phenomenon was referred to by GPs participating in this study, yet from an angle of excessive workload and staff capacity to perform the new service.

The further inter-domain analysis of facilitators and barriers ascertained during the interviews with GPs distinguished the three over-arching themes which spanned across the key TDF domains referred to above: prioritisation of resources, service organisation and integration, and knowledge and capabilities (**Figure 7.1**).

Prioritisation of resources

Reflecting the views of GPs who responded to feedback questionnaires during the PDAF study (section **3.4.5**), most interviewees felt that AF screening was important, primarily due to the perceived positive impact of stroke prevention on patient outcomes and healthcare economy. Nevertheless, all GPs recognised that the development and implementation of the national AF screening programme was limited by the lack of funding and additional workload at the time when general practice was barely able to meet the demands for essential clinical services. These themes were previously identified by qualitative studies in Australian primary care (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019a), the UK-based survey of AF screening (Taggar *et al.* 2016b) and the AHSN initiative (Wessex AHSN 2019), suggesting that the barriers of inadequate funding and staff capacity/workload

occur regardless of the healthcare system and are likely to play a central role in the development of future AF screening programmes. The introduction of appropriate regional or national funding streams was viewed by many GPs participating in this study as a solution to improving general practice staff capacity to support routine AF screening. Several interviewees criticised the effectiveness of funding arrangements delivered through the GMS contract and the QOF pay-for-performance scheme. Such views were in line with the findings of a recent systematic review, revealing that the QOF scheme did not necessarily improve the care or outcomes for patients with long-term illnesses and might instead distract clinicians from providing high-quality care outside of the scheme (Forbes *et al.* 2017). Indeed, current QOF indicators for AF relate to the maintenance of AF register and stroke prevention (NHS England and BMA 2019a), but not the active detection of 'new' AF, thereby missing an opportunity to address the Government's target to identify 85% of all AF cases in England by 2029 (Public Health England 2019c). Therefore, despite a near-perfect achievement of QOF indicators in most practices (NHS Digital 2019c), more than 30% of all AF cases in some parts of England remain undiagnosed (Public Health England 2019f). As proposed by one of the GPs interviewed here, an alternative to a separate QOF indicator for AF detection may be to establish it as a centrally commissioned enhanced service (NHS England 2020c). The recent introduction of the revised GMS contract and the inception of PCNs as part of it (NHS England 2020c), might facilitate the local implementation of this enhanced service through additional staff capacity created by allied healthcare professionals, such as CPs or paramedics (NHS England and BMA 2019c).

Apart from funding and staff capacity, GPs interviewed by the present study appraised the technical resources required to facilitate the screening, primarily focusing on the advantages and disadvantages of pulse palpation and $_{SL}$ECG devices. Similar to multi-stakeholder feedback obtained during the PDAF study (**Chapters 3 and 4**) and previous AF screening initiatives using $_{SL}$ECG technology (Orchard *et al.* 2014; Lowres *et al.* 2015; Orchard *et al.* 2016; Halcox *et al.* 2017; Orchard *et al.* 2019a; Lown *et al.* 2020; da Costa *et al.* 2020), several interviewees praised the simplicity and user-acceptability of the KMD, which enabled AF screening by non-specialist staff, such as the HCAs. More than half of all participants had previously used $_{SL}$ECG devices to detect AF, however most focused on the clinical assessment or monitoring of symptomatic individuals. This approach somewhat contradicted both the ESC guidance, which recommends using $_{SL}$ECG for opportunistic screening of asymptomatic individuals (Kirchhof *et al.* 2016), and the recent NICE guidance, which does not support the use of $_{SL}$ECG technology to detect AF in symptomatic patients (NICE 2019b).

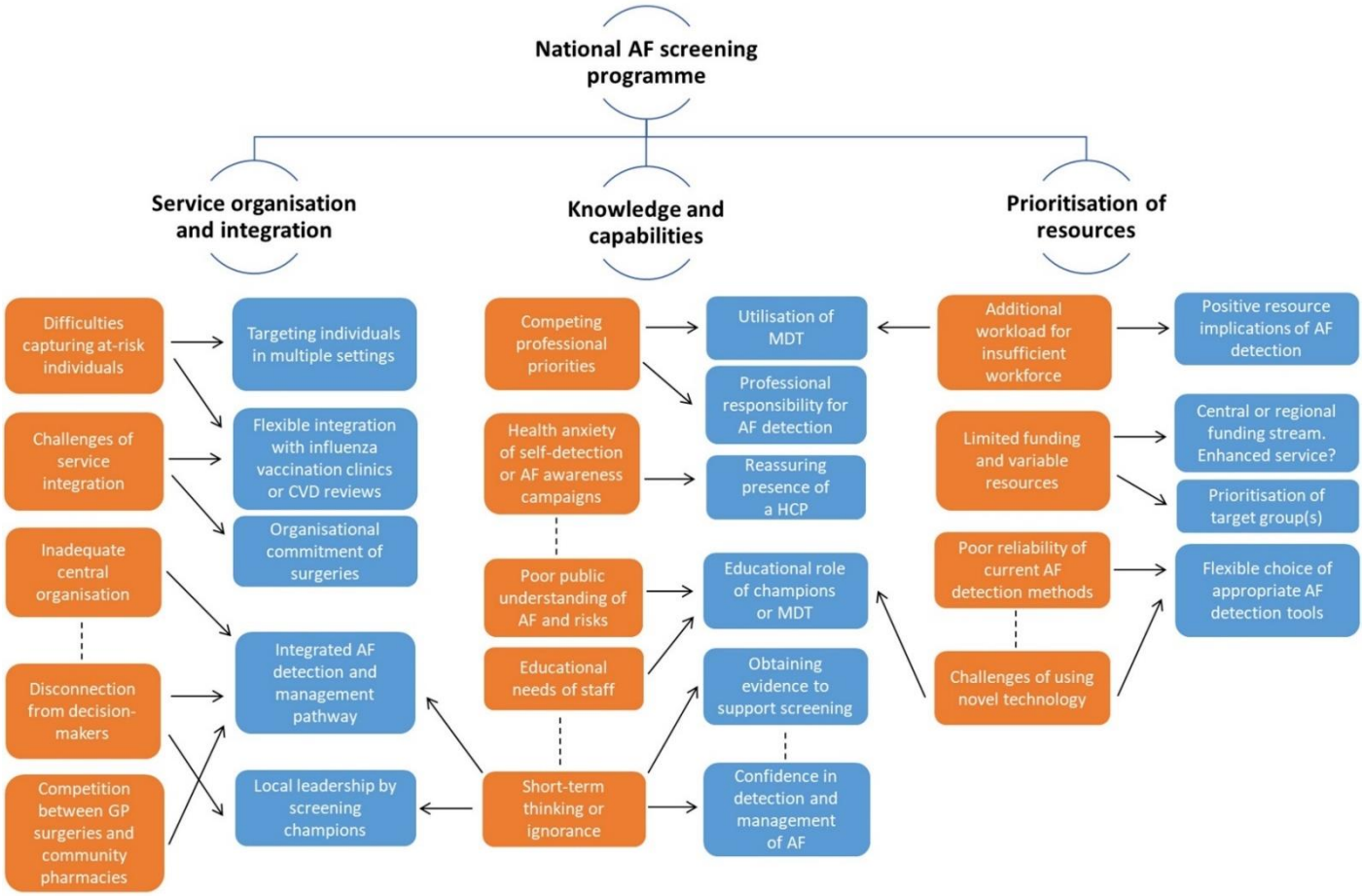


Figure 7.1 Key barriers (orange) and facilitators (blue) in relation to the national AF screening programme

Presented under the three main qualitative themes identified during the present study. The arrows emerge from each barrier and point towards a facilitator which may be used to overcome the respective barrier. Dotted lines relate to a potential relationship between the relevant barriers or facilitators. Abbreviations: AF – atrial fibrillation; CVD – cardiovascular disease; GP - general practitioner; HCP – healthcare professional; MDT – multidisciplinary team.

The discrepancy between clinical guidance and real-world practice is a well-documented phenomenon and may be a result of numerous contributing factors, for instance the personal beliefs/interests or the lack of up-to-date knowledge (Bosse *et al.* 2006; NICE 2007; Dispenza & Craig 2012; NICE 2018a). Some GPs interviewed here followed the stance of the UK NSC (2019) and did not conduct routine AF screening in asymptomatic individuals due to the absence of direct clinical outcome data from RCTs. As debated in the literature (Lown *et al.* 2017a), a number of interviewees were also concerned about the harm of OAC-related bleeding, although the results of a large cohort study suggested that the benefits of stroke prevention in patients with incidentally-detected AF might outweigh the risks of OAC therapy (Martinez *et al.* 2014).

Whilst the results of ongoing trials may ultimately help resolve this clinical dispute (Engdahl *et al.* 2017; ISRCTN Registry 2019), the widespread acceptance of novel AF detection tools amongst clinicians may take considerably longer. Similar to stakeholders involved in the AHSN initiative (Wessex AHSN 2019) or the Australian AF-SMART programme (Orchard *et al.* 2019a), some GPs interviewed here questioned the reliability and diagnostic accuracy of new technology, such as $_{SL}$ECG devices or PPG-capable smartphone applications. A few admittedly preferred the *'cheap'* and *'quick'* conventional pulse palpation regardless of the concerns about its poor diagnostic specificity for AF. This was surprising considering both the superior diagnostic accuracy of novel technology compared to pulse palpation (Taggar *et al.* 2016a) and the generally positive reception of $_{SL}$ECG devices amongst HCPs interviewed by previous AF screening programmes (Orchard *et al.* 2014; Lowres *et al.* 2015; Orchard *et al.* 2016; Savickas *et al.* 2020c). Besides the time and costs required to set up the new devices, this resistance to new technology may be partially explained by technical inexperience or the lack of IT support. As shown by this and several previous studies (Orchard *et al.* 2014; Lowres *et al.* 2015; Orchard *et al.* 2019a), technical problems, such as phone reception or concerns about privacy, may limit the use of electronic tools for AF detection and/or management. Targeted training and adequate IT support for HCPs using such technology may therefore be a crucial aspect of any future widespread AF screening programmes. It is also likely that such screening initiatives may have to utilise a flexible approach by personalising the selection of AF detection methods based on the needs of specific patients. Conforming with findings of Wessex AHSN (2019) and Orchard *et al.* (2019a), GPs interviewed by this study expressed their concerns about the universal adoption $_{SL}$ECG tools to screen older individuals who may not only struggle with new technology, but as demonstrated by the PDAF study in care homes (**Chapter 5**), may also be unable to use KMDs due to other comorbidities, for example rheumatoid arthritis. As showcased by Wiesel & Salomone (2017), such patients may instead be successfully

screened using the mBPMs, which in the future may be extended to include other wearable devices, such as ECG-capable watches or patches (Giebel & Gissel 2019).

The consideration of patient's age and comorbidities also played an important role in the prioritisation of target groups for AF screening. Much like the stakeholders of the PDAF qualitative evaluation (section **4.4.4**), GPs interviewed here reached a consensus to prioritise older individuals who were more likely to develop AF (Ball *et al.* 2013) and experienced a greater burden of risk factors for stroke, such as hypertension or diabetes (Olesen *et al.* 2011). The common age threshold for AF screening mentioned by study participants was 65 years and in agreement with the ESC guidance (Kirchhof *et al.* 2016). Half of all GPs interviewed by the present study conducted opportunistic pulse palpation in selected, typically older asymptomatic patients, and some viewed it as essential clinical care rather than a screening service. Resembling the AF-SMART programme in Australia (Orchard *et al.* 2019a; Orchard *et al.* 2019b), two interviewees reflected on the success of automatic prompts to perform opportunistic pulse checks in ≥ 65s, which suggested that such electronic tools had a place in AF detection and management in UK primary care should they be implemented consistently. Some GPs were in favour of screening younger patients, for example, those in their 50s, provided they had multiple risk factors for stroke and hence displayed a high enough CHA_2DS_2-VASc score to qualify them for OAC therapy (Olesen *et al.* 2011). This targeted approach had been given some consideration by the international medical community (Kirchhof *et al.* 2016; Freedman *et al.* 2017) but appears to be less cost-effective than the opportunistic screening strategy in ≥ 65s (Hobbs *et al.* 2005).

Service organisation and integration

Regardless of their involvement in the PDAF study, a number of GPs advocated for routine AF screening during seasonal influenza vaccination clinics which were thought to offer access to the at-risk group of individuals. Others echoed the concerns of stakeholders interviewed by Orchard *et al.* (2016), Orchard *et al.* (2019a) and the PDAF study (section **4.4.5**), pointing out the time-pressured influenza vaccination clinics which would require additional staff capacity to facilitate AF screening as a regular service. Similar to all stakeholder groups during the PDAF study, a few GPs also thought that seasonal influenza vaccinations attracted the *'healthy volunteers'* whilst missing those at-risk individuals who may not proactively engage with healthcare (Froom *et al.* 1999). Considering the focus on risk factors for stroke, opportunistic AF detection amongst patients attending their annual reviews for long-term conditions, such as IHD, was seen as a viable alternative. Several interviewees recalled their experience of either GP- or nurse-led opportunistic pulse

palpation for patients undergoing routine BP checks, which was in essence comparable to the concept of CVD 'MOT' collated by the PDAF study stakeholders (section **4.4.4**) or previous studies in community pharmacies (Twigg *et al.* 2016; Lowres *et al.* 2015; da Costa *et al.* 2020). As proposed by one of the interviewees, ambitious CVD detection targets set out in the Government's plan (Public Health England 2019c) may in fact warrant a mixed approach of annual AF screening as part of seasonal influenza vaccinations and opportunistic AF detection during routine appointments. Although overall not favourably viewed by GPs due to the younger eligibility age, NHS Health Checks incorporate routine pulse palpation and may also offer an opportunity to detect AF (Public Health England 2019d). This may for instance include formal AF screening of all ≥ 65-year-olds attending NHS Health Checks, perhaps by utilising a dual-function, high-accuracy mBPMs to detect AF and hypertension simultaneously (Twigg *et al.* 2016; Lown *et al.* 2018).

The availability of new electronic tools may also enable AF detection by patients themselves (Svennberg *et al.* 2015; Halcox *et al.* 2017), even though most GPs interviewed here followed the consensus of the PDAF study participants (section **4.4.4**) and did not support self-testing at home due to concerns about the unnecessary anxiety caused by false positive diagnoses. As mentioned by several participants of the PDAF focus groups, GPs preferred for any self-testing to take place within a safe healthcare environment, such as community pharmacies or GP surgeries, where patients would have access to a HCP should that be needed. Self-testing for hypertension using stationary monitors or kiosks in community and primary care settings had previously been shown to improve patient access to screening and may possibly help minimise the effects of the *'white coat syndrome'* (Houle & Tsuyuki 2013; Tompson *et al.* 2017). Whilst it remains unclear as to whether or not such an approach may help detect AF, the aspects of patient privacy and proficiency in self-testing techniques (Houle & Tsuyuki 2013; Tompson *et al.* 2017) would need to be addressed before the widespread implementation is achieved.

As such it was not surprising that the majority of GPs interviewed here would choose for AF screening programmes to be delivered in general practice which not only benefited from the regular presence of HCPs to support patients, but also had an established clinical infrastructure and access to universal health records (NHS Digital 2020). These facilitators appeared to outweigh the perceived inaccessibility of GP surgeries compared to community pharmacies or public locations, such as supermarkets. Similar to stakeholders of the PDAF qualitative evaluation (section **4.4.5**) and previous studies in community pharmacies (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018), GPs felt that screening in such settings may be limited by risks to patient's confidentiality and the lack of an established referral

pathway to general practice. As mentioned by interviewees of those studies, some GPs participating in this research also questioned whether or not community pharmacies had sufficient staff capacity to accommodate the non-essential services, such as AF screening. The introduction of new clinical services, such as influenza vaccinations, meant that the workload pressures faced by UK community pharmacies had been rising year on year (Hassell *et al.* 2011; Murray 2016), and are likely to increase further considering the proposals to deliver additional CVD screening in the new Community Pharmacy Contractual Framework (Royal Pharmaceutical Society 2019; Department of Health and Social Care 2019). As shown by comments from a few GPs participating in this study and the recent systematic review (Hindi *et al.* 2019), the development of new community pharmacy services may be further hindered by their competition with GP surgeries. The ongoing drive to improve the collaboration between community pharmacies and PCNs, for instance by establishing a clear post-CVD screening referral pathway to GP surgeries (Department of Health and Social Care 2019), may help refine the roles of each care provider and hence reduce the professional competition. This process may be facilitated by practice-based CPs who may act as a liaison between GPs and community pharmacies (NHS England and BMA 2019c). The potential for collaboration between GP surgeries, community pharmacies and secondary care had previously been showcased by the success of one-stop AF screening and management clinics in London (Antoniou *et al.* 2019), which were perceived as a means to improve patient convenience and reduce the practice workload by GPs interviewed here.

As illustrated by the findings of the PDAF study (**Chapter 5**), further work is also needed to improve the process of AF detection, diagnosis and management at the interface between GP surgeries and care homes. GPs participating in this study were in favour of targeting the at-risk residents in care homes or the housebound individuals, which concurred with qualitative feedback from the PDAF study stakeholders (section **4.4.4**). Some GPs showed a degree of flexibility and suggested that, where possible, AF screening should be delivered in more than one setting which might make it more convenient for patients and might help detect AF amongst those that did not routinely seek healthcare at their GP surgery. Provided the privacy and process concerns are addressed, this may be achieved through mobile clinics, which had previously been deployed in community settings to screen for conditions such as cervical cancer or glaucoma (Greenwald *et al.* 2017; Al-Aswad *et al.* 2017). As discussed in **Chapter 6**, the coverage of AF screening or indeed the combined AF-CVD screening programme as a whole may be further expanded by delivering the service within specific communities, such as ethnic minority groups (Rao *et al.* 2012; Eastwood *et al.* 2013; Macniven *et al.* 2019).

The discussion points raised above make it clear that the sustainability of AF screening programmes in primary care or community settings may depend on more than a funding stream, and may in particular require both adequate central support and integration within the existing clinical pathways. The lack of these elements during the recent AHSN initiative meant that only half of all KMD devices distributed as part of the programme were ever registered and that two thirds of participants stopped using the devices after screening no more than 25 patients (Wessex AHSN 2019). Similarly, only one out of 10 GPs interviewed here was involved in the England-wide AHSN initiative, primarily due to excessive bureaucracy, regional variations in the availability of $_{SL}$ECG devices and the lack of central guidance. Despite their leading role in clinical service commissioning (NHS Providers and NHS Clinical Commissioners 2018), GPs reported an ever-increasing gap between them and decision-makers, calling for more initiative or guidance from CCGs/PCNs and from national bodies, such as Public Health England. It is clear that whilst the *'General Practice Forward View'* programme (NHS England 2016b) may have resulted in certain improvements to primary care infrastructure or services, for instance by introducing modern technology (Royal College of General Practitioners 2018), the Government has some way to go to ensure the consistent and well-supported delivery of such services across the board. According to GPs interviewed by this study and by previous AF screening initiatives (Orchard *et al.* 2016; Wessex AHSN 2019; Orchard *et al.* 2019a), one of the main facilitators of this process would be to establish a centrally approved protocol for AF screening and follow-up, which would tie in with the current guidelines (NICE 2014a) and clinical pathways between different care settings referred to above (Department of Health and Social Care 2019). The creation of the AF screening programme as an enhanced service within a GMS contract may therefore seem to be a logical solution to ensuring its sustainability, owing to a steady funding stream and a comprehensive, centrally managed service specification (NHS England 2020c).

Besides the regional or national incentives, the success of widespread AF screening may depend on the commitment of individual practices and GPs (Orchard *et al.* 2019b; Wessex AHSN 2019). Instead of engaging with the central AHSN programme, some GPs interviewed here shared their success stories about the past or current locally organised AF screening initiatives, in some cases incorporating a defined AF detection pathway. One of the key barriers to the more widespread implementation of such initiatives was the resistance from GPs who perceived AF screening as an unnecessary task at the time of limited funding and workforce capacity. The resistance to change in healthcare resembles the previously discussed unwillingness to follow new clinical guidelines, and may be rooted in several factors: from toxic organisational culture and the inability to unlearn old care

models to personal reluctance due to a perception of being incompetent or the opposition to the aims and methods of the new programme (Gollop *et al.* 2004; LeTourneau 2004; Gupta *et al.* 2017; Mannion & Davies 2018). As a result, introducing new services or quality improvement in general practice may take a considerable amount of time and requires a concerted, multi-dimensional approach which has been summarised by NHS England as a *'Quality Improvement Wheel'* (NHS England 2019b). This cyclical approach is built on the classic *'Plan, Do, Study, Act'* model and may be facilitated by process mapping, engagement of staff and patients, the generation of supporting outcome data, setting clear expectations/accountability and empowering clinicians to become champions to drive the change (Gollop *et al.* 2004; Gesme & Wiseman 2010; NHS England 2019b). The champion aspect of quality improvement in particular was recognised as critical for the implementation and uptake of AF screening by studies included in this enquiry (**Chapters 4 and 6**) as well as by previous AF screening initiatives (Orchard *et al.* 2016; Orchard *et al.* 2019a; Wessex AHSN 2019; da Costa *et al.* 2020). Shaw *et al.* (2012) distinguished between two different types of change champions: *'project champions'* who led a specific programme, such as AF screening, and *'organisational change champions'* who led the change for entire organisations. The qualitative findings presented here suggest that some GPs, certainly GPwERs in cardiology, already act as champions for AF detection within their practice or their geographical area. Others feel intrinsically accountable for AF detection and may wish to become more involved, but instead assume the passive role of a *'follower'* (Gesme & Wiseman 2010) and may not engage in the initiative without the stimulus from local leaders. The views of GPs interviewed here suggested that a greater leadership and engagement of clinical specialists, such as cardiologists or stroke consultants, may help convince the unbelievers, adding to the positive impact of local organisational change exerted by GP champions.

Knowledge and capabilities

Although the majority of GPs participating in the present study considered themselves to be responsible for AF diagnosis, all of them recognised that the current general practice skill mix called for AF detection to be performed by other members of the MDT. The nurse- or HCA-led AF detection dominated such conversations which was not unexpected considering the stakeholder feedback collected during the PDAF study (**Chapters 3 and 4**) and the fact that these staff are typically responsible for routine pulse checks or the conduct of $_{12L}$ECGs (Taggar *et al.* 2016b). Nurses have traditionally been a HCP of choice to perform AF detection in primary care (Sudlow *et al.* 1998a; Morgan & Mant 2002; Hobbs *et al.* 2005; Kearley *et al.* 2014; Kaasenbrood *et al.* 2016; Lown *et al.* 2018) and have in most cases expressed a high degree of confidence to undertake such duties provided the appropriate

protocols were in place (Orchard *et al.* 2014; Orchard *et al.* 2016; Orchard *et al.* 2019a). Interestingly, despite their leading role in NHS Health Checks (NHS 2019b), none of the AF screening research to date utilised the skillset of HCAs. Whilst technically not qualified as HCPs, these members of clinical support staff may be trained to perform clinical procedures such as BP measurements or phlebotomy (Health Education England 2020), and have therefore formed almost 20% of all $_{SL}$ECG device users during the AHSN initiative (Wessex AHSN 2019). As stated in the evaluation of the AHSN programme, HCAs were able to effectively use such devices to detect AF and were the least likely of all user groups to stop performing AF screening (Wessex AHSN 2019). Considering their lower pay rate compared to HCPs (NHS 2020), one may thus hypothesise that the HCA-led AF screening followed by an immediate HCA-led $_{12L}$ECG confirmation may be more effective and cost-effective than the convoluted follow-up after a practice nurse-led pulse check. Nonetheless, in the absence of evidence, it remains unclear as to whether or not HCAs would be confident in performing routine AF detection and how much time or resources would be required to train them accordingly. For example, non-clinical staff (practice receptionists) who performed AF screening using the KMD in the study by Orchard *et al.* (2016) expressed their reluctance to engage with the initiative, could not respond to questions from patients and were unmotivated to learn new skills. In line with these findings, more than 20% of HCAs responding to the survey by Taggar *et al.* (2016b) were unsure about their role in performing pulse checks and 80% appealed for more training in this technique compared to 0% and 50% of equivalent responses from practice nurses.

Some interviewees of the present study were convinced that AF screening could be performed by allied healthcare professionals, including pharmacists, paramedics, social workers and the aforementioned receptionists. Similar to patients interviewed during the qualitative evaluation of the PDAF study (section **4.4.4**), most GPs interviewed here viewed pharmacists as capable and qualified HCPs, however a few struggled to rationalise adding AF screening to the portfolio of pharmacist-led services which were heavily focused on medicines supply and optimisation. As shown by the recent survey of general practice pharmacy services (Savickas *et al.* 2020a) and the SEARCH-AF study in community pharmacies (Lowres *et al.* 2015), the introduction of novel pharmacist-led clinical services, such as AF screening, may indeed be limited by their pre-existing competing professional priorities. Therefore, policy-makers and commissioners should be cautious when expanding the pharmacists' scope of practice to prevent the burn-out effects experienced by GPs (Hall *et al.* 2019). Considering the feasibility of AF screening by trained pharmacy professionals (e.g. pharmacy technicians) (Twigg *et al.* 2016) and even by pharmacy students (Zaprutko *et al.* 2019) (**Chapter 6**), future researchers and commissioners may also wish to redefine

the responsibilities of pharmacists in AF detection, delegating more of the initial screening responsibilities to support or technical staff.

Indeed, some GPs interviewed by the present study did not have any preference for the selection of staff to deliver AF screening provided they were appropriately trained. Apart from training in the use of $_{SL}$ECG devices, participants echoed the findings by Taggar *et al.* (2016b) and identified the need for further pulse palpation training, particularly amongst the non-GP staff. Some interviewees also felt that themselves or their peers might benefit from additional training and support with regards to the initiation and monitoring of OAC therapy. The QOF scheme and the introduction of analytical tools such as GRASP-AF (Shantsila *et al.* 2015), helped ensure that most eligible patients with AF in England were prescribed appropriate OAC therapy in 2019 (NHS Digital 2019c). However, the findings of this qualitative study indicate that certain historical barriers to OAC therapy, such as the perceived excessive risk of bleeding (Pugh *et al.* 2011), remain amongst GPs and need to be tackled if widespread AF screening was to be rolled out across the UK. The lack of GP confidence to initiate OACs may be partially addressed through the use of appropriate clinical decision support tools (Orchard *et al.* 2019b) and possibly through their direct involvement in AF screening initiatives, which appear to improve the HCP knowledge of AF and its risks (Lowres *et al.* 2015; Orchard *et al.* 2019a). As suggested by GPs interviewed here and by the recent qualitative meta-synthesis (Pritchett *et al.* 2020), further support from specialists and educational interventions may be necessary to facilitate the management of more complex AF cases. For instance, the cardiologist and stroke consultant-led, AF-focused anticoagulation clinics and educational programme at GP surgeries in Liverpool improved the rate of appropriate OAC prescribing from 77% to 95% at six-month follow-up (Das *et al.* 2015).

The reality however is that senior secondary care clinicians may not have the required workforce capacity to perform such routine duties in primary care (Hospital Consultants and Specialists Association 2015), and even if they did, consultant-led OAC clinics for AF patients may not be financially sustainable. The utilisation of CPs to deliver similar interventions may be a viable alternative considering their expertise of outpatient anticoagulation clinics and patient education for more than several decades (Witte *et al.* 1980; Pegg *et al.* 1985; Holleman *et al.* 2020). The CP integration within GP surgeries as part of the PCN agenda (NHS England and BMA 2019c) offers an excellent opportunity for them to become the champions of AF-related stroke prevention in primary care, providing GPs and other GPS with the necessary support mechanism. Close to one in five of practice-based CPs responding to a recent survey expressed an interest to become more involved

in the provision of anticoagulation services (Savickas *et al.* 2020a). In turn, several CP-led initiatives targeting patients with AF in GP surgeries reported optimised OAC prescribing, a decrease in inappropriate antiplatelet prescriptions and a reduction in AF-related strokes (Public Health England 2019e; Virdee & Stewart 2017; Chahal *et al.* 2019).

As shown by evidence presented in **Chapters 3, 4 and 6**, as well as other pharmacist-led AF screening initiatives (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018; da Costa *et al.* 2020), these professionals may also have a role in raising the general public awareness of the condition. Similar to HCPs and patients interviewed by previous AF screening programmes (Orchard *et al.* 2014; Orchard *et al.* 2016; Wessex AHSN 2019; Lown *et al.* 2020) (section **4.4.3**), GPs participating in the current study recognised the necessity to improve the general public awareness of AF and its risks. Most interviewees emphasised the need to make sure any AF awareness campaigns were centralised and considered the impact they might have on general practice workload. As with patient self-testing, *'health anxiety'* was the central term in these conversations. Similar to GPs involved in the AHSN initiative (Wessex AHSN 2019), interviewees of this study were concerned about the excess of false positive diagnoses that may overwhelm their surgeries following the community-based public health campaigns. These fears were not completely unfounded, considering the documented negative impact of false positive diagnoses on incremental healthcare costs and patient's mental health (Lafata *et al.* 2004; Hafslund *et al.* 2012). Nevertheless, the feedback from individuals attending AF screening in GP surgeries (Orchard *et al.* 2014; Lown *et al.* 2020) (**Chapters 3 and 4**) or community-based locations (**Chapter 6**) suggest that the presence of a HCP, such as a nurse or a CP, during the consultation may not only raise their awareness of AF, but may also help reassure those with a suspected AF diagnosis, possibly reducing the impact of health anxiety. Such consultations overall resemble the anxiety-free AF awareness and screening events recommended by one of the participating GPs, and may act as an opportunity to educate the patients about the risks and benefits of OAC therapy, perhaps by adopting one of the approaches discussed in section **4.5.1** (Clarkesmith *et al.* 2013; Vinereanu *et al.* 2017). In turn, the GP-agreed screening/referral pathway and a secure funding stream requested by GPs interviewed during this study, may help general practice prepare for the impact of AF awareness and/or screening programmes, particularly those occurring outside the GP surgeries. Where AF screening is a part of a central public health campaign, this closer collaboration between the organisers or commissioners and clinicians may increase the proportion of individuals with suspected abnormalities who are ultimately followed-up. For example, whilst the follow-up rate during the PDAF study in general practice reached 76% (section **3.4.4**), community-

based AF awareness campaign by da Costa *et al.* (2020) or the AF screening initiative at the Gurdwaras (section **6.4.4**) reported the follow-up rates of 20% and 5%, respectively.

7.5.2 Strengths and limitations

This study benefitted from the method of individual semi-structured interviews, which offered a quick and convenient approach to obtain the perspectives of time-pressured GPs (Breen 2006; Adams 2015; DeJonckheere & Vaughn 2019). The anonymity of one-to-one telephone interviews also minimised the influence of any pre-existing power relationships (Hofmeyer & Scott 2007; Vogl 2013), and enabled participants to express their personal views that might otherwise appear unpopular amongst their peers (Adams 2015; DeJonckheere & Vaughn 2019). For instance, the deviant case analysis (Mills *et al.* 2012) revealed that one GP had a preference for future AF screening to become integrated within the NHS Health Checks, rather than accompany the seasonal influenza vaccination clinics or the reviews of patients with long-term illnesses, which were the popular choices amongst most participants. The regional recruitment strategy also provided this research with access to a variety of GPs, some of whom participated in the PDAF study or the AHSN initiative, thereby facilitating a comparison of qualitative themes between the more and less engaged GPs, and between the participants of this study and the PDAF stakeholders (**Chapter 4**).

To our knowledge, this study was the first to explore the views of UK-based GPs with regards to AF screening initiatives and the national AF screening programme, contributing to the results of the AHSN evaluation which focused on the use of $_{SL}$ECG devices (Wessex AHSN 2019). The perspectives of primary care clinicians presented here therefore add the much needed qualitative feasibility element to previous evaluations of AF screening in UK primary care (Sudlow *et al.* 1998a; Somerville *et al.* 2000; Morgan & Mant 2002; Hobbs *et al.* 2005; Rhys *et al.* 2013; Kearley *et al.* 2014; Twigg *et al.* 2016; Halcox *et al.* 2017; Lown *et al.* 2018; Antoniou *et al.* 2019; Lown *et al.* 2020). The structured TDF approach employed by this study (Atkins *et al.* 2017; Savickas *et al.* 2020c) ensured that the fundamental aspects of the prospective AF screening programme were explored from multiple dimensions, assisting in the identification of key facilitators and barriers, which may inform the design of the future service specification.

As mentioned in section **4.5.2** however, the TDF approach is not without limitations, and due to its primarily deductive nature, may have restricted the identification of less predictable qualitative themes, which may emerge following a more inductive approach, such as the grounded theory (Gale *et al.* 2013). Considering the regional recruitment strategy, the transferability of findings beyond Kent and certainly beyond England may be

limited due to differences in organisation and healthcare policy of other UK regions or the devolved nations (Greer 2016). The qualitative themes derived here may have also been influenced by the inclusion of GPs involved in the PDAF initiative, although the data analysis did not show any substantial bias towards favouring AF screening programmes amongst these participants compared to the rest of the sample. Last but not least, the research team involved in this project overlapped with that of the PDAF study team, and the majority were registered pharmacists, thus potentially introducing a bias by steering the interviews and data analysis towards the pharmacist-led AF screening and AF detection as a whole (Stewart *et al.* 2007; Hiller & Vears 2016).

7.6 Conclusion

This chapter explored the perspectives of GPs with regards to the national AF screening programme, focusing on the key facilitators and barriers to the development and implementation of this complex intervention. The qualitative evidence presented here suggests that most GPs support the concept of routine AF screening, which is viewed as a long-term investment owing to the reduced negative impact of ischaemic stroke on patients, practices and the healthcare economy. The ever-increasing workload pressures experienced by general practice may limit the real-world sustainability of widespread AF screening unless it gains the backing of the Government and is firmly integrated within the GMS contract, perhaps as an enhanced service. The success of the programme will also depend on the availability of further direct evidence to support the clinical benefits of AF detection, and the development of a clear AF screening/follow-up pathway, which is incorporated into the existing clinical guidance. In line with the international medical consensus and the PDAF study stakeholders, interviewees of this study emphasised the need to prioritise the at-risk groups of individuals for AF screening, focusing on those aged ≥ 65 years and those with underlying medical conditions, such as diabetes, hypertension or IHD. Due to overlapping age eligibility or risk factors, seasonal influenza vaccination clinics and routine CVD reviews offered the key opportunities for AF detection, integrating well with the Government's cardiovascular agenda (Public Health England 2019c).

All interviewees agreed that nurses and HCAs should be the staff of choice to facilitate AF screening due to the suitability of their skillset and the current involvement in opportunistic AF detection. Pharmacists were viewed as an alternative, provided they had a workforce capacity to combine AF detection with their medicines-centred roles, which should be considered when expanding the spectrum of CP-led services in primary care (NHS England and BMA 2019c). With some exceptions, the majority of GPs were sceptical about the added benefits of novel AF detection tools compared to pulse palpation, hinting that a pure

distribution of new technology tested during the AHSN initiative may not be effective and may instead require additional clinical and technological support. Most GPs did not favour AF self-detection by patients and preferred for AF screening to take place within the established general practice environment, although screening in community pharmacies, mobile clinics and care homes was viewed as an option provided an established pathway was in place. The resistance of fellow GPs to engage in a new service was identified as a key barrier, and may require the support of local champions, such as clinical specialists, to facilitate the cultural change. The integration of practice-based CPs within the PCNs places them in an ideal position to contribute to this process by providing GPs with targeted education about the risks and benefits of OAC therapy and by working with their community pharmacy counterparts to deliver one-stop AF screening clinics. In turn, CPs and local AF screening champions, for instance stroke consultants or GPswER in cardiology, should liaise with national organisations, such as Public Health England, to raise AF awareness amongst the public and staff in a structured manner which prevents the unnecessary health anxiety and reduces the negative impact of false positive diagnoses.

The results of the much-awaited SAFER trial may act as a catalyst to convincing the doubters about the benefits of AF screening on clinical outcomes, such as stroke prevention (ISRCTN Registry 2019). Nonetheless, the qualitative perspectives of GPs presented here imply that clinical evidence constitutes only a small part in the framework of barriers to more widespread AF screening. Considering the strong case for AF detection in selected asymptomatic individuals (Kirchhof *et al.* 2016; Freedman *et al.* 2017), it therefore urges policy makers and commissioners to construct the specifications of a prospective AF screening service around the facilitators presented in this report and the previous AF screening evaluations, including those discussed in **Chapters 3-6**. The complexity of this process forms the grounds for future qualitative and quantitative research (MRC 2006), such as an exploration into the combined AF screening-CVD 'MOT' service in general practice, care homes or community settings. The lessons from the England-wide AHSN initiative (Wessex AHSN 2019) and data presented here also suggest that smaller, centrally managed, but locally championed pilots with adequate guidance and support may provide the foundations for the success of the national AF screening programme. Further qualitative and quantitative research is also warranted to refine the pathways for AF detection and follow-up between the different care settings and to explore the roles of the primary care MDT within this process.

Chapter 8: Discussion and Conclusions

8.1 Summary of key findings

This thesis investigated the role of primary care CPs in the detection of AF using a mixed-methods research approach recommended for the development and evaluation of complex healthcare interventions (MRC 2006). An in-depth literature review at the start of the enquiry defined AF as a growing public health issue and helped identify the evidence in support of various AF detection or screening strategies, particularly the use of digital technology and pharmacist-led AF screening in primary care (**Chapter 1**). The evidence appraised during this process also revealed the primary gaps in the literature, which to date had almost entirely focused on pharmacist-led AF detection in community pharmacies (section **1.3.4**). The rapid evolution of pharmacists' roles in UK general practice (Butterworth *et al.* 2017; Bradley *et al.* 2018), and their consistent integration within the primary care infrastructure (NHS England and BMA 2019c) warranted a further exploration into routine AF detection by practice-based CPs. In turn, the overlapping age criteria for opportunistic AF screening and seasonal influenza vaccinations (Kirchhof *et al.* 2016; Public Health England 2020a), as well as the findings of previous AF screening initiatives (Rhys *et al.* 2013; Orchard *et al.* 2016; Kaasenbrood *et al.* 2016), suggested that targeting individuals attending seasonal influenza vaccination clinics may help detect at-risk patients with AF who would benefit from the OAC therapy.

The PDAF feasibility study in GP surgeries therefore hypothesised that trained practice-based CPs were sufficiently qualified to accurately detect AF amongst individuals aged ≥ 65 years during the influenza vaccination season, using either the conventional pulse palpation or $_{SL}$ECG-based KMDs, whilst producing economic benefits for the NHS. The cross-sectional quantitative component of this study (**Chapter 3**) investigated the participant recruitment, diagnostic accuracy, acceptability and economic elements of the CP-led AF screening intervention proposed. The mixed systematic population and opportunistic AF screening strategy in four GP surgeries helped achieve the desired sample size (≥ 600 participants) over a period of seven months split between two influenza vaccination seasons, providing a potentially more efficient AF screening strategy than reported in other primary care settings, such as community pharmacies (Lowres *et al.* 2014; Zaprutko *et al.* 2019) (**Figure 8.1**). This CP-led AF screening strategy also provided access to the relevant, at-risk group of individuals, 4.3% of whom had a suspected AF at the time of screening (1.3% 'unknown') and qualified for OAC therapy (Kirchhof *et al.* 2016). The 0.7% yield of 'new' AF was in line with the results of other similar studies in community pharmacies or GP

surgeries (Lowres *et al.* 2014; Orchard *et al.* 2016; Sandhu *et al.* 2016; Quinn *et al.* 2018). The use of KMDs also helped diagnose non-AF cardiovascular abnormalities in 5.0% of participants, some of whom required a further intervention from their GP. Most importantly, whilst CPs were able to detect AF using either pulse palpation or $_{SL}$ECG, the reliance on the automated KMD algorithm appeared to be substantially more accurate than pulse palpation, producing 15.4% and 5.2% fewer false negative and false positive AF diagnoses with reference to the cardiologist's interpretation, respectively. This finding agreed with pre-existing evidence suggesting that pulse palpation may have a lower diagnostic accuracy for AF than the modern AF detection tools (Lowres *et al.* 2014; Taggar *et al.* 2016a; Quinn *et al.* 2018). For the first time however, this argument was supported by direct comparative cost-effectiveness analysis which showed that, although both AF screening using pulse palpation and KMD were cost-effective compared to no screening, the superior diagnostic accuracy of KMD translated into an additional £70 million net benefit over 10 years. The cost-effectiveness of AF screening could be further improved by increasing the uptake of the intervention and by reducing the proportion of inconclusive diagnoses, thus highlighting the potential role for trained CPs or other HCPs in raising service awareness and interpreting the less complex $_{SL}$ECG traces. Similar to other KMD-based initiatives (Orchard *et al.* 2014; Orchard *et al.* 2016; Halcox *et al.* 2017), the acceptability of CP-led AF screening using this technology was substantiated by favourable feedback from study participants, CPs and GPs completing the evaluation questionnaires who praised the device's simplicity and convenience, appreciated the reassurance/educational role of CPs and were overall in favour of AF screening programmes. The multi-stakeholder feedback also uncovered several potential barriers to future AF screening strategies in this setting, primarily the poor public awareness of AF or pharmacists' roles and the lack of funding.

Some of the themes from feedback questionnaires were also referred to by previous AF screening initiatives (Lowres *et al.* 2015; Orchard *et al.* 2016; Sabater-Hernandez *et al.* 2018; Lown *et al.* 2020), and were therefore further explored during the qualitative multi-stakeholder evaluation (**Chapter 4**). This component of the study utilised a method of focus group interviews and the structured TDF approach (Atkins *et al.* 2017) to explore the facilitators and barriers to the development and implementation of the CP-led AF screening strategy in GP surgeries from the perspectives of the PDAF study participants (patients), CPs and GPS.

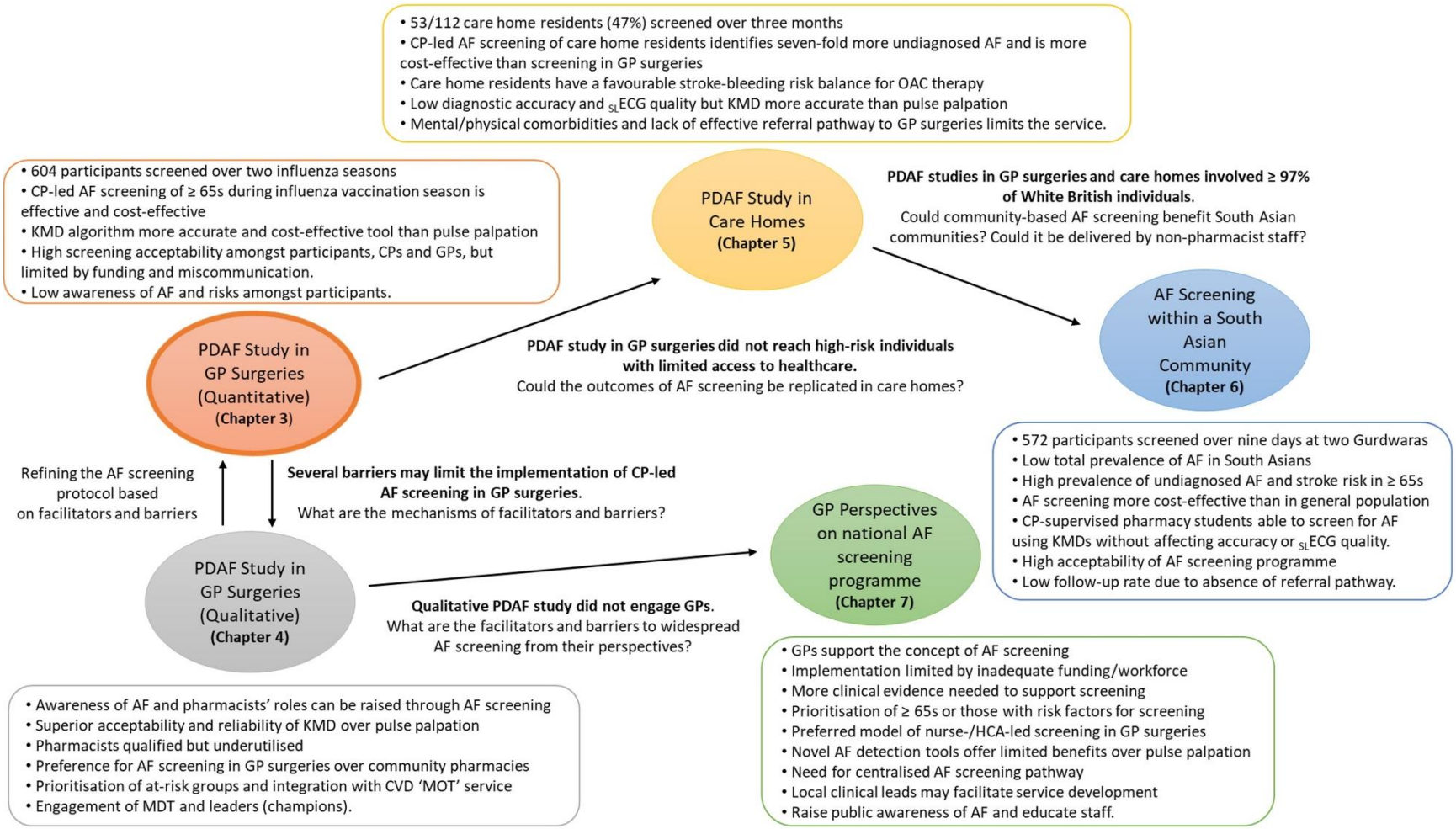


Figure 8.1 Summary of key findings and questions which progressed the enquiry

Abbreviations: AF – atrial fibrillation, CP – clinical pharmacist, CVD – cardiovascular disease; GP – general practitioner; HCA – healthcare assistant; KMD – Kardia Mobile® device, MDT – multidisciplinary team; MOT - Ministry of Transport [check for motor vehicles]; PDAF – Pharmacists Detecting Atrial Fibrillation; SLECG – single-lead electrocardiogram.

The qualitative data analysis revealed that the majority of facilitators and barriers to the AF screening strategy proposed mapped onto five key TDF domains, each of which were shared by at least two stakeholder groups: 'Environmental context and resources', 'Goals', 'Social or professional role and identity', 'Knowledge' and 'Social influences'. The inter-domain analysis helped distinguish the three overarching themes which connected these domains, namely knowledge and awareness, prioritisation of resources and environmental considerations.

The finding of poor AF awareness amongst patients and even amongst GPS concurred with the results of the PDAF study feedback questionnaires (section **3.4.5**) and previous qualitative studies (Orchard *et al.* 2014; Sabater-Hernandez *et al.* 2018; Lown *et al.* 2020), altogether advocating for structured AF education and awareness interventions. All stakeholder groups agreed that the educational skillset of pharmacists was an underutilised resource at the time of general practice workforce crisis, and that they might be ideally placed to deliver AF screening, reassure the patients and raise AF awareness in GP surgeries. The success of the AF screening service was also perceived to depend heavily on the effective multidisciplinary collaboration and engagement of leaders, such as GPs, practice managers and commissioners, who may champion the programme. In support of the quantitative PDAF data (section **3.4.5**) the convenient and accurate testing using the KMDs was viewed as a facilitator compared to unreliable pulse palpation, however most patients did not support self-testing using such technology at home and instead preferred the established general practice environment where they could be reassured by a qualified HCP. Despite some concerns about the hectic influenza vaccination clinics and the general practice inaccessibility, this setting was favoured by many over community pharmacies where issues surrounding commercialisation, staffing and patient confidentiality were raised as previously reported (Lowres *et al.* 2015; Sabater-Hernandez *et al.* 2018). In order to increase the effectiveness of the AF screening programme, all stakeholder groups proposed prioritising the groups of individuals who may not routinely seek healthcare at GP surgeries but might be at risk of CVD, such as the housebound individuals, care home residents or those with CVD risk factors encountered in public locations. These discussions culminated in the concept of a CVD 'MOT' service, which might incorporate AF screening as part of a personalised screening/management plan for those at risk of CVD or those with established comorbidities, such as diabetes or hypertension.

The findings of the PDAF study (**Chapters 3 and 4**) provided foundations for CP-led AF screening service in GP surgeries, and identified the direction for further research to develop and refine this complex intervention. In particular, it highlighted the need to make

AF screening more available to those groups of individuals who may have a limited access to healthcare in GP surgeries yet experience a high CVD burden, such as the aforementioned care home residents (Gordon *et al.* 2014; Victor *et al.* 2018). The PDAF study extension in care homes built on the experience in GP surgeries and the previous reports which demonstrated that the prevalence of AF amongst these at-risk individuals may be as high as 19%, with approximately 7% of it undiagnosed (Krüger *et al.* 2012; Khan *et al.* 2020) – nine-fold above the 0.8% population average in England (Public Health England 2017a). It adapted the AF screening protocol tested in GP surgeries to determine the feasibility of the intervention in a care home setting from the perspectives of participant recruitment, diagnostic accuracy and cost-effectiveness.

A total of 53 individuals residing in four care homes in Kent were screened by a single CP over a period of three months during the influenza vaccination season, identifying a 'Possible AF' in 13.5% of residents. Of these, 9.6% had an 'unknown' AF and 1.9% were diagnosed with a 'new' AF after a $_{12L}$ECG, which was approximately three times the yield of 'new' AF diagnosed following the PDAF study in GP surgeries. All residents with cardiologist-suspected AF were aged > 80 years, qualified for OAC therapy and, contrary to the popular belief (Alcusky & Lapane 2018), had an overall lower risk of bleeding than their counterparts with AF in GP surgeries, demonstrating the potential of AF screening to benefit this largely overlooked population group. Less than 30% of eligible care home residents with AF were however prescribed OAC therapy at follow-up emphasising the Government-recognised demand for targeted CP-led medicines optimisation in this setting (NHS England and BMA 2019c). We also found that, compared to the PDAF study in GP surgeries, care home residents referred for a $_{12L}$ECG had to wait on average nine days longer and fewer of them were followed-up. Whilst the referral pathways between primary care and community settings may be improved through closer service alignment and collaboration (NHS England 2020b), additional staff capacity created by new PCN roles of CPs may facilitate this process and enhance care home resident access to healthcare as a whole (NHS England and BMA 2019c). The feasibility of AF screening in care homes was also somewhat limited by the prevalence of physical and mental illnesses, which meant that less than 50% of all residents could be screened using both pulse palpation and KMD, thus advocating the use of alternative screening methods, for instance mBPMs, in this care setting (Wiesel & Salomone 2017). Possibly affected by such comorbidities, the quality of $_{SL}$ECG recordings produced during this study was significantly below that observed in GP surgeries, leading to a lower diagnostic accuracy for AF, although the use of the automated KMD algorithm remained more accurate than the conventional pulse palpation. The high prevalence of undiagnosed AF in care homes compared to GP surgeries appeared to

counterbalance the poorer diagnostic performance of the KMD, overall producing a more favourable cost-effectiveness profile of AF screening, with base-case ICERs of £6,223 and £14,460/QALY gained in care homes and GP surgeries, respectively.

Despite showcasing the feasibility of CP-led AF screening in GP surgeries and care homes during the influenza vaccination season, the PDAF study did not sufficiently engage individuals from the BAME groups, with ≥ 97% of study participants in each setting declaring their ethnicity as White British (**Chapters 3 and 5**). Considering the multi-ethnic populations of England and Wales, and Kent (Kent County Council 2011; Office for National Statistics 2018b), this under-representation of BAME groups limited the generalisability of findings beyond the study sample and encouraged this enquiry to pursue a separate investigation focusing on the feasibility of AF screening within a community setting of a selected ethnic group (**Chapter 6**). This study targeted individuals of South Asian origin, the largest ethnic minority group in England and Wales (Office for National Statistics 2018c), who experience a greater than average burden of CVD (Wild & Mckeigue 1997; George *et al.* 2017), yet paradoxically display up to 13-fold lower prevalence of AF compared to the general population (Mathur *et al.* 2013; Gillott *et al.* 2017). Hypothesising that this low prevalence of AF may be a result of their limited engagement with conventional healthcare owing to multiple barriers (Szczepura 2005; Netto *et al.* 2010), this initiative investigated the feasibility of AF screening within a specific South Asian community, namely the British Indian individuals attending local Gurdwaras, or places of worship of the Sikh religious group. The AF screening protocol adapted for this study built on the results of the PDAF study (**Chapters 3-5)**, excluding the less accurate pulse palpation and focusing on AF detection using the automated KMD algorithm, which was operated by trained pharmacy undergraduates under the supervision of CPs, thus postulating that AF detection itself could be undertaken by less clinically-qualified staff. Similar to the PDAF study in GP surgeries (**Chapter 3**), the feasibility of this adapted AF screening intervention was examined from the perspectives of participant recruitment, diagnostic accuracy, user acceptability and economic impact. In order to increase the uptake and impact of AF screening, it was delivered in conjunction with the AF Association, timed with the public health campaign/event and a religious occasion, and facilitated by language and ethnocultural concordance between the participants and the research team (Waibel *et al.* 2018; da Costa *et al.* 2020).

This approach to recruitment proved to be highly efficient, and a total of 572 British Indian participants underwent AF screening with students at the two Gurdwaras over a period of nine days. The majority of individuals (528/572) were screened at the Gurdwara in Kent

with a smaller proportion (44/572) attending the one-day public health event at the Gurdwara in South Yorkshire. Individuals recruited in Kent were older and accounted for all suspected AF cases (1.0%), none of which were previously known. This level of AF prevalence within a South Asian community was marginally above the findings of previous studies (Lip *et al.* 1998; Gill *et al.* 2011; Mathur *et al.* 2013; Gillott *et al.* 2017), although overall rejected the hypothesis that the low prevalence of AF in this ethnic minority group could be a result of their poor engagement with healthcare, implying that other physiological or anatomical factors may be responsible instead (O'Neill & Tayebjee 2018; O'Neill *et al.* 2018b). The prevalence of 'unknown' AF in the ≥ 65-year-old sub-group (1.5%) however conformed with the results of the PDAF study in GP surgeries (1.3%, **Chapter 3**) and all ≥ 65s qualified for OAC therapy, indicating that AF screening within this community setting may still benefit a substantial group of South Asian individuals who are at a heightened risk of ischaemic stroke. To our surprise, the quality of $_{SL}$ECG recordings and the diagnostic accuracy of the KMD algorithm for AF during this study were comparable to or above the levels observed during the PDAF study in GP surgeries, irrespective of the fact that the device was operated by less qualified pharmacy students or that the screening took place in a public location. This finding proved the hypothesis that community-based AF screening using the KMDs could be undertaken by staff other than CPs without compromising the diagnostic performance. Another interesting albeit unexpected diagnostic finding of this study was the higher prevalence of 'Sinus Tachycardia' and the lower prevalence of ectopic beats amongst the British Indian individuals compared to either of the two PDAF study cohorts (**Chapters 3 and 5**). Whilst this may purely reflect the variations in the KMD algorithm or differences in the screening environment, it may also relate to the *'autonomic dysfunction'* hypothesis by O'Neill *et al.* (2019) and warrants a further exploration as a protective mechanism against AF in individuals of South Asian origin. Since 89% of all 'Sinus Tachycardias' detected by the study in South Asian community were mild and did not require a follow-up, this finding also supports a potential model for dual-pharmacy screening service whereby pharmacists overread the $_{SL}$ECGs recorded by less qualified staff, e.g. pharmacy technicians, before referring the patient to their GP.

The sustained diagnostic performance of the KMD algorithm and the literature-comparable prevalence of 'unknown' AF (Lowres *et al.* 2013) meant that the AF screening intervention within the high-stroke-risk community of South Asian individuals was in fact more cost-effective than the CP-led AF screening in GP surgeries or care homes (**Chapters 3 and 5**), producing an ICER of £3,283/QALY gained for the screening of ≥ 65s. The favourable economic profile of the intervention was supported by positive questionnaire feedback from study participants who perceived AF screening as a valuable cause for their local

community and appreciated the improved access to healthcare provided by the initiative. Similar to the PDAF study in GP surgeries (section **3.4.5**) they were also impressed with the speed and non-invasiveness of the $_{SL}$ECG test, and were supportive of other health screening initiatives at the Gurdwara, particularly those for CVD risk factors, which aligned well with the 'MOT' concept collated by stakeholders of the PDAF study (section **4.4.4**). As observed in GP surgeries however, ≤ 50% of respondents were aware of AF or its risks prior to being screened, demonstrating the magnitude of this issue across different ethnic groups. Besides the lack of awareness, other key barriers to South Asian engagement with health screening that emerged from participant feedback were the language, cultural norms and the lack of health education. The first two barriers were successfully tackled by this study through language and ethnocultural concordance, offering screening to 30% of the sample who were non-English speakers. As shown here, the issue of health education in South Asian individuals may also be addressed by similar community-based AF awareness/screening campaigns, perhaps by integrating them with more widespread CVD risk factor and perception programmes delivered by HCPs who are champions within their local communities (Eastwood *et al.* 2013). The appropriate referral pathway to GP surgeries from such community locations will be crucial to increasing the proportion of those with AF or inconclusive diagnoses who are ultimately followed up, from 5% seen by this study to 76% observed by the PDAF study in GP surgeries (section **3.4.4**).

This vast gap in the follow-up rates between the AF screening programmes delivered in community and general practice settings pointed out the significance of direct GP involvement in the planning and execution of similar future initiatives, particularly at the time of the UK general practice workforce crisis (Gibson *et al.* 2017; NHS Digital 2019b). The qualitative evaluation of the PDAF study (**Chapter 4**) failed to recruit GPs who may have offered their perspective about the development and implementation of the CP-led AF screening service proposed. As detailed above, the questionnaire feedback obtained from GPs during the quantitative component of the PDAF study (section **3.4.5**) implied that several barriers, such as the lack of funding, may hinder the implementation of more widespread AF screening. Some of these themes aligned with pre-existing literature, which also revealed the time/workload and the lack of guidance or clear protocols as key barriers to AF screening (Orchard *et al.* 2014; Orchard *et al.* 2016; Taggar *et al.* 2016b; Orchard *et al.* 2019a; Wessex AHSN 2019). The final component of this enquiry therefore aimed to qualitatively explore such barriers and indeed any associated facilitators to AF screening from the perspectives of GPs, using the previously tested multi-dimensional TDF methodology (Atkins *et al.* 2017; Savickas *et al.* 2020c) and the convenient method of individual semi-structured interviews. It was anticipated that, in the absence of previous AF-

screening focused qualitative studies with UK-based GPs, the results of this research would contribute to both the refinement of the PDAF study intervention and the development and implementation of the future national AF screening programme.

The analysis of qualitative data obtained during the interviews with 10 GPs in Kent highlighted the five key TDF domains which were expected to influence the development and/or the implementation of the widespread AF screening service. It was rather interesting to note that four of these domains matched the ones identified during the analysis of qualitative data collected during the multi-stakeholder focus groups of the PDAF study (section **4.4.2**). 'Beliefs about capabilities' was an exception to this trend, potentially showcasing a degree of scepticism amongst GPs with regards to the logistics of AF detection, especially the 'new' AF detection tools, which was less apparent amongst the stakeholders of the PDAF study. The inter-domain analysis of qualitative data identified three overarching themes which linked the five TDF domains: prioritisation of resources, service organisation and integration, and knowledge and capabilities. Overall, the great majority of interviewees were in agreement with GPs responding to the PDAF study questionnaires (section **3.4.5**) and supported the concept of AF screening, which was deemed to be beneficial owing to the positive impact of stroke prevention on patients, general practice and the healthcare economy. The costs and workload were perceived as primary barriers to the more widespread provision of AF screening services, and a central, sustainable funding stream was viewed as crucial for the success of the national AF screening programme. A proposal was therefore made to establish AF screening as an enhanced service within the GMS contract, which may tie in well with workforce capacity created through the GMS-embedded PCNs (NHS England and BMA 2019c). This recommendation was in line with the common request for improved leadership of national organisations, for example the Public Health England, and the development of the centrally endorsed AF detection-management pathway. The introduction of such a pathway was considered to be particularly important for any AF awareness/screening programmes taking place outside general practice, thus voicing the follow-up struggles encountered after AF screening in care homes (**Chapter 5**) or the South Asian community setting (**Chapter 6**). A number of GPs also concurred with the recommendations of the UK NSC (2019), appealing for more evidence to prove that AF detection amongst the largely asymptomatic individuals helped achieve the clinical endpoints such as a reduction in the risk of ischaemic stroke or mortality. Some interviewees reported local resistance to new services amongst their peers, and reflected on additional training for GPs or other HCPs, which may be necessary to improve the detection of AF and to dispel any myths about the excessive risks of OAC therapy. As noted in **Chapter 4**, strong leadership from local champions, such as GPswERs

in cardiology or stroke physicians, was perceived as indispensable when attracting resources and facilitating the clinical-cultural change in general practice to enable more widespread AF screening.

All GPs followed the international consensus (Freedman *et al.* 2017; Mairesse *et al.* 2017) and agreed that if the national AF screening programme was to be successful, it would need to prioritise the resources to target at-risk groups individuals, particularly those aged ≥ 65 years and those with risk factors for stroke, such as diabetes and hypertension. Seasonal influenza vaccination clinics and routine CVD reviews, which provided access to high-risk patients, were therefore viewed as ideal companion services for opportunistic AF detection, in principle agreeing with the CVD 'MOT' concept collated by the PDAF study stakeholders (section **4.4.4**). Indeed, half of all GPs already performed opportunistic pulse checks in ≥ 65s, and some made the use of electronic prompts or $_{SL}$ECG devices, which were praised for their simplicity. Other GPs did not display as much enthusiasm about the 'new' AF detection tools, raising concerns about their diagnostic accuracy, privacy and technical issues. This finding agreed with the evaluation of the nationwide AHSN initiative (Wessex AHSN 2019), urging commissioners of future AF screening programmes to provide GPs with structured guidance and technical support prior to the widespread distribution of AF detection tools, such as the KMDs. Even though the automated algorithm of such devices was seen by a few as an enabler for self-screening by patients, GPs generally preferred for any AF testing to occur within a safe and established general practice environment. As discussed by stakeholders of the PDAF study (**Chapter 4**), community pharmacies or public locations were recognised by GPs as an alternative setting for AF screening, which might also offer opportunities to educate the public about AF, provided patients had access to a HCP and an approved GP referral pathway to minimise the risk of health anxiety. The established health-testing roles of nurses and HCAs (Taggar *et al.* 2016b; NHS 2019b) meant that most GPs considered them as staff of choice to conduct routine AF screening. Pharmacist-led AF detection was viewed by some as an option, however concerns about their competing professional duties in relation to medicines optimisation were raised.

8.2 Strengths and limitations

The advantages and disadvantages of specific research methods employed by this enquiry are discussed in **Chapter 2**, whereas the strengths and limitations pertaining to each component study are outlined in individual **Chapters 3-7**. Besides the study-specific strengths, this thesis benefitted from the MRC guidance for the development and evaluation of complex interventions (MRC 2006; Craig *et al.* 2008), which was used as a structured cyclical framework to identify the relevant research questions, to develop and refine the

intervention, to evaluate its effectiveness and cost-effectiveness, and to help understand the processes or behaviours which may affect the success of the intervention in real-world settings. In turn, the mixed-methods approach to research advocated by the MRC guidance (MRC 2006; Giddings & Grant 2006) helped this enquiry ascertain comprehensive information about the role of primary care CPs in the detection of AF, which was identified as a key research phenomenon of the thesis in **Chapters 1 and 2**. The quantitative research components presented in **Chapters 3, 5 and 6** provided an opportunity to test the feasibility of the AF screening intervention using two different AF detection tools in various primary care or community settings and with a varying degree of involvement of CPs who either led (**Chapters 3 and 5**) or supervised the screening process (**Chapter 6**). This vigorous and diverse feasibility testing process allowed us to estimate the recruitment rates/efficiency or predicted sample sizes, revealed potential acceptability/implementation problems (e.g. follow-up attrition after community-based screening), and also helped evaluate the provisional outcomes of effectiveness and cost-effectiveness of CP-led AF screening in different care settings. The qualitative research components of this thesis (**Chapters 4 and 7**) provided an insight into the facilitators and barriers which may affect the widespread implementation of CP-led AF screening and indeed AF screening as a whole, from the perspectives of service users (patients), service providers (CPs), potential champions or commissioners (GPs) and primary care staff (GPS). Qualitative findings also helped revise the design and execution of the intervention tested during the quantitative components of this thesis, for instance by increasing the proportion of pre-booked appointments during the second influenza season of the PDAF study (**Chapter 3**) or by excluding the less accurate method of pulse palpation from the study within a South Asian community (**Chapter 6**).

The strong feasibility-focus of the MRC (2006) guidance and hence this enquiry may also be considered a limitation. Whilst the mixed-methods results of this thesis may act as comprehensive foundations for commissioners or policy makers considering the development and implementation of pharmacist-led AF screening services, they are by and large explorative in nature and warrant a further confirmation through definitive research, such as RCTs (MRC 2006; Victora *et al.* 2004). Perhaps the main deficiency of this feasibility-driven enquiry as indeed of many previous AF screening studies (Hobbs *et al.* 2005; Lowres *et al.* 2014; Svennberg *et al.* 2015) was that it did not measure the effect of AF detection on clinical endpoints, such as the risk of stroke or mortality, which are a subject of future research (Engdahl *et al.* 2017; ISRCTN Registry 2019; ClinicalTrials.gov 2020b). Considering the cyclical nature of the MRC guidance, several component studies included in this enquiry (**Chapters 5-7**) also evolved from the findings or limitations of the PDAF study and were not planned simultaneously. The differences in research design,

methodology and methods between these studies therefore limit the value of direct comparison between their findings. For instance, the findings of the qualitative study with GPs (**Chapter 7**) primarily relate to the development and implementation of the national AF screening programme rather than AF screening interventions investigated by other component studies (**Chapters 3-6**), although where appropriate connections with qualitative multi-stakeholder feedback obtained during the PDAF study (**Chapter 4**) were drawn.

The real-world applicability of findings presented in this enquiry may be limited by the clinical research setting itself, which at times was not firmly integrated with pre-existing clinical infrastructure or pathways (Sacristán 2015). During the PDAF study (**Chapters 3-5**), only one of the participating CPs was officially employed by a GP surgery, whereas during the study within a South Asian community (**Chapter 6**) patients were referred to their GP without an established pathway in place. Last but not least, it should be noted that studies included in this thesis were designed, delivered and reported in line with the recommendations outlined in the 2016 ESC guidelines for the management of AF (Kirchhof *et al.* 2016). Close to the submission time of this thesis, the 2020 ESC guidelines for AF were published, and whilst no major updates were introduced in the area of AF screening, it is possible that some of the research outcomes presented here would vary in light of the new recommendations (Hindricks *et al.* 2020). For instance, the recommendation to introduce a *'structured referral platform'* for individuals with screening-detected AF may increase the follow-up rates observed by studies included in this thesis. In turn, the recommendation encouraging a periodic re-assessment of individual's risk of bleeding and stroke may alter the proportion of those with 'new' AF who are offered the long-term OAC therapy.

8.3 Implications for research and contribution to knowledge

The findings of this enquiry made an original contribution to pre-existing research knowledge (**Chapter 1**) and helped address the research questions or hypotheses which emerged along the course of the research programme (**Chapters 3-7**). First and foremost, this enquiry demonstrated the feasibility, acceptability, effectiveness and cost-effectiveness of pharmacist-led AF screening services outside the traditional community pharmacy environment, which had dominated all of the previous investigations (section **1.3.4**). The PDAF study (**Chapters 3-5**) showcased the potential of CPs to detect AF in GP surgeries or care homes using either the conventional pulse palpation or modern $_{SL}$ECG technology in a stakeholder-acceptable and cost-effective manner. This enquiry also proposed an alternative and possibly even more cost-effective model of community-based AF screening, whereby AF detection using the automated KMD algorithm is performed by less clinically

qualified staff, such as pharmacy students, under the supervision of a qualified CP (**Chapter 6**), thus providing additional evidence to support the previous reports of receptionist- or student-led AF screening in primary care (Orchard *et al.* 2014; Zaprutko *et al.* 2019; Anderson *et al.* 2020).

Secondly, this thesis adds knowledge to previous studies (Rhys *et al.* 2013; Orchard *et al.* 2016; Kaasenbrood *et al.* 2016; Jacobs *et al.* 2018) by supporting the effectiveness and cost-effectiveness of CP-led opportunistic or population-based AF screening of ≥ 65s during the influenza vaccination season, which offered access to the at-risk group of individuals with AF in either GP surgeries or care homes (**Chapters 3 and 5**). In turn, the qualitative feedback in relation to this model (**Chapters 4 and 7**) suggested that its real-world implementation may be limited by logistical barriers, such as staff capacity or time-pressured clinic environment, thus proposing a flexible approach of opportunistic AF screening either during the seasonal influenza vaccination clinics or during the routine CVD appointments. The care home-based AF screening programme included in this enquiry was the first of its kind in the UK (**Chapter 5**), demonstrating that the prevalence of undiagnosed AF in this setting may be 12-fold above the population average (Public Health England 2017a), and that unlike commonly held beliefs, patients with AF in this setting may display a favourable risk-benefit balance for stroke prevention with OAC therapy. This thesis also incorporated the first-ever AF screening intervention targeting a selected UK ethnic minority group which showed that population-based AF screening within a South Asian community setting may be a beneficial and cost-effective strategy regardless of the low AF prevalence (**Chapter 6**).

The findings of this enquiry contribute to the growing body of research evidence, which supports the favourable diagnostic accuracy, user-acceptability and cost-effectiveness profile of modern $_{SL}$ECG devices as the preferred method for AF detection in primary care or community settings (Lowres *et al.* 2014; Lowres *et al.* 2015; Aronsson *et al.* 2015; Halcox *et al.* 2017; Svennberg *et al.* 2017; Tarride *et al.* 2017; Jacobs *et al.* 2018; Orchard *et al.* 2019a; Lown *et al.* 2020). Several previous studies suggested that AF screening using modern $_{SL}$ECG devices may in fact be more accurate than the use of conventional pulse palpation (Lowres *et al.* 2014; Quinn *et al.* 2018). The results of the PDAF study (**Chapters 3-5**) support the superiority argument of $_{SL}$ECG devices over pulse palpation with quantitative and qualitative multi-stakeholder feedback, comprehensive diagnostic accuracy data, and for the first time, a direct cost-effectiveness comparison. Lastly, to our knowledge, this thesis presents the findings of the first qualitative study with UK-based GPs aimed specifically at exploring their perspectives about the national AF screening

programme (**Chapter 7**). The results suggest that previously-highlighted funding, workload or technical considerations (Orchard *et al.* 2016; Taggar *et al.* 2016b; Wessex AHSN 2019) may form only a part in the framework of barriers to widespread AF screening, and that further quantitative and qualitative research evidence will be necessary to explore such barriers and to get all GPs on board.

8.4 Implications for practice and policy

The contribution to research knowledge and clinical evidence made by this enquiry may lead to several substantial practice and/or policy developments. Firstly, the evidence supporting the CP-led AF screening in GP surgeries and care homes presented here (**Chapters 3-5**) comes at a convenient time when practice-based CPs are being integrated into PCNs to provide increasingly more clinical services, including those for care home residents (NHS England and BMA 2019c). The primary target audience of such medicines optimisation-focused clinical activities are older individuals experiencing long-term illnesses and/or polypharmacy (NHS England and BMA 2019c), a large proportion of whom may be at risk of AF and ischaemic stroke (Benjamin *et al.* 1994; Olesen *et al.* 2011). Their participation in routine CP-led clinical medication reviews at GP surgeries or care homes may therefore offer an opportunity to detect AF in a similar manner to the CVD 'MOT' model proposed by the PDAF study stakeholders (**Chapter 4**). The fact that most CPs are expected to become independent prescribers, and in some cases, lead on the anticoagulation agenda within their practice (NHS England and BMA 2019c), may also help fast-track the management of patients with newly detected AF who are eligible for OAC therapy, using a simplified model of the one-stop community pharmacy clinics (Antoniou *et al.* 2019). A recent survey suggested that 76% of UK general practice-based CPs may have an independent prescribing qualification and that over a third of them wished to expand their expertise in diabetes/endocrinology and cardiology, thus fitting the profile of the future combined AF screening-CVD 'MOT service (Savickas *et al.* 2020a). A third of the responding workforce also hoped to provide more care home services whereas one in five aimed to become more involved in anticoagulation (Savickas *et al.* 2020a), implying that a one-stop CP-led AF screening and OAC clinic in GP surgeries, perhaps with an outreach to care homes, may be a sustainable future model. In turn, CP-led identification and management of undiagnosed AF or other CVD risk factors, such as hypertension, may help achieve the targets set out in the Government's CVD agenda (Public Health England 2019c). As shown by the AF screening study within a South Asian community setting (**Chapter 6**), CPs may also play a role in tackling health inequalities by improving healthcare access amongst ethnic minority groups who may not routinely visit their GP yet experience

an elevated risk of CVD (Public Health England 2017c; NHS England 2018a). Whilst much work had be done to deliver CVD risk factor assessment programmes in South Asian communities (Mathews *et al.* 2007; Patel *et al.* 2007; Rao *et al.* 2012), the findings of this study urge policy makers and commissioners to consider AF screening as a routine outreach service to this at-risk population within the CVD screening package.

The comments from PDAF study participants (**Chapter 3 and 4**) and South Asian individuals (**Chapter 6**) both suggested that AF screening initiatives may also help raise the inadequate public awareness of AF or its risks – a widespread barrier to AF detection services which was highlighted throughout this enquiry (**Chapters 3, 4, 6 and 7**). Of course, a question remains as to whether or not practice-based CPs, who are already affected by increasing workload pressures (Savickas *et al.* 2020a), may have sufficient time to provide AF screening/awareness services, certainly at the out-reach locations, which may be outside the scope of their professional commitments. This concern was raised by GPs (**Chapter 7**), and may require a further consideration from workforce planners, perhaps by improving the utilisation of practice-based pharmacy technicians, who may perform AF screening using the automated KMD algorithm in a similar way to pharmacy students (**Chapter 6**) before referring selected patients to the CP. The AF screening service in community pharmacies remains an alternative due to its accessibility, however the issues of patient confidentiality, commercialisation and poor integration within the existing clinical pathways, which were stressed by both service users (**Chapter 4**) and service providers or potential decision-makers (**Chapter 7)**, may hinder its widespread implementation. Another alternative model of future AF screening service may exclude pharmacy staff altogether and would instead focus on HCAs or practice nurses who were commonly identified by patients and staff interviewed during this enquiry (**Chapters 4 and 7**) as displaying the most optimal skillset to facilitate AF detection. Considering their current roles in the delivery of seasonal influenza vaccinations and healthcare testing (e.g. NHS Health Checks) (Royal College of Nursing 2019; NHS 2019b), AF screening may possibly be combined with either of the two services provided an appropriate service specification, training and funding/workforce are in place as emphasised by stakeholders of this enquiry (**Chapters 4 and 7**).

The qualitative findings presented by this thesis also make it clear that the success of any future AF screening services, whether it is pharmacist or non-pharmacist-led, will depend heavily on both the central support from the Government and even more importantly, on the leadership of local clinicians and decision-makers. The concept of the *'screening champion'* (Orchard *et al.* 2016; Orchard *et al.* 2019a) was therefore referred to in different contexts throughout this enquiry (**Chapters 4, 6, 7**), and encourages commissioners or policy-

makers to formalise this role within the existing CVD agenda. The closer collaboration between the AHSNs and Sustainability and Transformation Partnerships or Integrated Care Systems (Dodge 2017; The AHSN Network 2019b) offers a chance to develop these roles by utilising the expertise of leading primary and secondary care clinicians, researchers and community leaders. As pointed out by this enquiry, GPwERs in cardiology and stroke consultants already champion AF detection and management within their routine practice (**Chapter 7**). Their joint efforts may be complemented by PCN-integrated CPs who could offer their expertise as AF awareness and OAC champions, together contributing to the much needed positive culture shift to deliver appropriate AF screening and OAC prescribing in general practice at the ground level. Indeed, as shown here, CPs of BAME origin may also act as champions within their local communities by helping overcome the traditional language and/or cultural barriers to participation in AF screening or awareness campaigns.

The results of this enquiry may affect the existing guidelines and recommendations for AF screening or detection (NICE 2014a; Hindricks *et al.* 2020). The evidence presented here suggests that $_{SL}$ECG devices may be a more accurate, cost-effective and acceptable means of AF detection compared to conventional pulse palpation, urging policy makers and international medical consensus to consider these tools as the first-line option for opportunistic or population-based AF screening of asymptomatic individuals aged ≥ 65 years. Further clinical and technological guidance, and the integration of opportunistic silent AF screening within the national AF pathways (NICE 2014a) is also warranted to ensure that clinicians are informed and equipped to use $_{SL}$ECG devices for appropriate purposes in their daily practice. Finally, the preliminary evidence gathered by this enquiry supports the effectiveness and cost-effectiveness of asymptomatic AF screening amongst care home residents and individuals of South Asian origin, advocating for the future guideline inclusion of specific population groups, which may help minimise the impact of health inequalities.

8.5 Recommendations for future research

As discussed in **Chapters 3-7**, the findings of this enquiry raise a number of further questions or recommendations for future research. Perhaps the most important question of all is whether or not the quantitative outcomes ascertained during the PDAF study (**Chapters 3 and 5**) or the AF screening initiative within the South Asian community (**Chapter 6**) could be replicated on a larger scale and in an appropriately-designed RCT, the widely-regarded “gold” standard of primary research evidence (CEBM 2009; Kirchhof *et al.* 2016). Despite requiring a larger sample size and more complex data analysis, cluster RCTs may offer an efficient approach to investigating an organisation-level complex intervention, such as widespread AF screening (Donner & Klar 2004; Dreyhaupt *et al.*

2017). As such this RCT design had been employed by both the parent SAFE study (Hobbs *et al.* 2005) and the ongoing SAFER research programme in GP surgeries (ISRCTN Registry 2019) – two of the largest AF screening trials to date. However, in line with stepwise guidance for complex interventions (MRC 2006), a more cost-effective approach may be to conduct several smaller, adequately-powered, mixed-methods individual RCTs which would investigate a particular AF screening strategy prior to rolling it out across the clusters of practices (Torgerson 2001). Based on the findings of this enquiry, the key service designs and single-time point AF screening strategies to be explored by such two- or multiple-arm RCTs in general practice may include:

- CP-led opportunistic AF screening during routine (medication) reviews of ≥ 65s with an established CVD or risk factors for ischaemic stroke
- CP-, nurse- or HCA-led opportunistic/population-based AF screening of patients eligible for seasonal influenza vaccinations and
- Nurse-, HCA- or CP-led opportunistic AF screening of ≥ 65s attending other health testing (e.g. NHS Health Checks).

Intermittent self-screening by patients at home should also be given a consideration, yet it is already a subject of the SAFER and STROKESTOP II trials (Engdahl *et al.* 2017; ISRCTN Registry 2019), and according to stakeholders interviewed by this enquiry (**Chapters 4** and **7**) may be difficult to implement on a larger scale. In turn, RCT-generated evidence is required to support AF screening in other primary care or public locations, which was referred to throughout this thesis, including care homes, community pharmacies or places of worship of selected ethnic minority groups. Nevertheless, the execution of RCTs in such settings may be currently limited by logistical barriers, particularly the lack of established referral pathways, which may be a subject of future qualitative research.

Considering the ample demographic, diagnostic and cost-effectiveness evidence presented by previous AF screening studies and this enquiry, the outcomes of future studies, including the RCTs, should focus on deriving the data pertaining to clinical endpoints, such as the effects of opportunistic AF detection on the risk of ischaemic stroke/TIA/SEE, major/non-major haemorrhage and stroke/all-cause mortality, which had previously been included in major AF-related RCTs of OAC therapies (Connolly *et al.* 2009; Patel *et al.* 2011; Granger *et al.* 2011). A sub-group analysis of a future RCT may also wish to explore the benefits of AF screening intervention in patients with different patterns of AF, such as those with PAF or persistent disease, which together with global endpoint data, may ultimately present enough evidence to support the UK national AF screening programme (UK NSC 2019). A

head-to-head RCT of conventional pulse palpation versus modern AF detection tools, such as $_{SL}$ECG devices or mBPMs, may consolidate the findings of superior diagnostic accuracy and cost-effectiveness of these methods compared to pulse checks presented in this feasibility-focused enquiry. In practice however, the value of such an RCT may be questionable, and although it may convince some of the doubters who resist the introduction of newer technology, the strong evidence base supporting the use of $_{SL}$ECG devices means they will likely form the basis of future AF screening investigations regardless.

8.6 Conclusion

This enquiry employed a mixed-methods approach to explore the role of primary care CPs in the detection of AF, focusing on CP-led AF screening interventions in GP surgeries, care homes and community settings. Research evidence presented here constitutes an original contribution to the development of CP-led AF screening services in primary care at the time of their rapid role evolution, and demonstrates that these qualified yet underutilised professionals may deliver, or facilitate, AF detection in an accurate and cost-effective manner. It also urges commissioners and policy makers to reconsider the most optimal methods for opportunistic detection of asymptomatic AF, transitioning from conventional but less accurate pulse palpation to more capable modern technology, such as $_{SL}$ECG devices. The results of this enquiry suggest that, as a complex healthcare intervention, AF screening service is underpinned by multiple layers of potential implementation barriers that need to be addressed by the Government and local leaders prior to its formal integration within the primary care infrastructure. As part of this process, future researchers are encouraged to evaluate the effectiveness and economic benefits of several potential models or strategies of AF screening, for instance, incorporating it with services for patients with long-term conditions. The ongoing expansion of general practice pharmacy roles and workforce offers a unique opportunity to facilitate the development and implementation of such novel combined public health services which may benefit the patients, the practice and the healthcare economy.

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Appendices

Appendix 1 The history of literature search conducted on MEDLINE database

#	Query	Limiters/Expanders	Results
S25	S9 AND S20 AND S23	Limiters - Date of Publication: 20000101-20200831; English Language; Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	18
S24	S9 AND S20 AND S23	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	18
S23	S21 OR S22	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	39,051
S22	pharmacist*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	39,051
S21	(MH "Pharmacists")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	16,724
S20	S12 OR S19	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	21,964
S19	S15 AND S18	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	21,964
S18	S16 OR S17	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	2,814,973
S17	detect*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	2,357,043
S16	screening	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	615,653
S15	S13 OR S14	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	218,301

S14	AF	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	162,159
S13	atrial fibrillation	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	82,911
S12	S10 AND S11	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	215
S11	(MH "Mass Screening+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	127,064
S10	(MH "Atrial Fibrillation")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	55,045
S9	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	403,993
S8	primary care	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	219,269
S7	GP practice*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	2,745
S6	GP surger*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	531
S5	general practice	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	106,082
S4	community pharmac*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	11,281
S3	(MH "General Practice+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	74,134
S2	(MH "Primary Health Care+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	158,680
S1	(MH "Pharmacies")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	7,905

Appendix 2 The history of literature search conducted on CINAHL database

#	Query	Limiters/Expanders	Results
S25	S9 AND S20 AND S23	Limiters - Published Date: 20000101-20200831; English Language; Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	9
S24	S9 AND S20 AND S23	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	9
S23	S21 OR S22	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	25,412
S22	pharmacist*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	25,412
S21	(MH "Pharmacists")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	15,545
S20	S12 OR S19	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	2,869
S19	S15 AND S18	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	2,869
S18	S16 OR S17	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	373,464
S17	detect*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	234,764
S16	screening	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	170,242
S15	S13 OR S14	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	36,393
S14	AF	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	12,431

S13	atrial fibrillation	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	34,087
S12	S10 AND S11	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	0
S11	(MH "Mass Screening+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	238
S10	(MH "Atrial Fibrillation")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	24,779
S9	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	143,804
S8	primary care	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	112,970
S7	GP practice*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	2,019
S6	GP surger*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	394
S5	general practice	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	34,752
S4	community pharmac*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	4,855
S3	(MH "General Practice+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	398
S2	(MH "Primary Health Care+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	63,555
S1	(MH "Pharmacies")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	0

Appendix 3 The history of literature search conducted on Cochrane Library

ID	Search	Hits
#1	MeSH descriptor: [Pharmacies] explode all trees	93
#2	MeSH descriptor: [Primary Health Care] explode all trees	7131
#3	MeSH descriptor: [General Practice] explode all trees	2432
#4	community pharmac* OR general practice OR GP practice* OR primary care	109586
#5	#1 OR #2 OR #3 OR #4	111903
#6	MeSH descriptor: [Atrial Fibrillation] explode all trees	4542
#7	MeSH descriptor: [Mass Screening] explode all trees	3717
#8	#6 AND #7	21
#9	atrial fibrillation OR AF	21085
#10	screening OR detect*	133950
#11	#9 and #10	2517
#12	#8 OR #11	2517
#13	MeSH descriptor: [Pharmacists] explode all trees	575
#14	pharmacist*	5136
#15	#13 OR #14	5136
#16	#5 AND #12 AND #15 with Cochrane Library publication date Between Jan 2000 and Aug 2020	65

Appendix 4 Characteristics and findings of studies selected for the literature review

Participant age expressed as a mean ± standard deviation. Abbreviations: $_{12L}$ECG – 12-lead electrocardiogram; AF – atrial fibrillation; BMI – body mass index; BP – blood pressure; CHA_2DS_2-VASc – Hypertension, Age ≥ 75 years, Diabetes, previous Stroke/TIA/thromboembolism, Vascular disease, Age 65-74 years, Sex category; CVD – cardiovascular disease; DOAC – direct-acting oral anticoagulant; ECG – electrocardiogram; GP – general practitioner; HCP – healthcare professional; KMD – Kardia Mobile® device; mBPM – modified BP monitor; NPV – negative predictive value; OAC – oral anticoagulant; PPV – positive predictive value; QALY – quality-adjusted life year; $_{SL}$ECG – single-lead electrocardiogram; UK – United Kingdom; US – united states.

Study and location	Design and aim(s)	Study participants	Methodology/ methods	Significant outcomes/results	Limitations/ biases
Lowres *et al.* (2014) Screening Education And Recognition in Community pHarmacies of Atrial Fibrillation (SEARCH-AF) Australia	Cross-sectional, diagnostic accuracy and economic evaluation (feasibility study) **Aim:** To determine the feasibility, impact and cost-effectiveness of community pharmacy-based screening using $_{SL}$ECG.	Persons entering one of 10 community pharmacies aged ≥ 65 years with/without a history of AF recruited over 8 months (n = 1000; mean age 76.0 ± 7.0 years).	**Intervention** Single time point opportunistic AF screening by trained pharmacists using 30-second pulse palpation followed by 30-60-second $_{SL}$ECG recording using KMD. Estimation of yield and diagnostic accuracy of pulse palpation and pharmacist/algorithm interpretation of $_{SL}$ECG (index tests) vs. cardiologist's interpretation of $_{SL}$ECG and $_{12L}$ECG where available (reference standard). Individuals referred to GP if AF suspected by cardiologist. Eight-item questionnaire administered to assess	**Screening outcomes** Total AF prevalence on $_{SL}$ECG: 6.7% Yield of 'new' AF on $_{SL}$ECG: 1.5% (all CHA_2DS_2-VASc ≥ 2; 60% asymptomatic) Yield of 'new' AF on $_{12L}$ECG: 0.7% Started on OAC therapy: 0.3% (20.0% of 'new' AF cases). **Diagnostic accuracy** *Sensitivity* $_{SL}$ECG algorithm: 98.5% $_{SL}$ECG pharmacist: 77.0% Pulse palpation: 77.0%` *Specificity* $_{SL}$ECG algorithm: 91.4% $_{SL}$ECG pharmacist: 87.0% Pulse palpation: 93% Inter-rater agreement (Cohen's Kappa): $_{SL}$ECG algorithm: Not determined $_{SL}$ECG pharmacist: 0.40	Involved a single region of Australia – results may not be generalisable to the wider population. Sampling method not stated – risk of non-random sampling bias. Response rate not stated – risk of non-response bias. Recruited individuals with and without AF – risk of recall or reporting bias. Unclear if pharmacists/cardiologist blinded to results of prior tests – risk of diagnostic review bias.

			pharmacists' knowledge of AF before and after study. **Cost-effectiveness** Simulated comparison of screening using KMD vs. no screening in Australian population over the time horizon of 10 years (Monte Carlo simulation). Estimation of incremental cost/QALY gained and /stroke prevented. All AF patients receiving warfarin at base case.	Pulse palpation: 0.52 **Cost-effectiveness** Positive cost-effectiveness with $AUD 5,988/QALY gained and $AUD 30,481/stroke prevented (at 55% adherence to OAC therapy). Costs greater in DOAC-dominated (90%) model than 100%-warfarin model: $AUD 14,044/QALY gained. Cost-effectiveness improved with adherence to OAC therapy ($AUD 3,888/QALY gained at 80% adherence). **Impact measures** Significant improvement in pharmacists' knowledge post-study ($p < 0.001$). 44% of individuals with known AF unaware of diagnosis – potential for educative role of pharmacists.	Interval between index tests and cardiologist's interpretation not stated – risk of disease progression bias. $_{12L}$ECG performed for 14/15 patients with AF but combined with $_{SL}$ECG interpretation by cardiologist as a reference standard – risk of partial/differential verification and misclassification biases. Economic analysis did not appear to consider the costs of OAC-related bleeding, inconclusive diagnoses or the probability of cost-effectiveness – may limit real-life applicability. Economic analysis assumed non-inferiority for DOACs vs. warfarin, which may be clinically conservative and may underestimate the possible net clinical benefit with DOACs over warfarin.
Sandhu *et al.* (2016)	Cross-sectional with follow-up	Persons entering one of 30 pharmacies	**Intervention** Single time point AF screening by trained	**Screening outcomes** Yield of 'new' AF on $_{SL}$ECG: 2.4%	Recruited individuals with and without AF – risk of

The Program for the Identification of 'Actionable' Atrial Fibrillation in the Pharmacy Setting (PIAAF-Pharmacy) Canada	(referred to by authors as a prospective cohort study) **Aim** To identify 'actionable AF' ('new' AF or known AF but not on OAC therapy) and the rates of CVD risk factors, and to determine the feasibility of combined CVD screening in community pharmacies.	aged ≥ 65 who did not take OAC therapy for AF recruited over six months (n = 1145; mean age 77.2 ± 6.8 years).	volunteers with a 30-second HeartCheck®-based $_{SL}$ECG recording interpreted by a technician. Volunteers also checked participants' blood pressure using a PharmaSmart® kiosk, helped complete a Canadian Diabetes Risk Assessment Questionnaire and provided educational materials/counselling on stroke risk factors. $_{SL}$ECG interpreted and quality-rated by two independent cardiologists. If AF suspected on $_{SL}$ECG, individuals referred for $_{12L}$ECG within 24-72 hours. If $_{12L}$ECG demonstrated SR, external cardiac monitoring was recommended. **Follow-up** Participants with 'actionable AF' followed-up at six weeks (mostly with a GP) and three months (with a specialist), and completed a three-item feedback questionnaire at three-month follow-up. Estimation of enrolment rate, the proportion with 'actionable	Yield of 'actionable AF' on $_{SL}$ECG: 2.5% (93% had a CHA_2DS_2-VASc ≥ 2) Yield of 'new' AF on $_{12L}$ECG: 0.3% Proportion initiated on OAC therapy at six-week follow-up: 0.4% (17% of 'actionable AF'). Proportion initiated on OAC therapy at three-month follow-up: 1.1% (45% of 'actionable AF'). **Follow-up findings** Proportion attended six-week follow-up: 24.1% Proportion attended three-month follow-up: 79.3% At 3 months, 83% of those with 'actionable AF' were aware of AF risks, all satisfied with screening and 96% satisfied with educational materials for stroke risk factors. **Other findings** Quality of $_{SL}$ECG: 37.0% excellent, 56.4% acceptable, 6.6% poor, 1.2% uninterpretable. Inter-rater agreement between technicians and cardiologist: 0.79. Proportion with suboptimal BP: 55% (n = 616/1122; 51.7% amongst those with 'actionable AF) Most of those screened had intermediate (47.0%, n = 231/492) or high risk (43.4%, n = 214/492) of diabetes.	recall or reporting bias (for inter-rater agreement). Sampling method not stated – risk of non-random sampling bias. Response rate not stated – risk of non-response bias. Self-reported medical history – risk of recall and selection biases. Screening performed by volunteers and not pharmacists – unclear what the role of pharmacists was in the screening process or how it could be integrated with existing services. No built-in automated algorithm of the $_{SL}$ECG device – limited real-life applicability. Interval between the index test and reference standard not stated – risk of disease progression bias. Unclear if cardiologist blinded to results of index

			AF', those with suboptimal blood pressure control; rates of low/intermediate/high risk for diabetes, use of OAC in those with 'actionable' AF at three months, quality of $_{SL}$ECG and the agreement between technician's & cardiologist's interpretations of $_{SL}$ECG (index test and reference standard, respectively).		test – risk of diagnostic review bias. Feedback questionnaire administered only to those with 'actionable AF' at follow-up – risk of non-response bias, and results may not reflect the feasibility in the general population. Low follow-up rate at six-week follow-up (< 25%) questions the effectiveness of the follow-up pathway to GPs. The 24-72 h target for $_{12L}$ECGs to confirm AF may not be realistic in certain healthcare systems and real-life settings.
Zaprutko *et al.* (2019) Poland	Cross-sectional, diagnostic accuracy (feasibility study) **Aim:** To evaluate the feasibility and diagnostic	Persons entering one of 10 community pharmacies aged ≥ 65 years without a history of AF recruited over 11 months (n = 525; mean age 73.7 ± 6.5 years).	Single time point opportunistic AF screening by trained students under the supervision of pharmacists with a 30-second KMD-based $_{SL}$ECG recording interpreted by an automated algorithm. Estimation of yield and diagnostic accuracy of $_{SL}$ECG interpretation by the algorithm (index test) vs.	**Screening outcomes** Total AF prevalence on $_{SL}$ECG: 2.3% Yield of 'new' AF on $_{SL}$ECG: 1.3% (all men had CHA_2DS_2-VASc ≥ 1; single female had a score of 2) **Diagnostic accuracy** Sensitivity: 100% Specificity: 99% PPV: 65% NPV: 100%	No sample size calculation – outcomes derived may not be a reliable estimate. Sampling method not stated – risk of non-random sampling bias. Response rate not stated – risk of non-response bias.

	accuracy of $_{SL}$ECG screening in community pharmacies.		cardiologist's interpretation of $_{SL}$ECG (reference standard) within 48 hours. Individuals referred to GP if AF suspected by cardiologist.	**Other findings** Inconclusive (Unclassified) diagnoses by $_{SL}$ECG: 2.7% Unreadable/non-interpretable diagnoses by $_{SL}$ECG: 11.0% (4.6% by cardiologist) High level of inconclusive/non-analysable diagnoses may be a result of KMD use by non-professionals (students) or noise levels in pharmacies.	Unclear if cardiologist blinded to results of index test – risk of diagnostic review bias. No $_{12L}$ECG performed – risk of misclassification bias. No follow-up of individuals post-screening to check if OAC therapy initiated – unclear if screening benefits population.
Cunha *et al.* (2020) Portugal	Cross-sectional (pseudo-longitudinal), diagnostic accuracy (feasibility study) **Aim:** To test the feasibility of an awareness event including opportunistic AF screening by pharmacists and diagnostic accuracy of	Persons in a community pharmacy, a nursing home or an outpatient cardiology clinic aged ≥ 40 years without a history of AF (unless they had AF and were not prescribed OAC therapy) recruited over one month during an AF awareness campaign (n = 205 out of 223 involved in an awareness event; mean age	Single time point opportunistic AF screening by pharmacists with a 30-second KMD-based $_{SL}$ECG recording interpreted by an automated algorithm. Estimation of yield and diagnostic accuracy of $_{SL}$ECG interpretation by the algorithm (index test) vs. the cardiologist's interpretation of $_{12L}$ECG (reference standard). Individuals from community pharmacies referred to GP or to physician responsible for a nursing home if AF suspected by pharmacist.	**Screening outcomes** Proportion with irregular pulse: 22% Yield of 'new' AF on $_{12L}$ECG: 6.3% (1.0% in a community pharmacy; 9.9% in an outpatient clinic and 13.0% in a nursing home) **Diagnostic accuracy (in the outpatient clinic)** Sensitivity: 90.9% Specificity: 97.4% **Other findings** Unclassified diagnoses by $_{SL}$ECG: 14.0% Unreadable diagnoses by $_{SL}$ECG: 0.5% 18% of incidentally found known AF cases not prescribed OAC therapy. Difficulties arranging $_{12L}$ECG in a nursing home highlighted.	Involved a single region of Portugal – results may not be generalisable to the wider population. Involved individuals aged ≥ 40 years who may not benefit from OAC therapy if AF was detected. No sample size calculation and small sample (especially in a nursing home; n = 23) – outcomes derived may not be a reliable estimate. Sampling method not stated – risk of non-random sampling bias.

	SLECG screening.	66.0 ± 15.0 years; 48% recruited in community pharmacy).			Self-reported medical history – risk of recall and selection biases. Yield of 'new' AF obtained across all three settings – skewed by yields in the nursing home and the outpatient clinic. Unclear if cardiologist blinded to KMD result – risk of diagnostic review bias. Interval between the index test and reference standard not stated – risk of disease progression bias. Diagnostic accuracy evaluated in a hospital sample only (n = 101) and excluded inconclusive diagnoses – may not be generalisable to primary care. No follow-up of individuals post-screening to check if OAC therapy initiated – unclear if screening benefits population.
Twigg *et al.* (2016)	Cross-sectional	Persons entering one of	Single time point opportunistic or targeted	**Screening outcomes**	Involved a single region of UK – results may not be

UK	(evaluation of a new service) **Aim:** To describe the outcomes from an AF service in UK community pharmacies in terms of referral outcomes and further interventions.	six community pharmacies aged ≥ 65 years or aged 50-64 years with risk factors but without a history of AF recruited over 4 months (n = 594; mean age 68.3 ± 8.9 years).	CVD risk and AF screening by trained pharmacists or other pharmacy staff with a Microlife WatchBP Office Afib®, and if positive, KMD-based $_{SL}$ECG recording using an automated algorithm. Diagnosis confirmed by cardiologist's interpretation of $_{SL}$ECG within 24 hours. Estimation of yield and follow-up actions. Individuals referred to GP if AF suspected by cardiologist. Individuals received advice on alcohol consumption, smoking, weight loss and hypertension, if risks were identified from the eligibility questionnaire or BP results.	Individuals identified as at-risk of having AF on $_{SL}$ECG and referred to GP: 1.5% Yield of 'new' AF confirmed after follow-up and prescribed medication: 0.8% Undiagnosed hypertension (referred to GP): 18.4% Proportion with a BMI of > 30 kg/m^2: 29.6% Proportion with an Audit C score of > 5 (harmful drinking): 22.1% Proportion of smokers: 9.9% **Other findings** Pharmacists provided 413 interventions in 54.9% individuals; 23.6% received multiple interventions. Pharmacists were able to provide appropriate and established pharmacy public health interventions to address multiple issues.	generalisable to the wider population. No sample size calculation – outcomes derived may not be a reliable estimate. Sampling method not stated – risk of non-random sampling bias. Response rate not stated – risk of non-response bias. Self-reported medical history – risk of recall and selection biases. Unclear who conducted the screening (pharmacists or pharmacy staff), but only pharmacists were trained – risk of misclassification bias. Unclear what the duration of $_{SL}$ECG recording was – risk of misclassification bias. Unclear if cardiologist blinded to results of index test – risk of diagnostic review bias.

					Unclear if AF diagnoses confirmed by 12LECG – risk of partial/differential verification and misclassification biases. Unclear what treatment was prescribed at follow-up. Lack of follow-up of individuals with suspected hypertension or those who received advice regarding weight reduction, alcohol consumption or smoking cessation – unclear what the benefits of the intervention might be for these individuals.
Antoniou *et al.* (2017) – conference abstract Multinational (Canada, New Zealand, Portugal, Spain, UK)	Cross-sectional (feasibility study) **Aim:** To raise awareness of AF and importance of pulse rhythm checks to general public and to	Persons entering one of 56 pharmacies aged ≥ 18 years recruited over one week during an AF awareness campaign (n = 1717; mean age 62.2 ± 15.5 years).	Single time point AF screening by trained pharmacists using pulse palpation. Individuals referred to GP if AF suspected after screening. Estimation of proportion with irregular pulse who were referred to GP and the yield of 'new' AF, including the proportion anticoagulated within 30 days.	Individuals with irregular heart rhythm detected and referred to GP: 4.5% Yield of 'new' AF within 30 days: 1.4% (all initiated on OAC therapy).	No sample size calculation – outcomes derived may not be a reliable estimate. Sampling method not stated – risk of non-random sampling bias. Involved individuals aged ≥ 18 years who may not benefit from OAC therapy if AF was detected (although all detected cases qualified for OAC therapy in this study).

	assess feasibility of pulse checks in community pharmacy.				Response rate not stated – risk of non-response bias. Unclear what the duration of $_{SL}$ECG recording was – risk of misclassification bias. Unclear if AF diagnoses confirmed by $_{12L}$ECG – risk of misclassification bias. Little demographic data provided (e.g. no details of comorbidities/risk factors) – not possible to verify the level of stroke risk amongst 'new' AF cases.
Bacchini *et al.* (2019) Italy	Cross-sectional (feasibility study) **Aim:** To raise awareness of AF and evaluate feasibility and reliability of AF screening in community pharmacies	Persons entering one of 74 community pharmacies aged ≥ 50 years with or without a history of AF recruited over 6 months (n = 3071; mean age for screen positives 73.7 ± 9.2 years; mean age for screen negatives 66.4 ± 9.9 years).	Single time point opportunistic AF screening by pharmacists with an automated MicrolifeAFIB® device. Estimation of AF yield by the device and risk factors amongst those with suspected AF. Individuals referred to GP if AF suspected or to emergency department if symptomatic AF following the screening.	**Screening outcomes** Total AF prevalence determined by mBPM: 3.2% 'new' AF identified by mBPM: 1.4% (87.7% had CHA_2DS_2-VASc ≥ 2). **Other findings** More than 50% of AF positive patients unaware of AF diagnosis. 16% of those with known AF not prescribed OAC therapy despite CHA_2DS_2-VASc > 2. High prevalence of stroke in patients with 'new' AF diagnoses (9%).	Involved a single region of Italy – results may not be generalisable to the wider population. Involved individuals aged ≥ 50 years who may not benefit from OAC therapy if AF was detected. Self-reported medical history – risk of recall bias. No sample size calculation – outcomes derived may not be a reliable estimate.

	using a mBPM.				Sampling method not stated – risk of non-random sampling bias. Response rate not stated – risk of non-response bias. Unclear if any ECG tool was used to confirm suspected AF diagnoses – risk of misclassification bias. Smoking, alcohol, tea, coffee, heavy meals or strenuous physical activity in the previous two hours before screening were not permitted – results may not be representative of real-life opportunistic screening. No follow-up of individuals post-screening to check if OAC therapy initiated – unclear if screening benefits the population.
Antoniou *et al.* (2019) – conference abstract UK	Cross-sectional (feasibility study) **Aim:** To assess the	Persons entering one of 21 community pharmacies aged	Single time point AF screening by trained pharmacists using pulse palpation and KMD-based $_{SL}$ECG recordings. Individuals referred to one-stop clinic if any irregularity	**Screening outcomes** Individuals with irregularity referred to one-stop clinic: 6.7% Yield of 'new' AF within 30 days: 1.6% Yield of known AF not on OAC therapy ('actionable AF'): 1.2%	Unclear if involved a single region or multiple UK regions – results may not be generalisable to the wider population.

	feasibility of screening by community pharmacists with onward referral to an innovative one-stop AF clinic to enable identification of new cases of AF and subsequent initiation OAC therapy.	≥ 65 years (mean age 69 ± 3.5; n = 672).	was suspected. Estimation of proportion who were referred following the screening and the yield of AF within 30 days.	All new and actionable AF cases started on OAC therapy. **Other findings** Prevalence of hypertension in the entire sample: 92% Prevalence of diabetes in the entire sample: 36% Innovative pathway from community pharmacies to one-stop clinic could provide remote triage at scale and help address the missing people with undiagnosed and actionable AF.	No sample size calculation – outcomes derived may not be a reliable estimate. Sampling method not stated – risk of non-random sampling bias. Response rate not stated – risk of non-response bias. Unclear what the duration and order of index tests were, and whether all participants underwent both tests – risk of partial/differential verification and misclassification biases. Unclear if $_{12L}$ECG was used to confirm suspected AF diagnoses – risk of misclassification bias. Unclear if medical history was self-reported– risk of recall and selection biases.
Anderson *et al.* (2020) – US	Cross-sectional (feasibility study) **Aim:** To evaluate AF	Persons attending one of 13 health fairs with or without a history of AF (no age defined) recruited over 6	Single time point AF screening by trained pharmacy students using 30-second KMD-based $_{SL}$ECG recordings interpreted by an automated algorithm under	**Screening outcomes** Prevalence of AF on $_{SL}$ECG: 2.3% (all asymptomatic; none aware of previous diagnosis; 69.0% CHA_2DS_2-VASc ≥ 2). **Other findings** Unclassified diagnoses by $_{SL}$ECG: 1.1%	Involved a single region of US – results may not be generalisable to the wider population.

	screening and education at student pharmacist – driven health fairs.	months (mean age 56 ± 15; n = 697). Health fairs held at community centres, festivals, senior centres, carnivals, state capital buildings, state pharmacy meetings, and religious centres.	the supervision of a preceptor. Participant education was provided using an American Heart Association AF patient information sheet. Learning assessment was evaluated with a three-item questionnaire.	40% never heard of AF before screening. Most participants (72.2-92.3%) answered each learning assessment question correctly. > 95% of participants believed that screening for AF at health fairs was important or very important.	No sample size calculation – outcomes derived may not be a reliable estimate. No defined eligibility criteria – some individuals with AF identified through screening may not have benefitted from OAC therapy. Sampling method not stated – risk of non-random sampling bias. Response rate not stated – risk of non-response bias. Self-reported medical history – risk of recall bias. No $_{12L}$ECG performed – risk of misclassification bias. No follow-up of individuals post-screening to check if OAC therapy initiated – unclear if screening benefits the population.
Da Costa *et al.* (2020) Multinational (Canada, New Zealand, Portugal,	Cross-sectional quantitative and qualitative study.	**Quantitative** Persons in participating 104 community pharmacies, three community	**Intervention** Single time point opportunistic AF screening by trained pharmacists using pulse palpation with or without KMD-based $_{SL}$ECG recordings	**Screening outcomes** Proportion referred to GP: 5.8% Yield of new possible AF on $_{SL}$ECG: 4.5% (mean CHA_2DS_2-VASc 2.6 ± 1.7) Yield of new possible AF on $_{SL}$ECG in ≥ 65s: 3.3% (mean CHA_2DS_2-VASc 3.7 ± 1.4)	**Quantitative** Variation in healthcare systems – results may not be generalisable across the spectrum of countries.

Spain, UK, Czech Republic, France, Hong Kong, Hungary and Switzerland)	**Aims:** To test a model for raising AF awareness and opportunistic early detection of AF (EDAF) involving pharmacists globally. To identify the enablers and barriers to program implementation.	care centres, two hospital outpatient clinics, and one nursing home aged ≥ 40 years who did not take OAC therapy for AF recruited over one month during an AF awareness campaign (n = 2,762 out of 4,193 involved in an awareness event; n = 1346 for $_{SL}$ECG recordings; mean age 65.3 ± 13.0 years; 63% recruited in community pharmacies) **Qualitative** All country co-ordinators (pharmacists; no number indicated; n = 10?).	interpreted by an automated algorithm. Individuals referred to GP if abnormal heart rate or rhythm were detected, when having symptoms suggestive of AF or in the presence of a high CHA_2DS_2-VASc score. Estimation of the yield of new or actionable AF. Pharmacists also used educational materials to promote self-care and increase awareness of AF. **Qualitative study** Ascertaining barriers and enablers to program implementation by way of interviews with all country coordinators facilitated by one researcher. Exploring the referral pathway and the influence of the setting, country and communication format on the effectiveness of EDAF. Interviews audio-recorded, transcribed verbatim, coded and analysed by two other researchers using Charmaz's iteration of constant comparative analysis (grounded theory).	Yield of new possible AF on $_{SL}$ECG in community pharmacies: 1.8% (mean CHA_2DS_2-VASc 3.2 ± 1.3) Yield of new possible AF on $_{SL}$ECG in a nursing home: 13.0% (mean CHA_2DS_2-VASc 4.7 ± 1.5) Yield of new possible AF on $_{SL}$ECG in outpatient clinics: 7.1% (mean CHA_2DS_2-VASc 3.6 ± 1.6) Yield of new possible AF on $_{SL}$ECG in community care centres: 7.2% (mean CHA_2DS_2-VASc 3.9 ± 1.3) Yield of known AF not on OAC therapy ('actionable AF'): 1.0% Yield of 'new' AF confirmed after follow-up: 0.2% (all in ≥ 65s detected in community pharmacies) Yield of atrial flutter or bradycardia: 0.1% each. **Other findings** Unclassified diagnoses by $_{SL}$ECG: 8.1% Unreadable diagnoses by $_{SL}$ECG: 0.4% Feedback from referred patients obtained: 19.9% of cases. More frequently a confirmed diagnosis was obtained following a manual pulse check without KMD (n = 10/1416 vs. n = 2/1346). **Qualitative findings** Local champion instrumental in enabling community pharmacists to successfully undertake EDAF (helps find innovative ways to combine with existing services	No sample size calculation – outcomes derived may not be a reliable estimate. Sampling method not stated – risk of non-random sampling bias. Involved individuals aged ≥ 40 years who may not benefit from OAC therapy if AF was detected. Small sample in a nursing home (n = 23) – outcomes derived may not be a reliable estimate. Low follow-up rate (19.9%) questions the effectiveness of the programme. Self-reported medical history in some countries – risk of recall bias. Unclear if AF diagnoses confirmed by $_{12L}$ECG – risk of misclassification bias. Assessment of symptoms and risk factors undertaken only in some countries – inconsistency in data collection and reporting.

			Analysis conducted until clear themes were identified, data saturation was reached and principle themes were agreed by all authors.	and enables flexibility in service provision, e.g. checking for AF on public transport). Combining with existing services a useful way to engage with EDAF and enhance recruitment; patients liked the addition of EDAF to medication reviews, or to other CVD risk factor clinics (increased patient acceptance of AF screening). Pharmacists were more willing to engage with combined AF screening if they had prior experience of offering enhanced services. AF screening itself was motivational and gave pharmacists a greater understanding about the potential for a wider scope of practice. The need for effective referral pathway at the time of rapid pharmacist's role evolution identified. Provision of bright inviting materials encourages patient engagement. Avoid complex language or text-dense materials which may act as barriers, particularly in populations of varying health literacy. Successfully identifying AF a major enabler to sustained service provision due to increased sense of value and camaraderie between GPs and pharmacists.	$_{SL}$ECG recordings performed only in some individuals – inconsistency and risk of partial/differential verification and misclassification biases. Unclear what the duration of $_{SL}$ECG recording was – risk of misclassification bias. Yield of 'new' AF obtained across multiple settings – skewed by high yields in non-community pharmacy settings. No follow-up of individuals post-screening to check if OAC therapy initiated – unclear if screening benefits population. **Qualitative** Lack of explicit information about the philosophical perspectives or epistemological positions, although interpretivism/constructivism could be implied from the use of grounded theory

				Simplicity and curiosity of screening using KMD an enabler of patient engagement with the service. Younger and technologically aware individuals more likely to engage. Some older patients felt that GP surgeries were already offering such services and were not willing to engage with EDAF in pharmacies. Good patient and pharmacist relationships/communication with GPs crucial for the success of pharmacy-based EDAF. Conducting EDAF improves relationships/collaboration with other team members, such as pharmacy technicians. Some local physicians (e.g. cardiologists) resist to pharmacists providing EDAF and/or may not offer feedback making experience less rewarding. Financial constraints a major challenge in sustaining the service (needs formal commissioning).	methodology and the underlying theoretical hypothesis. Not explicitly stated whether individual semi-structured or focus group interviews were conducted, however individual interviews may be implied from the topic guide. Unclear if interviews were conducted face-to-face or by telephone. No direct feedback from service users or clinicians. The sample size or duration of the interviews not provided. No statement about the cultural/theoretical perspectives of researcher(s) involved in qualitative data collection and analysis. No acknowledgement of how such perspectives or other researcher-specific factors may potentially influence the data

					collection/analysis (no reflexivity statement).
Tarride *et al.* (2017) 'Actionable' Atrial Fibrillation in the Pharmacy Setting (PIAAF-Pharmacy) Canada	Economic evaluation of the intervention by Sandhu *et al.* (2016). **Aim** To evaluate the economic impact of the PIAAF-Pharmacy study to better inform decision-makers about the value of screening for AF in Canadian pharmacies.	Persons entering one of 30 pharmacies aged ≥ 65 years who did not take OAC therapy for AF recruited over six months (n = 1145; mean age 77.2 ± 6.8 years).	**Intervention** Single time point AF screening by trained volunteers with a 30-second HeartCheck®-based SLECG recording interpreted by a technician. See Sandhu *et al.* (2016) above. **Cost-effectiveness** Simulated comparison of screening using the HeartCheck®-based SLECG vs. no screening in a Canadian population over a lifetime horizon (Monte Carlo simulation/Markov model). Assuming the PPV of the SLECG device was 65.4%. Proportions of patients receiving DOACs and warfarin were 48% and 52%, respectively. Estimation of short-term costs (costs of screening), outcomes (new cases of AF), and long-term costs and benefits associated with stroke prevention (incremental cost/QALY gained).	Cost per person screened: $CA 66. Pharmacy screening intervention would result in higher expected costs ($CA 26), more life-years (0.0032) and more QALYs (0.0035) over a lifelong time horizon. Positive cost-effectiveness with $CA 7,480/QALY gained. Costs greater in 100%-DOAC model than 100%-warfarin model: $CA 8,611/QALY gained and $CA 5,985/QALY gained, respectively. Probability of cost-effectiveness 91% and 94% if WTP is CA$ 50,000 and $CA 100,000/QALY gained, respectively. Costs < WTP of CA$ 50,000/QALY in all sensitivity analyses unless < 20% of AF cases received OAC therapy, PPV of the device was ≤ 20% or ≥ 50% of cases were diagnosed through routine care.	PPV value obtained from unpublished data – may not reflect the true accuracy of the SLECG device used during the PIAAF-Pharmacy study. No other diagnostic accuracy measures apart from PPV considered during the economic analysis – may not provide a valid reflection of the true economic value of AF screening due to false negative diagnoses which were not taken into account. Probabilities of clinical events derived from the general registry data and may not reflect those amongst the population with incidentally detected AF. Economic analysis did not appear to include the costs of SLECG interpretation by technicians (no automated algorithm), the follow-up appointments with GPs or

					specialists and the cost of inconclusive diagnoses.
Lowres *et al.* (2015) Australia	Qualitative study **Aim** To explore the experience of implementing an AF screening service from the pharmacist's perspective including the process of study implementation; perceived benefits; barriers and enablers; and challenges for future sustainability of AF screening within pharmacies.	Pharmacists participating in the SEARCH-AF screening initiative (n = 9). See Lowres *et al.* (2014) above.	Data collected during face-to-face or telephone-based individual semi-structured interviews (of a median 17-minute duration) facilitated by one of two researchers approximately two months after completing the SEARCH-AF study. Interviews were audio-recorded and transcribed verbatim by a professional transcription service. Transcriptions were initially coded and analysed by one researcher using the principles of grounded theory. Initial analyses were further interpreted by the team of three researchers until cohesive and conceptually clear themes were identified. These were discussed amongst all authors to reach a consensus on the principal themes.	**Acceptability** Pharmacists were positive about the overall role for AF screening in community pharmacies and were comfortable performing the screening. The benefits of offering screening in pharmacies in addition to traditional methods of screening (increases the reach). Overwhelmingly positive customer feedback. Customers engaged and comfortable with a pharmacist performing the screen. Many unaware pharmacies could offer such services. One pharmacist reported the lack of interest from their customers, mainly related to the expectation of the pharmacist's role. Both cardiologists and GPs were supportive of the pharmacy screening and appeared interested in the KMD technology. Negative feedback received from a minority of GPs who trivialised the screening. **Perceived benefits** Pharmacists valued the opportunity to learn and to apply learning in an educative role when building AF awareness in the community.	Lack of explicit information about the philosophical perspectives or epistemological positions, although interpretivism/constructivism could be implied from the use of grounded theory analysis. No direct feedback from service users or clinicians. No statement about the cultural/theoretical perspectives of researcher(s) involved in qualitative data collection and analysis. No acknowledgement of how such perspectives or other researcher-specific factors may potentially influence the data collection/analysis (no reflexivity statement).

				Providing screening improved customer relations, fostered enhanced customer care, increased the customer's confidence in the pharmacist and improved community awareness of pharmacy services. **Implementation** Customer's confidence regarding the pharmacist's ability to offer screening/clinical services integral to the recruitment success. Clear and simple explanations were needed to overcome the initial fear of being screened. Novelty of KMD technology acted as an incentive for customers to engage in screening. Customers valued the ability to see ECG in real time, which acted as an educational tool to discuss AF. Advertising of the new service required a layered approach: using promotional materials, staff directly approaching customers and utilising health promotion events (within pharmacy and in community locations). Managing workflow by far the greatest barrier to AF screening (additional pharmacy staff was needed during busy periods). Booking appointments may hinder the ability to offer screening to everyone. Flexible approach of pre-	

				booked and spontaneous appointments may be an option. Most pharmacists offered AF screening in combination with other health screening such as BP, cholesterol or blood sugar monitoring. This was more time- efficient and provided greater levels of satisfaction for both the pharmacist and customers. All pharmacists reported the KMD screening as quick, simple and easy. Initial familiarisation period was required to become proficient in using the KMD, especially if not comfortable with technology. Technical issues related to poor mobile phone reception or WiFi could slow down the process and act as barriers for recruitment. Access to a private counselling area was an enabler and added a sense of professionalism. **Sustainable future implementation** Requirement for appropriate remuneration/government funding to sustain future screening – a consistent theme. Charging customers for screening generally not feasible. Integrating AF screening within a CVD screening package or MedsChecks was	

				a common future vision, especially if the service was customer-paid. Reducing time burden on the pharmacist by upskilling pharmacy staff to engage customers, discuss the benefits of screening, and if trained, perform the initial screen before referring to pharmacist. Customers can self-complete the initial health questionnaire before undergoing the screening. Good communication/working relationship with GPs, and effective referral/follow-up processes emphasised.	
Sabater-Hernández *et al.* (2018) Australia	Qualitative study **Aim** To use a stakeholder co-design approach to develop a pharmacist-led community pharmacy service aimed at enhancing self-management	1) Potential service users aged > 65 with hypertension and/or AF recruited through existing networks and non-profit association that organises social activities for the elderly (n = 8; age 70-88 years; n = 3 for AF history; n = 5 for hypertension history (two had both); n = 4 for	A three-step co-design process using qualitative interviews facilitated by one researcher: 1) Face-to-face or telephone-based semi-structured individual interviews (unclear duration) and a focus group (2.5 hour-long) with service users to identify the key needs and concerns. 2) A focus group with mixed stakeholders to generate a preliminary model of the service (4.5 hour-long)	**Service users** Low awareness and knowledge of AF amongst those who had AF and non-existent among those who did not. Advertising materials designed to increase awareness and knowledge of AF considered to be counter-productive because of the negative language used and the lack of explanation for the term of 'atrial fibrillation. Those who had experienced frightening symptoms of AF more aware of their condition and prepared for its consequences. Most individuals had few AF symptoms and monitoring was not a priority. One	Lack of explicit information about the philosophical perspectives or epistemological positions, although interpretivism/constructivism could be implied from the use of thematic analysis. Risk of power-hierarchical relationships that may have prevented the less vocal individuals from expressing their opinions during a heterogenous multi-stakeholder focus group. Only one GP, one cardiologist and one nurse

	of AF (by promoting self-monitoring and screening).	focus group participants, n = 4 for individual interviews). 2) Mixed group of purposely selected stakeholders with a vested interest in the aimed community pharmacy service (n = 8; one service user from previous group; two community pharmacy owners/managers/service providers; one GP, cardiologist, heart failure nurse practitioner, research nurse with expertise in AF and a representative from the Australian Stroke	3) A focus group with community pharmacy owners and managers to explore the feasibility and appropriateness of the co-designed model (2.0-hours-long). All focus groups and interviews were facilitated by one researcher with experience in qualitative research. Interviews and focus groups were audio-taped and transcribed verbatim. Data was analysed by the same researcher with support of two other researchers using the Bazeley's framework of 'describe-compare-relate' to identify themes and intersections between the themes (a variation of thematic analysis). The JeMa2 model was used to organise the analysed data and build a theoretical model of the service.	participant with AF thought that having a monitoring device may help differentiate between emotional distress due to AF or other causes. Participants who did not have AF or hypertension expressed concerns about being over-serviced by self-monitoring. Participants were unconcerned by the possibility of AF being detected at home where a HCP was not immediately present to explain the findings. Widespread support for pharmacists to assist with the monitoring of AF. Pharmacist engagement in the management of AF must be in partnership with GPs. Important that participants' privacy was maintained and that information sharing between pharmacies and GPs must be conducted only with explicit permission. The fee for the service needs to be 'reasonable' and should vary according to individual level of government funded benefits. **Stakeholders and managers** Individuals aged ≥ 65 years with hypertension, with or without existing AF, and with or without a previous history of stroke should be the priority target group for screening. Service could	practitioner interviewed by the study – may not reflect the views of other non-pharmacist HCPs. The average duration of individual semi-structured interviews with service users not provided. No statement about the cultural/theoretical perspectives of researcher(s) involved in qualitative data collection and analysis. No acknowledgement of how such perspectives or other researcher-specific factors may potentially influence the data collection/analysis (no reflexivity statement).

		Foundation each). 3) Community pharmacy owners and managers purposely selected due to their previous experience in community pharmacy service delivery. (n = 4).		be rolled out to Aboriginal & Torres Strait Islander people as the second tier of implementation. Low awareness and knowledge of AF amongst high risk individuals – education a fundamental component of the service. Close attention to the language of educational materials – varying levels of health literacy amongst patients. Use different educational methods/techniques, e.g., pharmacists providing demonstrations on how to use the device, patient self-learning by taking information home and materials such as information sheets, websites, videos, podcast. Educational materials for patients should be endorsed by leading cardiovascular organisations. Importance of implementing reliable programmes that employ accurate devices (self-monitoring over 2-4 weeks). Concerns over reliability of current self-monitoring practices given the poor accuracy and performance of many mBPMs available on the market. Need for a confirmatory ECG. Since few patients felt a personal need/interest for AF screening it would be difficult to charge a fee and service may be uneconomic. Self-monitoring of AF/BP may be more valuable than sole in-pharmacy screening and might	

				facilitate the remuneration of the service. Patients could pay a fee for both renting the device and for professional advice. In-pharmacy consultations with patients, effective referrals to GPs and follow-up are of paramount importance to self-monitoring service. Doubts from pharmacy owners/managers regarding the success of follow-up consultations after the device is sold to customers (may not return). Communication methods would need to be formalised and agreed upon prior to the roll-out. Pharmacists anticipated low levels of success in communicating or collaborating with GPs due to misunderstandings regarding professional boundaries and the misinterpretation of the actions of pharmacists. Service must be provided by a pharmacist with appropriate qualification and should not be delegated to other staff. The need for a private consultation area to provide the service emphasised. Pharmacies need to be staffed by a sufficient number of pharmacists at any given time to continue the normal business. Regular visits to the pharmacy by a nurse practitioner to deliver	

				the service or facilitate coordination/communication may be an alternative (not supported by pharmacists).	

Appendix 5 Critical appraisal checklist for studies reporting prevalence data

Adapted from: JBI (2020). The items were scored 'yes' if the study met the defined criteria, 'no' if the study clearly did not meet the defined criteria and 'unclear' if insufficient information was provided by study authors. Abbreviations: $_{12L}$ECG – 12-lead electrocardiogram; AF – atrial fibrillation; ECG – electrocardiogram; $_{SL}$ECG – single-lead ECG.

No.	Criteria	Lowres *et al.* (2014)	Zaprutko *et al.* (2019)	Cunha *et al.* (2020)	Twigg *et al.* (2016)	Antoniou *et al.* (2017)	Bacchini *et al.* (2019)	Antoniou *et al.* (2019)	Anderson *et al.* (2020)	Da Costa *et al.* (2020)	Sandhu *et al.* (2016)
1	Was the sample frame appropriate to address the target population?	Yes (but single region)	Yes	Unclear (included younger individuals aged ≥ 40 years; single region)	Yes (but single region)	Unclear (included younger individuals aged ≥ 18 years)	Unclear (included younger individuals aged ≥ 50 years; single region)	Yes (but unclear if single or multiple regions involved)	Unclear (eligibility criteria not specified)	Unclear (included younger individuals aged ≥ 40 years)	Yes
2	Were study participants sampled in an appropriate way?	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)
3	Was the sample size adequate?	Yes	Unclear (sample size not estimated)	Unclear (sample size not estimated)	Unclear (sample size not estimated)	Unclear (sample size not estimated)	Unclear (sample size not estimated)	Unclear (sample size not estimated)	Unclear (sample size not estimated)	Unclear (sample size not estimated)	Yes
4	Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes	No (little demographic data provided)	Yes	Yes	Yes	Yes	Yes
5	Was the data analysis conducted with	Unclear (response	Unclear (response	Unclear (small	Unclear (response	Unclear (response	Unclear (response	Unclear (response	Unclear (response	Yes (but small sample	Unclear (response rate

	sufficient coverage of the identified sample?	rate not stated)	rate not stated)	sample size)	rate not stated	rate not stated)	rate not stated)	rate not stated)	rate not stated)	size in a nursing home)	not stated)
6	Were valid methods used for the identification of the condition?	Yes	Yes (but no 12LECG performed)	Yes	Yes	Yes (but unclear if AF confirmed by 12LECG)	No (did not specify if AF diagnoses confirmed by ECG)	Yes (but unclear if AF confirmed by 12LECG)	Yes (but no 12LECG performed)	Yes (but unclear if AF confirmed by SLECG and/or or 12LECG in all individuals)	Yes
7	Was the condition measured in a standard, reliable way for all participants?	No (12LECG not performed for all participants)	Yes	Yes	Unclear (did not state who conducted the tests; unclear if 12LECG performed for all individuals)	Yes	Unclear (did not state if and which individuals had diagnoses confirmed by ECG)	Unclear (did not state if all participants had both index tests)	Yes	No (some individuals had pulse palpation and some SLECG)	Yes
8	Was there appropriate statistical analysis?	Yes	Yes	Yes	Yes	Yes (albeit not specifically stated)	Yes	Yes (albeit not specifically stated)	Yes	Yes	Yes
9	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Yes (estimated sample size reached)	Unclear (response rate not stated)	Unclear (response rate not stated)	Unclear (response rate not stated)	Unclear (response rate not stated)	Unclear (response rate not stated)	Unclear (response rate not stated)	Unclear (response rate not stated)	Yes	Unclear (response rate not stated)

Appendix 6 Critical appraisal checklist for diagnostic test accuracy studies

Adapted from: JBI (2020). The items were scored 'yes' if the study met the defined criteria, 'no' if the study clearly did not meet the defined criteria and 'unclear' if insufficient information was provided by study authors. 'N/A' (Not applicable) was indicated where criteria proposed did not apply to a particular study. Abbreviations: $_{12L}$ECG – 12-lead electrocardiogram; AF – atrial fibrillation; $_{SL}$ECG – single-lead electrocardiogram.

No.	Criteria	Lowres *et al.* (2014)	Zaprutko *et al.* (2019)	Cunha *et al.* (2020)	Sandhu *et al.* (2016)
1	Was a consecutive or random sample of patients enrolled?	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)	Unclear (sampling method not stated)
2	Was a case control design avoided?	No (involved those with and without AF)	Yes	No (recall bias led to inclusion of those with known AF, but low impact due to automated $_{SL}$ECG testing)	No (involved those with and without AF)
3	Did the study avoid inappropriate exclusions?	Yes	Yes	Yes	Yes
4	Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear (blinding status not indicated)	Unclear (blinding status not indicated, but low impact due to use of automated $_{SL}$ECG testing)	Unclear (blinding status not indicated, but low impact due to use of automated $_{SL}$ECG testing)	Unclear (blinding status not indicated)
5	If a threshold was used, was it pre-specified?	N/A	N/A	N/A	N/A
6	Is the reference standard likely to correctly classify the target condition?	Yes	Yes (but not as likely as $_{12L}$ECG)	Yes	Yes
7	Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear (blinding status not indicated)	Unclear (blinding status not indicated)	Unclear (blinding status not indicated)	Unclear (blinding status not indicated)

8	Was there an appropriate interval between index test and reference standard?	Unclear (interval not stated for $_{SL}$ECG interpretation)	Yes	Unclear (interval not stated for $_{SL}$ECG interpretation)	Unclear (interval not stated for $_{SL}$ECG interpretation)
9	Did all patients receive the same reference standard?	No	Yes	No (only those with suspected abnormalities and those in outpatient clinic)	Yes
10	Were all patients included in the analysis?	Yes	Yes	Yes	Yes

Appendix 7 Critical appraisal checklist for economic evaluations

Adapted from: JBI (2020). The items were scored 'yes' if the study met the defined criteria, 'no' if the study clearly did not meet the defined criteria and 'unclear' if insufficient information was provided by study authors. Abbreviations: OAC – oral anticoagulant; $_{SL}$ECG – single-lead electrocardiogram.

No.	Criteria	Lowres et al. (2014)	Tarride *et al.* (2017)
1	Is there a well-defined question?	Yes	Yes
2	Is there comprehensive description of alternatives?	Yes	Yes
3	Are all important and relevant costs and outcomes for each alternative identified?	Yes	Yes
4	Has clinical effectiveness been established?	Yes	No (questionable data used to derive diagnostic accuracy and probabilities of clinical events)
5	Are costs and outcomes measured accurately?	No (no cost of OAC-related bleeding or inconclusive diagnoses)	No (no cost of $_{SL}$ECG interpretation, healthcare appointments or inconclusive diagnoses)
6	Are costs and outcomes valued credibly?	Yes	Yes
7	Are costs and outcomes adjusted for differential timing?	Yes	Yes
8	Is there an incremental analysis of costs and consequences?	Yes	Yes
9	Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?	Yes	Yes
10	Do study results include all issues of concern to users?	No (probability of cost-effectiveness not stated)	Yes
11	Are the results generalizable to the setting of interest in the review?	Unclear (see point 5 above)	Unclear (see points 4 and 5 above).

Appendix 8 Critical appraisal checklist for qualitative research

Adapted from: JBI (2020). The items were scored 'yes' if the study met the defined criteria, 'no' if the study clearly did not meet the defined criteria and 'unclear' if insufficient information was provided by study authors.

No.	Criteria	Lowres *et al.* (2015)	Sabater-Hernández et al. (2018)	Da Costa *et al.* (2020)
1	Is there congruity between the stated philosophical perspective and the research methodology?	Yes (although philosophical perspectives or epistemological positions not explicitly stated)	Yes (although philosophical perspectives or epistemological positions not explicitly stated)	Yes (although philosophical perspectives or epistemological positions not explicitly stated)
2	Is there congruity between the research methodology and the research question or objectives?	Yes	Yes	Yes
3	Is there congruity between the research methodology and the methods used to collect data?	Yes	Yes	Yes (the method of individual semi-structured interviews not explicitly stated)
4	Is there congruity between the research methodology and the representation and analysis of data?	Yes	Yes	Yes
5	Is there congruity between the research methodology and the interpretation of results?	Yes	Yes	Yes
6	Is there a statement locating the researcher culturally or theoretically?	No	No	No
7	Is the influence of the researcher on the research, and vice- versa, addressed?	No	No	No
8	Are participants, and their voices, adequately represented?	Yes (but no direct feedback from service users or clinicians)	Unclear (may have been influenced by hierarchical	Yes (but no direct feedback from service users or clinicians)

			relationships within a heterogenous focus group)	
9	Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body?	Yes	Yes	Yes
10	Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data?	Yes	Yes	Yes

Appendix 9 Theoretical Domains Framework used during the qualitative studies of this enquiry

Adapted from: Cane et al. (2012); Atkins et al. (2017).

Knowledge	
• Knowledge (of condition/scientific rationale) • Procedural knowledge • Knowledge of task environment	
Skills	
• Skills • Skills development • Competence	• Interpersonal skills • Practice • Skill assessment
Social/professional role and identity	
• Professional identity • Professional role • Social identity • Identity	• Professional boundaries • Professional confidence • Group identity • Leadership • Organisational commitment
Beliefs about capabilities	
• Self-confidence • Perceived competence • Self-efficacy • Perceived behavioural control	• Beliefs • Self-esteem • Empowerment • Professional confidence
Optimism	
• Optimism • Pessimism	• Unrealistic optimism • Identity
Beliefs about consequences	
• Beliefs • Outcome expectancies • Characteristics of outcome expectancies	• Anticipated regret • Consequents
Reinforcement	
• Rewards • Incentives • Punishment • Consequents	• Reinforcement • Contingencies • Sanctions

Intentions	
• Stability of intentions • Stages of change model	• Transtheoretical model and stages of change
Goals	
• Goals (distal/proximal) • Goal priority • Goal/target setting	• Goals (autonomous/controlled) • Action planning • Implementation intention
Memory, attention and decision processes	
• Memory • Attention • Attention control	• Decision making • Cognitive overload/tiredness
Environmental context and resources	
• Environmental stressors • Resources/material resources • Organisational culture/climate	• Salient events/critical incidents • Person x environment interaction • Barriers and facilitators
Social influences	
• Social pressure • Social norms • Group conformity • Social comparisons • Group norms • Social support	• Power • Intergroup conflict • Alienation • Group identity • Modelling
Emotion	
• Fear • Anxiety • Affect • Stress	• Depression • Positive/negative affect • Burn-out
Behavioural regulation	
• Self-monitoring • Breaking habit	• Action planning

Appendix 10 Atrial Fibrillation Association's data collection sheet

AF Association®
Unit 6B
Essex House
Cromwell Business Park
Chipping Norton
OX7 5SR
✆+44 (0) 1789 867502
@ info@afa.org.uk
➚www.afa.org.uk
➚www.afa-international.org

Providing information, support and access to established, new or innovative treatments for atrial fibrillation

DATA COLLECTION SHEET

CODE OF DATA COLLECTION SITE				
NUMBER OF PATIENT (SEQUENTIAL)				
TO BE FILLED IN BY PATIENT				
AGE				
GENDER	Male		Female	
DO YOU HAVE ANY OF THE FOLLOWING SYMPTOMS?	YES	NO	DON'T KNOW	
Palpitations				
Shortness of breath				
Tiredness				
Chest pain				
Dizziness				
Irregular pulse / heart rhythm				
DO YOU HAVE ANY OF THE FOLLOWING CONDITIONS?			YES /NO /DON'T KNOW	
High blood pressure				
Heart muscle disease (also known as failure)				
Diabetes				
Peripheral arterial disease (painful muscle cramping in the hips, thighs or calves when walking, climbing stairs or exercising)				
Have you ever had any of the following?			YES /NO /DON'T KNOW	
Stroke or transient ischaemic attack				
Clot in the body (not the veins of the lungs)				
Heart attack				
CURRENT THERAPY (TO BE FILLED IN BY PHARMACIST): PLEASE INDICATE ONLY ANTIPLATELET AND ANTICOAGULANT THERAPIES				
MEDICINE				
TO BE FILLED IN BY PHARMACIST				
Manual pulse check	**Heart rhythm (regular/irregular):** **Heart rate (bpm):**			
Do you have AliveCor Kardia (or equivalent)	Yes(next) /No (end)			
AliveCor Kardia result:	No irregularity ☐ Atrial Fibrillation ☐ Unclassified trace☐			

Appendix 11 Clinical pharmacist consent form for the Pharmacists Detecting Atrial Fibrillation study

Clinical Pharmacist Consent Form

(one copy to be retained by the participant and one by the researcher)

Title of Study: Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Please **initial** each box as appropriate	Yes
I confirm that I have read and understood the protocol for the named project and I have had the opportunity to ask questions which have been answered to my satisfaction.	
I confirm that I will attend all of the necessary training and education sessions in pulse palpation and electrocardiogram recording, arranged by the University of Kent.	
I agree that all anonymised-data collected during the pilot can be disseminated through normal scientific forums (e.g. peer-reviewed publications and conferences).	
I understand that I am free to withdraw from the study at any time. If I decide to withdraw, any data collected up to the point of withdrawal will be retained.	
I agree to be contacted to take part in future research (i.e. participation in a focus group) about this research.	
I agree to participate in this atrial fibrillation screening study.	

Clinical Pharmacists Name (Block Capitals):

Clinical Pharmacists Signature: ***Date:***

To be completed by the University of Kent research team.

I the undersigned have taken the time to fully explain the nature and the purpose of this study and provided them with a detailed protocol. I have invited them to ask questions on any aspect of the study that concerned them.

Name (Block Capitals):

Signature: ***Date:***

University of Kent

Appendix 12 Promotional poster for the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Research Study

PDAF

Pharmacists Detecting Atrial Fibrillation

If you are aged 65 years or over you may be eligible for a **free** pulse check with the clinical Pharmacist between September and December 2017 with your annual Flu vaccination.

Your surgery is offering you the opportunity to have your pulse tested, by the **clinical Pharmacist** as part of a study with researchers at the **University of Kent**, to find the best way to screen people at risk of developing **Atrial Fibrillation**.

What is Atrial Fibrillation (AF)?

- AF is an irregular heart rhythm which means the heart has to work harder.

What are the Risks of having AF?

- Increases the risk of **stroke** and **heart failure**

Why should you get your pulse checked?

- A simple pulse check could help detect and **abnormal heart rhythm** or **rate**.

What's involved? A clinical Pharmacist will measure your pulse and electrical activity of your heart using a non-invasive, painless **single-lead electrocardiogram (ECG)** as pictured here.

What do I have to do? If you would like to have your pulse tested you can **book an appointment** at reception. They will tell you if you are eligible to participate. **Or for more information:** Please pick up a leaflet from your surgery or visit www.msp.ac.uk/afstudy or scan the QR code.

University of Kent

Appendix 13 Promotional leaflet for the Pharmacists Detecting Atrial Fibrillation Study

Atrial Fibrillation Research Study

PDAF

Pharmacists Detecting Atrial Fibrillation

If you are aged 65 years or over you may be eligible for a free pulse check with the clinical Pharmacist between September and December 2017 with your annual Flu vaccination.

Your surgery is working with researchers at the University of Kent to find the best way to screen and diagnose patients at-risk of developing atrial fibrillation by using a simple pulse check and a mobile heart monitoring device.

What is Atrial Fibrillation (AF)?

- AF is an irregular heart rhythm which means the heart has to work harder.

What are the Risks of having AF?

- Increases the risk of stroke and heart failure.

Why should you have your pulse checked?

- A simple pulse check could detect an abnormal heart rhythm or rate and save your life! If detected and manage appropriately, AF is not considered to be a life threatening condition.

What happens?

- A clinical pharmacist will take your pulse and check the activity of the heart using a non-invasive and painless mobile heart monitor, as shown below. The appointment will last approximately 20 minutes, and you will be given provisional results immediately after. All data recorded will then be verified by a specialist Cardiologist within 72 hrs. Verified results of the test will be posted to you and any follow-up appointments arranged.

University of Kent

PDAF

Pharmacists Detecting Atrial Fibrillation

Who is eligible?

- Anyone aged 65 years or older, who does not have a pacemaker and is eligible for the Flu vaccination.

How do I find out more?

- Pick up an information leaflet from reception or visit our webpage [insert web link] or scan the QR code at the bottom of the page.

How do I get involved?

- You can book your appointment at reception, at the same time as your Flu vaccine. Or enquire on the day of your Flu vaccination.

- You will be given an information pack about the study and asked to provide written consent.

Get involved and get your pulse checked!

Mobile Heart Monitor device

University of Kent

Appendix 14 Homepage contents of the Pharmacists Detecting Atrial Fibrillation study website

Atrial Fibrillation Research Study

PDAF

Pharmacists Detecting Atrial Fibrillation

If you are aged 65 years or over you may be eligible for a free pulse check with the clinical Pharmacist between September and December 2017 with your annual Flu vaccination.

Your surgery is offering you the opportunity to have your pulse tested, by the clinical Pharmacist as part of a study with researchers at the University of Kent [MSoP research webpage], to find the best way to screen people at risk of developing Atrial Fibrillation.

What is Atrial Fibrillation (AF)?

- AF is an irregular heart rhythm which means the heart has to work harder. Left untreated you have an increased risk of stroke and heart failure. If you would like more information please click the link [PIL]. Or contact us directly [contact details].

Why should you get your pulse checked?

- A simple pulse check could help detect an abnormal heart rhythm or rate.

What's involved? A clinical Pharmacist will measure your pulse and electrical activity of your heart using a non-invasive, painless single-lead electrocardiogram (ECG) as pictured here.

How can I get involved? First check that you are eligible to participate, by clicking on the link [eligibility criteria]. If you have answered yes to all the questions then you can book an appointment at your surgery for a pulse check with the Pharmacist. Alternatively please contact us [contact details] directly and we can assist you in making an appointment.

THANK YOU FOR TAKING PART

University of Kent

Appendix 15 Text message invitation for the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Test Message Invite

In addition to your Flu vaccine you can also have your pulse tested. For more information go to www.msp.ac.uk/afstudy or pick up a leaflet at your surgery or call 01634 888909.

Appendix 16 Eligibility document for the Pharmacists Detecting Atrial Fibrillation study in general practice

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Eligibility Self-Confirmation Form

Please read through the criteria listed below to see if you are eligible to participate in the study. If you AGREE with each statement, then you are eligible to make an appointment with the clinical Pharmacist for a pulse check.

I am older than 65 years	Agree	☐
	Disagree	☐
I do not have a pacemaker	Agree	☐
	Disagree	☐
I do not have a terminal illness	Agree	☐
	Disagree	☐
I understand what this study is about and what I am being asked to do	Agree	☐
	Disagree	☐

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Appendix 17 Participant information leaflet for the Pharmacists Detecting Atrial Fibrillation study in general practice

What is Atrial Fibrillation?

Atrial fibrillation or AF is a common heart rhythm disorder that occurs when the electrical activity in the heart becomes chaotic. The result of this is often an **irregular** and sometimes very **fast pulse**. AF is an **age-related** condition, the older you get, the more likely you are to develop it. If you develop AF it means that your heart is no longer working properly and left untreated it can lead to serious complications such as **heart failure** and **stroke**.

Why should we screen for AF?

It is estimated that approximately 500,000 people in the UK are living with undiagnosed AF. Many people with AF have no obvious symptoms. AF represents a significant and growing burden on the NHS, with AF-related illness costing the NHS an estimated **£2.2 billion** each year. Early detection of AF and treatment with **anticoagulants** has been shown to significantly reduce the incidence of stroke and death.

What will the Research Study involve?

We are asking all eligible patients over the age of 65 years who are attending the surgery for a Flu vaccination between September and December 2017 to also consent to having their **pulse checked** and a **single-lead electrocardiogram (ECG)** taken by a clinical pharmacist. This process should take no more than 10-15 minutes, and is a painless and non-invasive procedure. All ECGs will be verified by a **specialist Cardiologist** within 72 hrs.

ECG test.

What is the purpose of the study?

GPs and clinical pharmacists from your surgery are working together with academics from the **University of Kent** to find the best way of screening patients routinely, who are at high-risk of developing AF.

Who is eligible to take part?

All patients **over the age of 65** years, who **do not** have a pacemaker and who are eligible to receive a **Flu vaccination** have been invited to take part in this study.

What are the benefits of taking part?

You will have your pulse checked to see that it is normal. You will also be actively helping in the development of this study and your views will enable us to determine how best to implement, deliver and measure future screening programmes for AF.

I want to take part, what happens next?

When you book your Flu vaccination, you can also ask to have your pulse checked with the pharmacist. Or you can enrol at any Flu vaccine clinic, where a pharmacist is present. Before the pulse check you will be asked to confirm your **eligibility** and sign a **consent form**.

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If I decide not to take part, will this affect my future care?

You are not obliged to participate. Please be assured that all medical care required when someone is diagnosed with AF will be available, whether you decide to take part in the study or not.

What will happen if I withdraw from the study?

You are **free to withdraw** from the study at any point, without giving a reason and this will not affect any future medical care.

What will happen if I am diagnosed with AF?

All patients that are diagnosed with AF will receive the **necessary medical care** that is appropriate to your condition.

Will any data collected about me be kept confidential?

All data collected as part of the study will be kept **strictly confidential** and stored securely for a maximum of 5 years. If you provide any personal identifiable information (e.g. contact details) to participate in the focus group, this information (other than the signed consent forms) will be destroyed 1 month after the focus group. Any data which leaves the surgery/hospital/university will not identify individuals. All other data will be handled in accordance with the Data Protection Act 1988.

Will it cost me anything?

This service will be completely **free of charge**.

What happens afterwards?

Immediately after being screened, your clinical pharmacist will ask you to fill in a short questionnaire about the experience. You will also be given an information pack to take home that contains additional information about AF and an invitation to take part in a focus group in the New Year, 2018. All unidentifiable data collected from the study will be analysed and written into a full report that will be published.

Who is funding the study?

This study is being jointly funded by the University of Kent and by a medical education grant from the pharmaceutical company, Bayer UK. Bayer have no involvement in the design of this study and no information about you will be disclosed to them.

Who can I contact for further information?

Further information about the study can be obtained from our webpage: [insert webpage address] or by email: s.a.corlett@kent.ac.uk or by phone: 01634 888909 by post: Medway School of Pharmacy, Anson Building, Central Avenue, Chatham, ME4 4TB.

Who can I contact if I have concerns, worries or complaints?

If you would like to find out more general information about taking part in research studies then please contact by email: t.thomas@kent.ac.uk or by phone or post as listed above. If you have complaints about the study, please contact: g.lall@kent.ac.uk or by phone as listed above.

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Appendix 18 Participant consent form for the Pharmacists Detecting Atrial Fibrillation study

Patient Consent Form

(one copy to be retained by the participant and one by the researcher)

Title of Study: Atrial Fibrillation screening in general practice by Clinical Pharmacists

Surgery Name*:*

Patient ID Number:

Please **initial** each box as appropriate	Yes
I confirm that I have read and understand the **patient information leaflet** for the above project and I have had the opportunity to ask questions which have been answered to my satisfaction.	Initial Here
I have read the **eligibility criteria** and can **confirm** that I am eligible to participate in this study.	Initial Here
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. If I decide to withdraw, any data collected up to the point of withdrawal will be retained.	Initial Here
I understand that relevant sections of my medical notes and information collected during this research study may be looked at by individuals from the University of Kent, for the purpose of this research and that such data will be anonymised and kept private and confidential by the research team. I give permission for these individuals to have access to my records (or to parts taken from by practice staff).	Initial Here
I agree to be contacted to take part in future research e.g. optional participation in a focus group, as detailed in the patient information leaflet.	Initial Here
I agree to participate in the atrial fibrillation screening study.	Initial Here

Participant Name (Block Capitals):

Participant's Signature: ***Date:***

To be completed by the Clinical Pharmacist.

I the undersigned have taken the time to fully explain to the above patient the nature and the purpose of this study in a manner that they could understand. I have invited them to ask questions on any aspect of the study that concerned them.

Name (Block Capitals):

Signature: ***Date:***

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Appendix 19 Demographic form for the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

About You (Demographic Data)

Patient ID Number:

Practice:

Date:

What is your gender?

- Male ☐
- Female ☐

What is your age? _____

What is your ethnicity?

- White:British ☐
- White:Irish ☐
- Black/Black British/African ☐
- Black/Black British/Caribbean ☐
- Asian/Asian British/Indian ☐
- Asian/Asian British/Pakistani ☐
- Asian/Asian British/Bangladeshi ☐
- Chinese ☐
- Other ☐

Please specify: _____

Do you smoke?

- Yes ☐
- No ☐

Do you drink alcohol? (1 unit = small glass of wine/half pint of beer)

- Yes ☐ Units/Week ☐
- No ☐

What is your height? _____

What is your weight? _____

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Appendix 20 Pulse and electrocardiogram recording form for the Pharmacists Detecting Atrial Fibrillation study

Pulse & ECG Recording Sheet

Surgery name:
Pharmacist Name:

Patient ID Number:			
Date of Visit:	(dd/mm/yyyy)		
Time of Visit:			
Duration of Visit:			
Pulse Rate (bpm):	(beats per minute)		
Pulse Rhythm (tick as appropriate):	(Regular)	(Irregular)	(unclassified)
Tick as appropriate	**YES**	**NO**	
Do they have a hearing aid?	(Switch off)		
Quality of the ECG :	☐ **Excellent**	☐ **Acceptable**	
	☐ **Poor**	☐ **Unreadable**	
Number of ECG's Recorded:			

Tick as appropriate	**YES**	**NO**	**Comments**
Were you able to interpret the ECG?			
Is there a P wave?			
Is the P wave followed by a QRS complex?			
Is the interval between QRS complexes regular?			

Tick as appropriate	**Pharmacist**	**Kardia**	**Comments**
ECG is normal?			
ECG suggests AF?			
ECG is unclassified?			
ECG is unreadable?			

Letter given to participant? **Normal** ☐ **AF** ☐ **unclassified** ☐

Appendix 21 Letter of results indicating Normal Sinus Rhythm during the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Patient Results Letter – Definite Normal

Patient ID Number:

Surgery:

Surgery Address:

Date:

Dear

Thank you for taking part in this study.

Your pulse check and ECG tracing suggest that your heart rhythm is normal and no further action is needed.

The ECG tracing will now be verified by a cardiologist and if there are any unexpected results, both you and your GP will be informed.

Yours sincerely

University of Kent

Appendix 22 Letter of results indicating Possible Atrial Fibrillation during the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Patient Results Letter – Possible AF

Patient ID Number:

Surgery:

Surgery Address:

Date:

Dear

Thank you for taking part in this feasibility study with the clinical Pharmacist.

Your pulse check and ECG tracing suggest that your heart rhythm is irregular and that you have a condition called atrial fibrillation (AF).

Although this does not necessarily cause you any symptoms at this time, it is important that further investigations and treatment appropriate to the condition are pursued.

The ECG tracing will now be verified by a specialist Cardiologist and both you and your GP will be informed of the outcome. You will be contacted by your GP within the next 1-2 weeks.

We will provide you with a booklet from the British Heart Foundation giving you more details about this condition.

Yours sincerely

University of Kent

Appendix 23 Letter of results indicating Unclassified or Unreadable diagnoses during the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Patient Results Letter – Unclassified/Unreadable

Patient ID Number:

Surgery:

Surgery Address:

Date:

Dear

Thank you for taking part in this study.

The Pharmacist checking your pulse and ECG tracing could not come to a conclusion regarding the heart rhythm as the ECG quality was poor.

This does not necessarily mean that anything is wrong, just that the equipment has produced a poor quality trace which is difficult to read.

The ECG tracing will now be sent to the Cardiologist for review and both you and your GP will be informed of the outcome.

If the ECG shows a normal rhythm, no further action is needed. If the ECG shows an abnormal rhythm or still cannot be classified, a conventional 12-lead ECG and any further investigations will be offered by your GP.

Yours sincerely

University of Kent

Appendix 24 Participant feedback questionnaire for the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Patient Questionnaire

Please complete this questionnaire to tell us about your appointment with the clinical Pharmacist today for a **pulse check and ECG**.

Your feedback will enable us to identify areas that may need improvement. Your opinions are therefore very valuable.

There are no right or wrong answers. We are interested in your honest views.

By taking part you are giving your consent for your answers to be used as described in the patient information leaflet, that you received before having your appointment. It is important for you to know that your Practice will not know whether you have participated in the questionnaire or not, and that taking part will not affect your future care in any way.

For all queries regarding this study, please do not hesitate to contact:

Research Lead:

Dr Sarah Corlett

Tel: 01634 888909

Email: S.A.Corlett@kent.ac.uk

Instructions: Please answer all the questions on the following pages. Please tick or mark the box that best reflects your level of agreement. Please **indicate one response only** for each statement.

We think that it will take you about **5 minutes** to complete this questionnaire.

Thank you

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Practice Name:	
Date of Visit:	_____ [dd/mm/yyyy]

1. Your GP practice was part of a screening study that supports the early detection and diagnosis of atrial fibrillation. From your experience of it, how important was the screening for you? ☐ **Very Important** ☐ **Important** ☐ **Not Important**

2. Were you aware of this condition before you were screened? ☐ **Aware** ☐ **Not Aware**

3. Were you aware of any of the health risks associated with this condition, before you were screened? ☐ **Aware** ☐ **Not Aware**

4. How satisfied were you with the information provided before the appointment? ☐ **Very Satisfied** ☐ **Satisfied** ☐ **Dissatisfied** ☐ **Very Dissatisfied**

5. Did the Pharmacist clearly explain what was involved by having your pulse tested? ☐ **Yes** ☐ **No**

6. Did the Pharmacist clearly explain what is involved in having an ECG? ☐ **Yes** ☐ **No**

7. Afterwards did the Pharmacist clearly explain the results of the test to you? ☐ **Yes** ☐ **No**

8. How satisfied were you with the information provided after the appointment? ☐ **Very Satisfied** ☐ **Satisfied** ☐ **Dissatisfied** ☐ **Very Dissatisfied**

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9. Please rate how well you thought the Pharmacist carried out the tests:

☐ **Very Good** ☐ **Good** ☐ **Poor** ☐ **Very Poor**

10. Did the Pharmacist make you feel at ease? ☐ **Yes** ☐ **No**

11. How satisfied were you with the length of the appointment?

☐ **Very Satisfied** ☐ **Satisfied** ☐ **Dissatisfied** ☐ **Very Dissatisfied**

12. Overall how satisfied were you with the service that you received?

☐ **Very Satisfied** ☐ **Satisfied** ☐ **Dissatisfied** ☐ **Very Dissatisfied**

13. If the test was offered to you again next year, would you have it done?

☐ **Yes** ☐ **No**

14. Was there anything you particularly **LIKED** about the service?

☐ **Yes** ☐ **No**

If you particularly liked something about the service please tell us what it was and what was good about this?

15. Was there anything that you particularly **DISLIKED** about the service?

☐ **Yes** ☐ **No**

If you particularly disliked something, please tell us about this.

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16. Would you be happy to see the Pharmacist for **other screening tests** in the future?

☐ **Yes** ☐ **No**

What other screening tests would you like to receive from a Pharmacist?

17. Please add any further comments that may help us to **improve** this proposed AF screening strategy.

Further comments:

Thank you for taking the time to complete this questionnaire.

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Appendix 25 Enhanced demographic and follow-up form for the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Screen Positive Enhanced Demographics Form

Patient ID Number:
Practice:
Date:

Gender	☐ Male	☐ Female	
Weight (kg)	**Height (m)**	**BMI (kg/m²)**	
Blood Pressure:	Systolic:	Diastolic:	
Smoking Status	☐ Smoker	☐ Former Smoker	☐ Non- Smoker
Alcohol Use	☐ Yes	☐ No	
If yes	☐ <14 units/week	☐ ≥14 units/week	☐ ≥21 units/week

Medical History	☐ Hypertension	☐ Diabetes	☐ Stroke Ischaemic
	☐ TIA	☐ Previous CVD_MI/CCABG	☐ Previous History A Fib
	☐ PVD	☐ Intercranial Bleed	☐ Heart Failure
	☐ Thyroid Disease	☐ Renal Disease	

CHA_2DS_2VASc Score	
HAS-BLED Score	

Existing Medication History	☐ ACE	☐ Anti-arrthymic	☐ ARB's	☐ Betablocker
	☐ Calcium Channel Blocker	☐ Cholesterol Lowering Agents	☐ Digitalis Preparations	☐ Diuretics
	☐ Oral Anti-Thromb Agent	☐ Thyroid Replacement Therapy	☐ HRT	☐ Other

INVESTIGATIONS:

Echo	☐ Yes	☐ No	
Echo type	☐ Practice Based Echo	☐ Community Based Echo	☐ Hospital Based Echo
Date of Echo			
Echo Result			

Lone/Idopathic AF		☐ Yes	☐ No
If no, select	**Thyrotoxicosis**	☐ Yes	☐ No
	CAD	☐ Yes	☐ No
	Valvular Heart Disease	☐ Yes	☐ No
	Alcohol Intoxication	☐ Yes	☐ No
	Infection	☐ Yes	☐ No
	Other	☐ Yes	☐ No

Anticoagulation Initiated in Practice	☐ Yes	☐ No	
If yes, select	☐ Warfarin	☐ Dabigatran	☐ Rivaroxaban
	☐ Apixaban	☐ Aspirin	☐ Others
If No, select	☐ Not prescribed at this practice	☐ History of major bleeding	☐ Severe Ilness
	☐ Compliance	☐ Patient Refused anticoagulation	☐ Alcohol excess
	☐ History of falls	☐ Extreme Fragility	☐ Liver disease
	☐ Kidney Disease	☐ Other	

Other Medications	☐ ACE	☐ Anti-arrthymic	☐ ARB's	☐ Betablocker
	☐ Calcium Channel Blocker	☐ Cholesterol Lowering Agents	☐ Digitalis Preparations	☐ Diuretics
	☐ Oral Anti-Thromb Agent	☐ Thyroid Replacement Therapy		

Appendix 26 Pharmacist study feedback questionnaire for the Pharmacists Detecting Atrial Fibrillation study

medway school of pharmacy

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Pharmacist Feedback Form

We would be grateful if you would complete this questionnaire about your experience providing the atrial fibrillation screening service. Feedback from this survey will enable us to identify areas that may need improvement. Your opinions are therefore very valuable.

Please answer all the questions below. There are no right or wrong answers.

Please rate the following:

1. Your knowledge on atrial fibrillation and screening **before** this experience

	Very poor		Poor		Fair		Good		Very good

2. Your knowledge on atrial fibrillation and screening **after** this experience

	Very poor		Poor		Fair		Good		Very good

3. Accessing information, advice and resources

	Very poor		Poor		Fair		Good		Very good

4. The equipment used for the screening

	Very poor		Poor		Fair		Good		Very good

5. The overall experience

	Very poor		Poor		Fair		Good		Very good

On a scale of 1 to 5, please rate the following
(1= not very important and 5 = very important)

6. The roe of clinical pharmacists in general practice

	1 Not very important		2		3		4		5 Very important

7. The role of clinical pharmacists in screening and detecting atrial fibrillation

	1 Not very important		2		3		4		5 Very important

Please rate the following:

8. The training you were provided with

	Very dissatisfied		Dissatisfied		Neutral		Satisfied		Very satisfied

9. Support from the research team

	Very dissatisfied		Dissatisfied		Neutral		Satisfied		Very satisfied

10. Support from your general practitioner/ doctor

	Very dissatisfied		Dissatisfied		Neutral		Satisfied		Very satisfied

11. Support interpreting results

	Very dissatisfied		Dissatisfied		Neutral		Satisfied		Very satisfied

12. Do you think clinical pharmacists are well equipped with the knowledge and resources to screen and detect for atrial fibrillation?

Yes ☐
No ☐

Please specify:

_____
_____

13. Was there anything you particularly **LIKED** about the service?

Yes ☐
No ☐

If so please specify:

_____
_____

14. Was there anything you particularly **DISLIKED** about the service?

Yes ☐
No ☐

If so please specify:

_____
_____

Please add any further comments:

_____
_____
_____

About you

What is your **gender**?

Male	
Female	

What is your **age**? _____

What is your **ethnicity**?

White: British	
White: Irish	
Black/ Black British: African	
Black/ Black British: Caribbean	
Asian/ Asian British: Indian	
Asian/ Asian British: Pakistani	
Asian/ Asian British: Bangladeshi	
Chinese	
Other	

Please Specify: _____

How many years have you been a **qualified pharmacist**? _____ years

How many years have you worked as a **clinical pharmacist** in general practice? _____ years

Appendix 27 Pharmacist training evaluation questionnaire for the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Clinical Pharmacist Training Evaluation Form

We would appreciate if you could take the time to complete this course evaluation form. This will help us gain information which will help us with our quality assurances and continuous development and improvement. Your opinions are therefore very valuable.

Instructions: Please answer all the questions on the following pages. Please rate the sessions by ticking the box that best represents your view, on a scale of 1 to 5. Please add any specific comments in the boxes below each section: include things that you particularly enjoyed or found informative, things you felt could be improved/added or omitted.

1	=	Very Poor (irrelevant)
2	=	Poor (unhelpful)
3	=	OK (fairly useful)
4	=	Good (useful)
5	=	Excellent (very useful)

We think that it will take you about **5 minutes** to complete this questionnaire.

Thank you

		1	2	3	4	5
1	**Introduction to the AF study**	Very Poor				Excellent
Comments:						
		1	2	3	4	5
2	**AF presentation Signs and Symptoms, Differential Diagnosis**	Very Poor				Excellent
Comments:						
		1	2	3	4	5
3	**Clinical assessment – pulse palpation**	Very Poor				Excellent
Comments:						
		1	2	3	4	5
4	**Clinical assessment – ECG**	Very Poor				Excellent
Comments:						

		1	2	3	4	5
5	**Study Protocol:** Study documentation, Informed Consent, Confidentiality and safe guarding of patient data	Very Poor				Excellent
Comments:						
		1	2	3	4	5
6	**Optimising the Consultation: (Consultation skills)**	Very Poor				Excellent
Comments:						
		1	2	3	4	5
7	**Preparing for the study: Competency log/screening in practice**	Very Poor				Excellent
Comments:						
		1	2	3	4	5
8	**Reflection:**	Very Poor				Excellent
General comments about the training sessions, including guided materials, organisation, administration, refreshment etc.						

Thank you for taking the time to complete this questionnaire.

Appendix 28 General Practitioner feedback questionnaire for the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

GP Feedback Form

The purpose of this questionnaire is to obtain your views on the Atrial Fibrillation Screening Pilot study that your practice recently participated in.

Please complete all questions as fully as you can by ticking ☑ the appropriate box or by writing your answer in the space provided. The questions should be based on your own experience and views of the screening study rather than the overall view of the practice. There are no right or wrong answers.

Feedback from this survey will enable us to identify areas that may need improvement. Your opinions are therefore very valuable.

More information about the study is available from: www.msp.ac.uk/afstudy

By taking part you are giving your consent for your anonymised answers to be used in future reports and publications.

For all queries regarding this study, please do not hesitate to contact:

Research Lead:

Dr Sarah Corlett

Tel: 01634 888909

Email: S.A.Corlett@kent.ac.uk

We think that it will take you about **5 minutes** to complete this questionnaire.

Thank you

Your GP practice was part of a screening study that supports the early detection and diagnosis of atrial fibrillation (AF).

1. How important is it to screen patients, older than 65 years, for AF in primary care?

☐ **Very Important** ☐ **Important**
☐ **Not Important**

2a. Does your surgery have a 12-Lead ECG? ☐ **Yes** ☐ **No**

If Yes, please answer 2b and 2c below. If No, go to question 3

2b. Who would normally perform the 12-Lead ECG at your practice?

☐ **GP** ☐ **Nurse** ☐ **Nurse Practitioner** ☐ **Other HCP**

If 'other HCP' please indicate their profession

c

2c. Which healthcare professional at your practice normally makes the decision on whether a 12-Lead ECG shows AF?

☐ **GP** ☐ **Nurse** ☐ **Nurse Practitioner** ☐ **Other HCP**

If 'other HCP' please indicate their profession

3. How would you rate the AF screening service provided within this study?

☐ **Excellent** ☐ **Good** ☐ **Fair** ☐ **Poor**

4. How do you think the service has been received by patients?

☐ **Very well** ☐ **Well**
☐ **Okay** ☐ **Not well**

5. How do you think the service has been received by staff at the practice?

☐ **Very well** ☐ **Well**

☐ **Okay** ☐ **Not well**

6. Was there anything you particularly **LIKED** about the screening service?

☐ **Yes** ☐ **No**

If you particularly liked something about the service please tell us what it was and what was good about this?

7. Was there anything that you particularly **DISLIKED** about the service?

☐ **Yes** ☐ **No**

If you particularly disliked something, please tell us about this.

8. Would your practice employ Pharmacists to provide this service in the future?

☐ **Yes** ☐ **Possibly** ☐ **No**

Please tell us why?

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9. Would you commission Pharmacists to perform **other screening tests** in the future?

☐ **Yes** ☐ **Possibly** ☐ **No**

If Yes, please list those screening tests that you think would be suitable?

10. Would you want this screening service to be run again next year, in your practice?

☐ **Yes** ☐ **No**

11. On a scale of 1-10, where 1 is not at all and 10 is extremely likely, do you think this AF screening service model could become a national screening programme? ☐

12. Please add any further comments to explain your answer to question 11 (above) or that may help us to **improve** the proposed service.

Further comments:

Thank you for taking the time to complete this questionnaire

University of Kent

Appendix 29 Input parameters for the economic model of the Pharmacists Detecting Atrial Fibrillation study in general practice

Table S1 Input parameters for the PSA of the Markov cost-effectiveness model evaluating the PDAF AF screening strategy in GP surgeries using Kardia Mobile® devices.

Abbreviations: AF – atrial fibrillation; ECG – electrocardiogram; GP – general practitioner; PDAF – Pharmacists Detecting Atrial Fibrillation; PSA – probabilistic sensitivity analysis.

Cost Parameter		**Base Case (£)**	**Range in PSA (£)**		**References**
			Lower	Upper	
3-monthly AF screening costs/participant		286.96	143.48	430.44	NICE (2014b); NICE (2015); Welton *et al.* (2017); NHS Improvement (2017); AliveCor (2019c); NHS Employers (2019)
*Cost of single-lead ECG screening**		*0.90*	-	-	AliveCor (2019c); NHS Employers (2019)
*Cost of new diagnosis***		*127.95*	-	-	NICE (2015); Welton *et al.* (2017); NHS Improvement (2017)
Cost of oral anticoagulant therapy		*158.11*	-	-	NICE (2014b)
Cost of ischaemic stroke		3,395.08	1,697.54	5,092.62	
Cost of major bleed		325.73	162.87	488.60	
Transition Probabilities		**Base Case**	**Range in PSA**		**References**
			Lower	Upper	
Ischaemic stroke from stable AF	No screening	0.0076	0.0075	0.0077	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2017a); Office for National Statistics (2017b).
	Screening	0.0068	0.0067	0.0070	
Major bleed from stable AF	No screening	0.0055	0.0053	0.0056	
	Screening	0.0058	0.0057	0.0059	
Death from stable AF	No screening	0.0362	0.0360	0.0365	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride
	Screening	0.0351	0.0349	0.0354	

					(1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2017a); Office for National Statistics (2017b)
Death from ischaemic stroke	No screening	0.1340	0.1282	0.1399	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2017a); Office for National Statistics (2017b); Jacobs *et al.* (2018)
	Screening	0.1300	0.1240	0.1361	
Death from major bleed	No screening	0.0543	0.0498	0.0589	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Eikelboom *et al.* (2006); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2017a); Office for National Statistics (2017b)
	Screening	0.0527	0.0484	0.0571	

Utilities	**Base Case**	**Range in PSA**		**References**
		Lower	Upper	
Stable AF	0.8430	0.7587	0.9273	Jacobs *et al.* (2018)
Post-ischaemic stroke	0.4490	0.3610	0.5370	
Post-major bleed	0.6660	0.5355	0.7965	

Table S2 Input parameters for the PSA of the Markov cost-effectiveness model evaluating the PDAF AF screening strategy in GP surgeries using pulse palpation.

Abbreviations: AF – atrial fibrillation; ECG – electrocardiogram; GP – general practitioner; PDAF – Pharmacists Detecting Atrial Fibrillation; PSA – probabilistic sensitivity analysis.

Cost Parameter		**Base Case (£)**	**Range in PSA (£)**		**References**
			Lower	Upper	
3-monthly AF screening costs/participant		275.15	131.67	418.63	NICE (2014b); NICE (2015); Welton *et al.* (2017); NHS Improvement (2017); NHS Employers (2019)
*Cost of screening**		*0.87*	-	-	NHS Employers (2019)
*Cost of new diagnosis***		*116.17*	-	-	NICE (2015); Welton *et al.* (2017); NHS Improvement (2017)
Cost of oral anticoagulant therapy		*158.11*	-	-	NICE (2014b)
Cost of ischaemic stroke		3,395.08	1,697.54	5,092.62	
Cost of major bleed		325.73	162.87	488.60	
Transition Probabilities		**Base Case**	**Range in PSA**		**References**
			Lower	Upper	
Ischaemic stroke from stable AF	No screening	0.0076	0.0075	0.0077	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2017a); Office for National Statistics (2017b).
	Screening	0.0070	0.0068	0.0071	
Major bleed from stable AF	No screening	0.0055	0.0053	0.0056	
	Screening	0.0058	0.0056	0.0059	
Death from stable AF	No screening	0.0362	0.0360	0.0365	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2017a); Office for National Statistics (2017b)
	Screening	0.0353	0.0351	0.0356	

Death from ischaemic stroke	No screening	0.1340	0.1282	0.1399	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2017a); Office for National Statistics (2017b); Jacobs *et al.* (2018)
	Screening	0.1307	0.1247	0.1367	
Death from major bleed	No screening	0.0543	0.0498	0.0589	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Eikelboom *et al.* (2006); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2017a); Office for National Statistics (2017b)
	Screening	0.0530	0.0486	0.0574	

Utilities	**Base Case**	**Range in PSA**		**References**
		Lower	Upper	
Stable AF	0.8430	0.7587	0.9273	Jacobs *et al.* (2018)
Post-ischaemic stroke	0.4490	0.3610	0.5370	
Post-major bleed	0.6660	0.5355	0.7965	

*The cost of screening per participating individual in England and Wales (Office for National Statistics 2017a; Office for National Statistics 2017b) included the clinical pharmacist's time (11 min/appointment) and the acquisition cost of 6,000 Kardia Mobile® devices (for device-based model only) (The AHSN Network 2019a).

**The cost of a 'new' AF diagnosis was based on the prevalence of 'unknown' AF (1.3%) determined by the cardiologist's interpretation of single-lead ECG and the sensitivity of the index test for the identification of AF. It took into account the cost of 12-lead ECG procedures and associated GP interpretations following the initial referral as well as the cost of GP and cardiologist's appointments for 'new' AF diagnoses (10 minutes each). It also considered the hypothetical costs of extra 12-lead ECGs and GP interpretations which would have been incurred due to false positive AF and 'Unclassified'/'Unreadable' diagnoses resulting from the device's algorithm or pulse palpation.

Appendix 30 Topic guide for focus group interviews with patients conducted during the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Patient Topic Guide – Focus Group

	Topics/Questions	Probes/ follow ups
Introduction	• Welcome and thank you for taking part • Purpose of the focus group • Duration • Consent forms • Data reporting (confidentiality)	
Ice-breaker	We are delighted that you have taken the time to join us today and we are hoping that over the next hour you can tell us about your experience of the AF screening project. We are going to discuss all aspects of the service including for example how you found out about the study, what were your expectations of the service, whether the information we provided met your needs and so on. And before we start I would like to emphasise that there are no right and wrong answers. We are really just interested in exploring your views and experiences. So, if we are all OK to begin perhaps we could go around the table and if you could tell us your name and very briefly why coming today is important to you that would be great.	
1	What did you think about the information that was provided about the pulse check before the appointment?	Easy to understand/ Amount of information supplied, Format/ Anything missing?
2	Why did you decide to make an appointment to have your pulse checked? Was there anything that you were worried about beforehand?	Benefit to you? Concerns re health? Prior experience? Confirmation healthy? Taking part in research?
3	How easy was it to make the appointment? Did you have to make an appointment or were you screened when attending surgery for another reason?	Convenience Choice of appointment times – match your need
4	What were your expectations of the consultation? Is that because you have/have not had a previous consultation with a pharmacist?	Duration of consultation Professionalism/ Inter-personal skills of Pharmacist
5	Was it as you expected it to be? If not, can you tell me what was different? How different do you think this service would be if it was provided in community pharmacies as opposed to GP practices?	Information provided within consultation In-clinic environment Technology/device

6	How did you feel about the guidance that you were given at the end of the consultation? And if follow up was required? Was there anything that you would have liked to have known/ been given information about that wasn't provided?	Adequate? Anxious? Clear? Easy to understand? Efficient?
7	What is your general view of the capability of a Pharmacist to undertake these tests?	Changed perceptions? Confidence? Trust? Expertise? Knowledge? Professionalism? Care? Communication? - language
8	Overall how did you feel about the service that you received? How could we improve it?	Best thing? Improved access to healthcare? Faster diagnosis? Reassurance? Health improvement? Worst aspect? Promotion? National screening programme? Combining with existing services?
9	What other screening tests/services can you envisage pharmacists delivering in the future?	Blood pressure? Diabetes? Cancer? Cholesterol? Dementia? Heart problems?
10	Is there anything else that I have asked you that you would like to say?	
Closure	• Thank you for your participation and contribution • Next steps: data analysis and data reporting (reminder) • Check if anyone would like to receive a copy of report. • Goodbye.	

Appendix 31 Topic guide for focus group interviews with clinical pharmacists or general practice staff conducted during the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Pharmacist/ GP and Practice Staff Topic Guide – Focus Group

	Questions:	Probes/ follow ups
1	How important is it to screen patients for AF?	Benefits Risks of not screening Understanding pre/post study
2	What are the difficulties to carrying out routine screening for patients? Who should be responsible for screening?	Barriers? Time? Training?
3	Thinking more broadly than this study… Please describe your thoughts on how we can best use Pharmacists to contribute to the primary care team?	What are their strengths? What are their limitations?
3	Screening for AF is not a routine role for Pharmacists. Was the training provided for this study adequate?	Did you feel supported? - Pharmacists/ How much support had to be provided? – Practice staff/ GPs
4	Thinking about the AF study How do you feel that the study was received in general by others within the Practice? …… and by Patients?	What was good about it? What was not so good? Any examples of feedback provided to you?
5	Do you think that the study was a success?	What has gone well? Issues? Solutions? Concerns? Clinical skills Organisational skills Attitudes Interpersonal Technology/equipment
6	What would you change about the protocol?	Information for patients about the study? Mass screening vs. selective screening? Opportunistic vs. planned screening? Co-ordination with flu-screening? Combining screening with other clinics/services? Duration each appointment? Scheduling appointments? Screening process during the appointment? Paperwork? Processes for feedback/ follow-up with patients? Training? Clinical supervision? Raising awareness? Promotion?

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7	How could using Pharmacists in this way potentially affect the role of GPs or Nurses? Could this protocol be used as a model for national study? Why?	Increase/ decrease workload? Other roles they could perform? Would you support future screening clinics?

8	Is there anything else that the participants would like to state?	

Appendix 32 Invitation letter for patients participating in focus group interviews of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists
Patient Focus Group Invitation

Dear Sir/Madam

We are undertaking an evaluation of the Atrial Fibrillation (AF) Research Study which you have recently participated in by having your pulse checked by the Pharmacist. As this is a feasibility study it is important that we evaluate it to determine how acceptable it is to patients and whether it is worthwhile to extend this type of service to other GP Practices.

If you have already given us your feedback by completing the patient questionnaire, thank you. However, we would also like to talk directly to a few people to get a more detailed view of their experience of this service. We plan to organise a **group discussion** or **focus group** with between 8 and 10 patients. As someone who has experienced this service we would very much value your views.

The focus group will take around one hour and will be informal. It will be held at a convenient location for you. Travel and parking expenses will be paid. The purpose is simply to capture your views and thoughts on the activities as stated above. Your responses to the questions will be recorded using an audio digital recorder and will be confidential. **It is important to emphasise that no one at your practice will know if you have participated in the focus group, and that your decision to participate will not affect your care in any way.**

Your participation will be a valuable contribution to our research and findings from this study could lead to a greater understanding of this innovative approach to screening patients for AF. It will be shared with the practices who are participating in this study and may also be beneficial to other GP practices who are employing Pharmacists within their organisations.

A Participation Information Sheet and Consent Form are attached for further information. If you are willing to participate, please complete the expression of interest form and post to Dr Sarah Corlett using the pre-paid envelope.

Thank you for reading this invitation letter. If you have any questions, please feel free to contact me.

Regards,

Sarah Corlett, Medway School of Pharmacy, University of Kent.

University of Kent

Appendix 33 Participant information leaflet for patients participating in focus group interviews of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Patient Information Sheet

We would like to invite you to take part in a research study. This study is being run by the Medway School of Pharmacy and is sponsored by the University of Kent. It is funded by the University of Kent and by a medical education grant from the pharmaceutical company, Bayer UK. Bayer have no involvement in the design of this study and no information about you will be disclosed to them.. Before you decide whether you would like to participate, we would like you to understand why the research is being done and what it would involve for you.

Why have I been invited?

All patients whom have already taken part in the AF screening study have been invited to take part in this evaluation of the service.

What is the purpose of this study?

This is a feasibility study which aims to find out whether Clinical Pharmacists working with GPs can efficiently and effectively provide this screening service. The purpose of this study is for opinions and views to be sought from people who have experienced this service. The first hand perspective you provide, will be really useful to help us to improve the service and develop it further.

Do I have to take part?

You are not obliged to participate. It is up to you to decide whether you wish to participate in a focus group, or not. If you agree to take part then we will ask you to sign a consent form. You are, however, free to withdraw from the study at any time, without giving a reason. Your data will be retained up to the point of withdrawal.

What will happen to me if I take part?

Please note that participation in this study will not have any effect on your care.

If you have expressed an interest to participate, we will be send a confirmation letter with further details of the date, time and venue of the focus group discussion.

We will ask all participants to sign a consent form to indicate that they agree to participate in a focus group discussion. The focus group of up to 10 people will be held in a suitable meeting room (venue to be confirmed) and should last about one hour. Refreshments will be provided.

We will ask you about your initial thoughts about the screening service, the information that you were provided with before, during and after your consultation, and on your experience of the consultation itself. We will also ask you about anything which happened as a result of the screen, and your overall opinion of the value of the service, and the suitability of the Pharmacist to provide it. You will not be asked to talk about anything that you do not wish to talk about. However, if for any reason you do not feel comfortable at any point during the focus group, you are free to stop without giving a reason.

The focus group will be recorded on a voice recorder to enable an accurate recording of your thoughts and experience. Only the researchers will listen to the recordings in addition to an independent transcriber who will have access to participants' names, and audio-files in order to transcribe the data. The focus group recording will be transcribed so that we have a written record for the study to enable evaluation. The independent transcriber will sign a confidentiality agreement and name and other individual characteristics will be changed in the transcription so that the participants such as yourself will not be identifiable in any way in this study or subsequent reports.

Data will be securely stored in a locked cabinet at Medway School of Pharmacy at the University of Kent for 5 years after the last publication date. With an exception of signed consent forms, your personal identifiable information (e.g. contact details) will be destroyed 1 month after the focus group. The electronic recording files and written transcripts in electronic form will be held on the University of Kent's secure servers, and disposed of in accordance with the Universities data management protocol.

What will happen if I decide to withdraw from this study?

You are free to withdraw from the study at any point, without giving a reason. If you decide to withdraw from the study, you can contact [s.a.corlett@kent.ac.uk] at any point and state that you wish to withdraw. Focus Group participants have the right to withdraw from the group, but not to withdraw any recorded data after the session has been recorded.

What are the possible benefits of taking part in this study?

You will assist in the development of this research programme and your views will enable us to learn from the experience so that we can determine how best to implement, deliver and measure

this innovative service. This may not benefit you directly, but we hope that the information collected will enable us to develop this and similar services in the future.

What are the disadvantages?

We do not think there are any disadvantages of taking part in this study, apart from the time taken to participate. Travel and parking expenses will be paid.

What happens when the study comes to an end?

The findings of this study will be formally prepared as a report for presentation to Bayer UK. We also plan to publish the findings in an academic journal. As previously stated, all data will be anonymised in the report. A summary of the findings will be produced for the general public and available on the School's web site.

Confidentiality- who will know about me from this project?

Everything you tell us will stay confidential; we will not tell anyone else what you personally say. As mentioned above, you will not be identified in any study reports.

Safeguarding concerns – how are they addressed?

If you disclose anything during the study which the researchers consider to present the possibility of a risk to yourself or to others this will be discussed with you any potential action reviewed with the research team and your GP.

Who has reviewed the study? The study has been approved by London - Riverside Research Ethics Committee .

Further information and contact details:

If you would like further information, please contact the lead Researcher Dr Sarah Corlett (S.A.Corlett@kent.ac.uk, or by phone 01634 888909).

What if you have any concerns or complaints regarding this study?

Please contact Dr Gurprit Lall, Medway School of Pharmacy. Tel: 01634 202935.

University of Kent

Appendix 34 Consent form for patients participating in focus group interviews of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation screening in general practice by Clinical Pharmacists

Patient Focus Group Consent Form

(one copy to be retained by the participant and one by the researcher)

Title of Study: Atrial Fibrillation screening in general practice by Clinical Pharmacists.

Practice:

Please **initial** each box as appropriate	Yes
I confirm that I have read and understood the information provided for the above study and I have had the opportunity to ask questions which have been answered to my satisfaction.	Initial Here
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. If I decide to withdraw, any data collected up to the point of withdrawal will be retained.	Initial Here
I understand that any personal information collected during the focus group will be anonymised and remain confidential.	Initial Here
I understand that the focus group will be audio recorded and that this recording will be written up word for word.	Initial Here
I understand that exact quotes taken from the recording of our conversation may be used in publications and reports, but that these will be anonymised and not traceable to me.	Initial Here
I understand that by agreeing to participate, I agree not to disclose outside of the focus group, anything that was said within the context of the discussion.	Initial Here
I agree to take part in a focus group.	Initial Here

Participant Name (Block Capitals):

Participant's Signature: ***Date:***

To be completed by the Researcher.

I the undersigned have taken the time to fully explain to the above patient the nature and the purpose of this study in a manner that they could understand. I have invited them to ask questions on any aspect of the study that concerned them.

Name (Block Capitals):

Researcher's Signature: ***Date:***

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Appendix 35 Expression of interest form for patients participating in focus group interviews of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Expression of Interest Form

I would like to express my views and thoughts about the AF Research Study and I am interested in taking part in the group discussion.

Name: _____

Contact telephone: _____

Contact email: _____

How do you prefer to be contacted?

☐ Email

☐ Telephone

☐ No preference

Please indicate which dates you are available for the first focus group (please tick all available dates):

☐ [Date 1 to be inserted]

☐ [Date 2 to be inserted]

☐ [Date 3 to be inserted]

☐ [Date 4 to be inserted]

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Appendix 36 Invitation letter for pharmacists participating in a focus group interview of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists
Pharmacist Focus Group Invitation

Dear XX

We are undertaking an evaluation of the Atrial Fibrillation (AF) screening study, which you have participated in. As this is a new service it is important that we evaluate it to determine how acceptable the service is to both patients and staff, and whether it is worthwhile to extend this service to other GP Practices. We will therefore be conducting focus groups to better understand how feasible the study was, whether the training and support provided to you to carry out this role was adequate. We are also interested to explore with you how you think the study impacted on other staff within the Practice and to determine what improvements could be made to the study protocol. As a pharmacist carrying out this innovative role within the Practice you are in an ideal position to provide us with valuable first-hand information from your own perspective.

We would therefore like to invite you to participate in a focus group which will take around one hour and will be informal. It will be held at Venue [to be inserted]. Travel expenses will be paid, and parking will be available on site. Refreshments will be provided. The purpose is simply to capture your views and thoughts on the activities as stated above. Your responses to the questions will be recorded using a digital recorder and will be confidential.

Your participation will be a valuable contribution to our research and findings from this study could lead to greater understanding of this innovative approach to screening patients for AF. It will be shared with the Practices who are participating in this study and may also be beneficial to other GP Practices whom are employing Pharmacists within their organisations. A Participation Information Sheet and Consent Form are attached for further information. If you are willing to participate, please complete the expression of interest form and e-mail to XXX

If you have any questions, please do contact me.

Regards,

Sarah Corlett, Medway School of Pharmacy, University of Kent.

University of Kent

Appendix 37 Invitation letter for general practice staff participating in a focus group interview of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Invitation by e-mail to GPs and Practice Staff for Focus Group

Dear Sir/Madam

We are undertaking an evaluation of the Atrial Fibrillation (AF) Research Study which your practice has participated in. As this is a new service it is important that we evaluate it to determine how acceptable it is to both patients and staff, and whether it is worthwhile to extend this service to other GP practices. We will therefore be conducting focus groups to better understand how feasible the study was, whether the training provided to the Pharmacist was adequate, how the study impacted on other staff within the Practice and to determine what improvements could be made to the study protocol. As a non-pharmacist member of staff from the Practice you are in an ideal position to provide us with valuable first-hand information from your own perspective.

We would like to invite you to participate in a focus group which will take around one hour and will be informal. It will be held at [insert venue]. Any incurred travel expenses will be paid and refreshment provided. The purpose is simply to capture your views and thoughts on the activities as stated above. Your responses to the questions will be recorded using a digital recorder and will be confidential.

Your participation will be a valuable contribution to our research and findings from this study could lead to greater understanding of this innovative approach to screening patients for AF. It will be shared with the practices who are participating in this study and may also be beneficial to other GP practices whom are employing Pharmacists within their organisations. A Participation Information Sheet and Consent Form are attached for further information. If you are willing to participate, please complete the expression of interest form and e-mail to Sarah Corlett [s.a.corlett@kent.ac.uk].

Thank you for reading this e-mail. If you have any questions, please feel free to contact me.

Kind regards,

Sarah Corlett

University of Kent

Appendix 38 Participant information leaflet for pharmacists participating in a focus group interview of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Participant Information Sheet

We would like to invite you to take part in a focus group discussion. This study is being run by the Medway School of Pharmacy and is sponsored by the University of Kent. It is funded by the University of Kent and by a medical education grant from the pharmaceutical company, Bayer UK. Bayer have no involvement in the design of this study and no information about you will be disclosed to them. Before you decide whether you would like to participate, we would like you to understand why the research is being done and what it would involve for you.

Why have I been invited?

All pharmacists whom have taken part in the AF screening study have been invited to take part in this evaluation of the service.

What is the purpose of this study?

This is a feasibility study which aims to find out whether Clinical Pharmacists working with GPs can efficiently and effectively provide this screening service. The first hand perspective you provide, will be really useful to help us to improve the service and develop it further.

Do I have to take part?

You are not obliged to participate but we hope that you will agree to take part. If you agree to take part then we will ask you to sign a consent form. You are, however, free to withdraw from the study at any time, without giving a reason.

What will happen to me if I take part?

Please note that participation in this study will not have any effect on your future employment. We will ask all pharmacists who have taken part in the study to take part in a group discussion which will be held at (venue to be confirmed) and should last about one hour. Refreshments will be provided.

We will ask you to reflect upon your knowledge and understanding of the importance of screening for AF before and after the study, your thoughts about the training provided to support you in your role, the information and support that you were provided with before, and during the study, how efficiently the service ran, and how it could be improved. We will also ask your overall

opinion of the value of the service, and the suitability of the 'Pharmacist' to provide it. You will not be asked to talk about anything that you do not wish to talk about. However, if for any reason you do not feel comfortable at any point during the focus group, you are free to stop without giving a reason.

The focus group will be recorded on a voice recorder to enable an accurate recording of your thoughts and experience. Only the researchers will listen to the recordings in addition to an independent transcriber who will have access to participants' names, and audio-files in order to transcribe the data. The focus group recording will be transcribed so that we have a written record for the study to enable evaluation. The independent transcriber will sign a confidentiality agreement and name and other individual characteristics will be changed in the transcription so that the participants such as yourself will not be identifiable in any way in this study or subsequent reports.

Data will be securely stored in a locked cabinet at Medway School of Pharmacy at the University of Kent for 5 years after the last publication date. With an exception of signed consent forms, your personal identifiable information (e.g. contact details) will be destroyed 1 month after the focus group. The electronic recording files and written transcripts in electronic form will be held on the University of Kent's secure servers, and disposed of in accordance with the Universities data management protocol.

What will happen if I decide to withdraw from this study?

You are free to withdraw from the study at any point, without giving a reason. If you agree to take part and then decide to withdraw from the study, you can contact [s.a.corlett@kent.ac.uk] at any point and state that you wish to withdraw. Focus Group participants have the right to withdraw from the group, but not to withdraw any recorded data after the session has been recorded.

What are the possible benefits of taking part in this study?

You will assist in the development of this research programme and your views will enable us to learn from the experience so that we can determine how best to implement, deliver and measure this innovative service. This may not benefit you directly, but we hope that the information collected will enable us to develop this and similar services in the future.

What are the disadvantages?

We do not think there are any disadvantages of taking part in this study, apart from the time taken to participate. Travel and parking expenses will be paid.

What happens when the study comes to an end?
The findings of this study will be formally prepared as a report which will be shared with Bayer UK. We also plan to publish the findings in an academic journal. As previously stated, all data will be anonymised in the report. A summary of the findings will be produced for the general public and available on the School's web site.

Confidentiality- who will know about me from this project?
Everything you tell us will stay confidential; we will not tell your employer or anyone else what you personally say. As mentioned above, you will not be identified in any study reports.

Safeguarding concerns – how are they addressed?
If you disclose anything during the study which the researchers consider to present the possibility of a risk to yourself or to others this will be discussed with you any potential action reviewed with the research team and your GP.

Who has reviewed the study? The study has been approved by London - Riverside Research Ethics Committee.

Further information and contact details:
If you would like further information, please contact the lead Researcher Dr Sarah Corlett (S.A.Corlett@kent.ac.uk, or by phone 01634 888909)

What if you have any concerns or complaints regarding this study?
Please contact Dr Gurprit Lall, Medway School of Pharmacy. Tel: 01634 202935.

University of Kent

Appendix 39 Participant information leaflet for general practice staff participating in a focus group interview of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Participant Information Sheet

We would like to invite you to take part in a focus group discussion. This study is being run by the Medway School of Pharmacy and is sponsored by the University of Kent. It is funded by the University of Kent and by a medical education grant from the pharmaceutical company, Bayer UK. Bayer have no involvement in the design of this study and no information about you will be disclosed to them. Before you decide whether you would like to participate, we would like you to understand why the research is being done and what it would involve for you.

Why have I been invited?

The practice that you work in has taken part in the AF screening study. If you have been involved in this service, in any way such as booking patients in for screening appointments or providing advice and support to the pharmacists running the clinics then we would like to invite you to take part in a group discussion to evaluate the service.

What is the purpose of this study?

This is a feasibility study which aims to find out whether Clinical Pharmacists working with GPs can efficiently and effectively provide this screening service. The first hand perspective you provide, will be really useful to help us to identify any problems or issues and to improve the service and develop it further.

Do I have to take part?

You are not obliged to participate but we hope that you will agree to take part. If you agree to take part then we will ask you to sign a consent form. You are, however, free to withdraw from the study at any time, without giving a reason.

What will happen to me if I take part?

Please note that participation in this study will not have any effect on your future employment. The focus group will be held at (venue to be confirmed) and should last about one hour. Refreshments will be provided.

We will ask you to reflect upon the study, how efficiently the service was conducted, and whether and how it could be improved. We will also ask your overall opinion of the value of the service to patients and the Practice, and the suitability of the 'Pharmacist' to provide this

service. You will not be asked to talk about anything that you do not wish to talk about. However, if for any reason you do not feel comfortable at any point during the focus group, you are free to stop without giving a reason.

The focus group will be recorded on a voice recorder to enable an accurate recording of your thoughts and experience. Only the researchers will listen to the recordings in addition to an independent transcriber who will have access to participants' names, and audio-files in order to transcribe the data. The focus group recording will be transcribed so that we have a written record for the study to enable evaluation. The independent transcriber will sign a confidentiality agreement and name and other individual characteristics will be changed in the transcription so that the participants such as yourself will not be identifiable in any way in this study or subsequent reports.

Data will be securely stored in a locked cabinet at Medway School of Pharmacy at the University of Kent for 5 years after the last publication date. With an exception of signed consent forms, your personal identifiable information (e.g. contact details) will be destroyed 1 month after the focus group. The electronic recording files and written transcripts in electronic form will be held on the University of Kent's secure servers, and disposed of in accordance with the Universities data management protocol.

What will happen if I decide to withdraw from this study?

You are free to withdraw from the study at any point, without giving a reason. If you agree to take part and then decide to withdraw from the study, you can contact [s.a.corlett@kent.ac.uk] at any point and state that you wish to withdraw. Focus Group participants have the right to withdraw from the group, but not to withdraw any recorded data after the session has been recorded.

What are the possible benefits of taking part in this study?

You will assist in the development of this research programme and your views will enable us to learn from the experience so that we can determine how best to implement, deliver and measure this innovative service. This may not benefit you directly, but we hope that the information collected will enable us to develop this and similar services in the future.

What are the disadvantages?

We do not think there are any disadvantages of taking part in this study, apart from the time taken to participate. Travel and parking expenses will be paid.

What happens when the study comes to an end?

The findings of this study will be formally prepared as a report which will be shared with Bayer UK. We also plan to publish the findings in an academic journal. As previously stated, all data will be anonymised in the report. A summary of the findings will be produced for the general public and available on the School's web site.

Confidentiality- who will know about me from this project?
Everything you tell us will stay confidential; we will not tell your employer or anyone else what you personally say. As mentioned above, you will not be identified in any study reports.

Safeguarding concerns – how are they addressed?
If you disclose anything during the study which the researchers consider to present the possibility of a risk to yourself or to others this will be discussed with you any potential action reviewed with the research team and your GP.

Who has reviewed the study? The study has been approved by London - Riverside Research Ethics Committee .

Further information and contact details:
If you would like further information, please contact the lead Researcher Dr Sarah Corlett (S.A.Corlett@kent.ac.uk, or by phone 01634 888909).

What if you have any concerns or complaints regarding this study?
Please contact Dr Gurprit Lall, Medway School of Pharmacy. Tel: 01634 202935.

University of Kent

Appendix 40 Consent form for pharmacists or general practice staff participating in focus group interviews of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation screening in general practice by Clinical Pharmacists

Pharmacist / GP Practice staff Focus Group Consent Form

(one copy to be retained by the participant and one by the researcher)

Please **initial** each box as appropriate	Yes
I confirm that I have read and understood the information provided for the above study and I have had the opportunity to ask questions which have been answered to my satisfaction.	Initial Here
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason	Initial Here
I understand that any personal information collected during the focus group will be anonymised and remain confidential. If I decide to withdraw, any data collected up to the point of withdrawal will be retained.	Initial Here
I understand that the focus group will be audio recorded and that this recording will be written up word for word.	Initial Here
I understand that exact quotes taken from the recording of our conversation may be used in publications and reports, but that these will be anonymised and not traceable to me.	Initial Here
I understand that by agreeing to participate, I agree not to disclose outside of the focus group, anything that was said within the context of the discussion.	Initial Here
I agree to take part in a focus group.	Initial Here

Participant Name (Block Capitals):

Participant's Signature: ***Date:***

To be completed by the Researcher.

I the undersigned have taken the time to fully explain to the above participant the nature and the purpose of this study. I have invited them to ask questions on any aspect of the study that concerned them.

Name (Block Capitals):

Researcher's Signature: ***Date:***

University of Kent

Appendix 41 Expression of interest form for pharmacists participating in a focus group interview of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Expression of Interest Form - Pharmacists

I would like to express my views and thoughts about the AF Research Study and I am interested in taking part in the group discussion.

Name: _____

Contact telephone: _____

Contact email: _____

How do you prefer to be contacted?

☐ Email

☐ Telephone

☐ No preference

Please indicate which dates you are available for the first focus group (please tick all available dates):

☐ [Date 1 to be inserted]

☐ [Date 2 to be inserted]

☐ [Date 3 to be inserted]

☐ [Date 4 to be inserted]

University of Kent

Appendix 42 Expression of interest form for general practice staff participating in a focus group interview of the Pharmacists Detecting Atrial Fibrillation study

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

Expression of Interest Form – GPs and Practice Staff

I would like to express my views and thoughts about the AF Research Study and I am interested in taking part in the group discussion.

Name: _____

Role: _____

Contact telephone: _____

Contact email: _____

How do you prefer to be contacted?

☐ Email

☐ Telephone

☐ No preference

Please indicate which dates you are available for the first focus group (please tick all available dates):

☐ [Date 1 to be inserted]

☐ [Date 2 to be inserted]

☐ [Date 3 to be inserted]

☐ [Date 4 to be inserted]

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Appendix 43 Participant information leaflet for the Pharmacists Detecting Atrial Fibrillation study in care homes

Atrial Fibrillation Screening in General Practice by Clinical Pharmacists

What is Atrial Fibrillation?

Atrial fibrillation or AF is a common heart rhythm disorder that occurs when the electrical activity in the heart becomes chaotic. The result of this is often an **irregular** and sometimes very **fast pulse**. AF is an **age-related** condition, the older you get, the more likely you are to develop it. If you develop AF it means that your heart is no longer working properly and left untreated it can lead to serious complications such as **heart failure** and **stroke**.

Why should we screen for Atrial Fibrillation (AF)?

It is estimated that approximately 500,000 people in the UK are living with undiagnosed AF. Many people with AF have no obvious symptoms. AF represents a significant and growing burden on the NHS, with AF-related illness costing the NHS an estimated **£2.2 billion** each year. Early detection of AF and treatment with **anticoagulants** has been shown to significantly reduce the incidence of stroke and death.

What will the Research Study involve?

We are asking all eligible residents who are having a Flu vaccine between September and December 2018 to also consent to having their **pulse checked** and a **single-lead electrocardiogram (ECG)** taken by a clinical pharmacist. This process should take no more than 10-15 minutes, and is a painless and non-invasive procedure. All ECGs will be verified by a **specialist Cardiologist** within 72 hrs.

ECG test.

What is the purpose of the study?

GPs and clinical pharmacists from your surgery are working together with academics from the **University of Kent** to find the best way of screening patients routinely, who are at high-risk of developing AF.

Who is eligible to take part?

All residents **over the age of 18** years, who **do not** have a pacemaker and who are eligible to receive a **Flu vaccination** may take part in this study.

What are the benefits of taking part?

You will have your pulse checked to see that it is normal. You will also be actively helping in the development of this study and your views will enable us to determine how best to implement, deliver and measure future screening programmes for AF.

I want to take part, what happens next?

When you have your Flu vaccination, you can also ask to have your pulse checked with the pharmacist. Before the pulse check you will be asked to confirm your **eligibility** and sign a **consent form**.

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If I decide not to take part, will this affect my future care?

You are not obliged to participate. Please be assured that all medical care required when someone is diagnosed with AF will be available, whether you decide to take part in the study or not.

What will happen if I withdraw from the study?

You are **free to withdraw** from the study at any point, without giving a reason and this will not affect any future medical care.

What will happen if I am diagnosed with AF?

All patients that are diagnosed with AF will receive the necessary medical care that is appropriate to your condition. If the test shows that you have an irregular pulse your GP will probably want to carry out another test called an ECG. People usually go to the GP Practice to have this test. Dependent upon the result of the ECG the GP will decide the best treatment options with you. They may want to start you on medicines to reduce your risk of having a stroke. You do not have to have the ECG or take any new medicines if you don't want to.

Will any data collected about me be kept confidential?

All data collected as part of the study will be kept **strictly confidential** and stored securely for a maximum of 5 years. If you provide any personal identifiable information this information such as signed consent forms this will be stored securely and deleted at the end of the study. Any data which leaves the home/ surgery/hospital/university will not identify individuals. All other data will be handled in accordance with the Data Protection Act 2018.

Will it cost me anything?

This service will be completely **free of charge**.

What happens afterwards?

Immediately after being screened, the clinical pharmacist will ask you to fill in a short questionnaire about the experience. You will also be given an information pack that contains additional information about AF. All unidentifiable data collected from the study will be analysed and written into a full report that will be published.

Who is funding the study?

This study is being jointly funded by the University of Kent and by a medical education grant from the pharmaceutical company, Bayer UK. Bayer have no involvement in the design of this study and no information about you will be disclosed to them.

Who can I contact for further information?

Further information about the study can be obtained from our webpage: [insert webpage address] or by email: s.a.corlett@kent.ac.uk or by phone: 01634 888909 by post: Medway School of Pharmacy, Anson Building, Central Avenue, Chatham, ME4 4TB.

Who can I contact if I have concerns, worries or complaints?

If you would like to find out more general information about taking part in research studies then please contact by email: t.thomas@kent.ac.uk or by phone or post as listed above. If you have complaints about the study, please contact: g.lall@kent.ac.uk or by phone as listed above.

University of Kent

Appendix 44 Consultee declaration form the Pharmacists Detecting Atrial Fibrillation study in care homes

CONSULTEE DECLARATION FORM

Title of Study: Atrial Fibrillation screening in general practice by Clinical Pharmacists

Care Home:

Participant ID Number:

Please **initial** each box as appropriate	Yes
I [name of consultee] have been consulted about [name of potential participant]'s participation in this research project. I have had the opportunity to ask questions about the study and understand what is involved.	Initial Here
In my opinion he/she would have no objection to taking part in the above study.	Initial Here
I understand that I can request he/she is withdrawn from the study at any time, without giving any reason and without his/her care or legal rights being affected.	Initial Here
I understand that relevant sections of his/her medical notes and information collected during this research study may be looked at by individuals from the University of Kent, for the purpose of this research and that such data will be anonymised and kept private and confidential by the research team. I give permission for these individuals to have access to his/her records (or to parts taken from by practice staff).	Initial Here

Name of consultee	Date	Signature

Relationship to participant: _____

Name of person undertaking consultation (if different from researcher)	Date	Signature

Name of researcher	Date	Signature

When completed: 1 (original) to be kept in care record, 1 for consultee; 1 for researcher site file

University of Kent

Appendix 45 Input parameters for the economic model of the Pharmacists Detecting Atrial Fibrillation study in care homes

Table S3 Input parameters for the PSA of the Markov cost-effectiveness model evaluating the PDAF AF screening strategy in care homes using Kardia Mobile® devices.

Abbreviations: AF – atrial fibrillation; ECG – electrocardiogram; GP – general practitioner; PDAF – Pharmacists Detecting Atrial Fibrillation; PSA – probabilistic sensitivity analysis.

Cost Parameter		**Base Case (£)**	**Range in PSA (£)**		**References**
			Lower	Upper	
3-monthly AF screening costs/participant		225.67	112.83	338.50	NICE (2014b); NICE (2015); Welton *et al.* (2017); NHS Improvement (2017); AliveCor (2019c); NHS Employers (2019)
*Cost of single-lead ECG screening**		*0.74*	-	-	AliveCor (2019c); NHS Employers (2019)
*Cost of new diagnosis***		*66.81*	-	-	NICE (2015); Welton *et al.* (2017); NHS Improvement (2017)
Cost of oral anticoagulant therapy		*158.11*	-	-	NICE (2014b)
Cost of ischaemic stroke		3,395.08	1,697.54	5,092.62	
Cost of major bleed		325.73	162.87	488.60	
Transition Probabilities		**Base Case**	**Range in PSA**		**References**
			Lower	Upper	
Ischaemic stroke from stable AF	No screening	0.0207	0.0200	0.0214	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2014); Friberg *et al.* (2012)
	Screening	0.0188	0.0181	0.0195	
Major bleed from stable AF	No screening	0.0046	0.0042	0.0049	
	Screening	0.0053	0.0049	0.0056	
Death from stable AF	No screening	0.1017	0.1002	0.1032	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.*
	Screening	0.0979	0.0964	0.0994	

					(2011); Patel *et al.* (2011); Office for National Statistics (2014); Office for National Statistics (2017a); Office for National Statistics (2017b)
Death from ischaemic stroke	No screening	0.3762	0.3593	0.3932	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2014); Office for National Statistics (2017a); Office for National Statistics (2017b); Jacobs *et al.* (2018)
	Screening	0.3621	0.3444	0.3798	
Death from major bleed	No screening	0.1525	0.1258	0.1793	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Eikelboom *et al.* (2006); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2014); Office for National Statistics (2017a); Office for National Statistics (2017b)
	Screening	0.1468	0.1223	0.1714	

Utilities	**Base Case**	**Range in PSA**		**References**
		Lower	Upper	
Stable AF	0.8430	0.7587	0.9273	Jacobs *et al.* (2018)
Post-ischaemic stroke	0.4490	0.3610	0.5370	
Post-major bleed	0.6660	0.5355	0.7965	

*The cost of screening per participating care home resident in England and Wales (Office for National Statistics 2014) included the clinical pharmacist's time (9 min/appointment) and the acquisition cost of 166 Kardia Mobile® devices (The AHSN Network 2019a).

**The cost of a 'new' AF diagnosis was based on the prevalence of previously undiagnosed AF (9.6%) determined by the cardiologist's interpretation of single-lead ECG and the sensitivity of the index test for the identification of AF. It took into account the cost of 12-lead ECG procedures and associated GP interpretations following the initial referral as well as the cost of GP and cardiologist's appointments for 'new' AF diagnoses (10 minutes each). It also considered the hypothetical costs of extra 12-lead ECGs and GP interpretations which would have been incurred due to false positive AF and 'Unclassified'/'Unreadable' diagnoses resulting from the device's algorithm.

Appendix 46 Promotional poster/leaflet for atrial fibrillation screening within a South Asian community

Atrial Fibrillation Awareness Project

Get your free heart check here at Guru Nanak Darbar 11th - 24th November

Guru Nanak Darbar Gravesend, offers you an opportunity to have your heart beat tested for free by researchers from the University of Kent, to screen people at risk of developing Atrial Fibrillation.

What is Atrial Fibrillation (AF)?

AF is the most common type of irregular heart rhythm which means the heart has to work harder. Many people have this condition without knowing, this increases the risk of stroke and heart disease.

Why should you get your heart checked?

A simple and painless 30-second ECG check using a new mobile device could help detect an abnormal heart rhythm or rate, which can be treated.

Mobile ECG check

What do I have to do?

If you **are aged 18 years** or over you may be eligible for a free heart check! If you would like to have your heart beat tested, come to our stand within the Gurdwara between the 11th and 24th of November 2019.

For more information, please pick up a leaflet within the Gurdwara, visit www.msp.ac.uk/saaf or scan the QR code above.

ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਜਾਗਰੂਕਤਾ ਸੰਬੰਧੀ ਪ੍ਰਾਜੈਕਟ

ਗੁਰੁ ਨਾਨਕ ਦਰਬਾਰ ਵਿਖੇ ਆਪਣੇ ਦਿਲ ਦੀ ਮੁਫ਼ਤ ਜਾਂਚ 11 ਤੋਂ 24 ਨਵੰਬਰ ਤੱਕ ਕਰਾਵੋ

ਗੁਰੁ ਨਾਨਕ ਦਰਬਾਰ ਗਰੇਵਸੇਨਡ ਵਲੋਂ ਯੂਨਿਵਰਸਿਟੀ ਆੱਫ਼ ਕੈਨਟ ਦੇ ਖ਼ੋਜਕਰਤਾਵਾਂ ਦੁਆਰਾ ਤੁਹਾਡੇ ਦਿਲ ਦੀ ਧੜਕਣ ਦਾ ਮੁਲਾਂਕਣ ਕਰਵਾਉਣ ਦਾ ਇੱਕ ਮੌਕਾ ਪ੍ਰਦਾਨ ਕੀਤਾ ਜਾ ਰਿਹਾ ਹੈ, ਜਿਸ ਰਾਹੀਂ ਜਿਨ੍ਹਾਂ ਲੋਕਾਂ ਵਿਚ ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਦਾ ਖਤਰਾ ਰੱਧ ਰਿਹਾ ਹੈ ਉਹਨਾਂ ਨੂੰ ਸਕ੍ਰੀਨ 'ਤੇ ਪ੍ਰਦਰਸਿਤ ਕੀਤਾ ਜਾਂਦਾ ਹੈ।

ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ (ਏਐਫ) ਕੀ ਹੈ?

ਏਐਫ ਇਹ ਦਿਲ ਦੀ ਆਮ ਕਿਸਮ ਦੀ ਅਨਿਯਮਿਤ ਧੁਨ ਹੈ ਜਿਸਦਾ ਮਤਲਬ ਹੈ ਕਿ ਦਿਲ ਨੂੰ ਜਿਆਦਾ ਕੰਮ ਕਰਨਾ ਪੈਂਦਾ ਹੈ। ਬਹੁਤ ਸਾਰੇ ਲੋਕੀ ਇਸ ਤੋਂ ਪੀੜਤ ਹੁੰਦੇ ਹਨ, ਪਰ ਉਹ ਇਸ ਤੋਂ ਅਜਾਣ ਹੁੰਦੇ ਹਨ, ਇਸ ਨਾਲ ਸਟ੍ਰੋਕ ਅਤੇ ਦਿਲ ਦੀ ਬਿਮਾਰੀ ਦਾ ਖਤਰਾ ਵੱਧ ਜਾਂਦਾ ਹੈ।

ਤੁਹਾਨੂੰ ਆਪਣੇ ਦਿਲ ਦੀ ਜਾਂਚ ਕਿਉਂ ਕਰਵਾਉਣੀ ਚਾਹੀਦੀ ਹੈ?

ਇੱਕ ਨਵੇਂ ਮੋਬਾਈਲ ਯੰਤਰ ਦੀ ਵਰਤੋਂ ਨਾਲ ਸਾਧਾਰਨ ਅਤੇ ਦਰਦ ਰਹਿਤ 30 ਸਕਿੰਟਾਂ ਲਈ ਈਸੀਜੀ ਜਾਂਚ ਰਾਹੀਂ ਦਿਲ ਦੀ ਅਸਾਧਾਰਨ ਧੁਨ ਜਾਂ ਦਰ ਨੂੰ ਖੋਜਣ ਵਿਚ ਮਦਦ ਹੋ ਸਕਦੀ ਹੈ ਅਤੇ ਇਸ ਦਾ ਇਲਾਜ ਕੀਤਾ ਜਾ ਸਕਦਾ ਹੈ।

ਮੋਬਾਈਲ ਈਸੀਜੀ ਜਾਂਚ

ਮੈਨੂੰ ਕੀ ਕਰਨਾ ਚਾਹੀਦਾ ਹੈ?

ਜੇ ਤੁਸੀਂ 18 ਸਾਲ ਜਾਂ ਵੱਧ ਉਮਰ ਦੇ ਹੋ, ਤਾਂ ਤੁਸੀਂ ਦਿਲ ਦੀ ਮੁਫ਼ਤ ਜਾਂਚ ਕਰਾਉਣ ਦੇ ਯੋਗ ਹੋ ਸਕਦੇ ਹੋ! ਜੇ ਤੁਸੀਂ ਆਪਣੇ ਦਿਲ ਦੀ ਬਿਮਾਰੀ ਦੀ ਜਾਂਚ ਕਰਵਾਉਣਾ ਚਾਹੋ, ਤਾਂ ਗੁਰਦੁਆਰੇ ਦੇ ਅੰਦਰ 11 ਤੋਂ 24 ਨਵੰਬਰ 2019 ਦਰਮਿਆਨ ਸਾਡੇ ਸਟੈਂਡ 'ਤੇ ਆਓ।

ਵਧੇਰੇ ਜਾਣਕਾਰੀ ਲਈ, ਕਿਰਪਾ ਕਰਕੇ ਗੁਰਦੁਆਰੇ ਅੰਦਰੋਂ ਇੱਕ ਪਤ੍ਰਿਕਾ ਲਓ ਜਾਂ www.msp.ac.uk/saaf ਦੇਖੋ ਜਾਂ ਉਪਰ ਦਿੱਤਾ ਕਿਊਆਰ (QR) ਕੋਡ ਸਕੈਨ ਕਰੋ।

Appendix 47 Text message invitation for atrial fibrillation screening within a South Asian community

medway school of pharmacy

Text Message and Social Media Invitation

Atrial Fibrillation Screening using Single-lead ECG within a South Asian Community

If you are aged 18 years or over you may be eligible for a free heart check. If you would like to have your heart beat tested, come to our stand within the Guru Nanak Darbar Gravesend between the 11th and 24th of November 2019. For more information, please pick up a leaflet within the Gurdwara or visit www.msp.ac.uk/saaf.

medway school of pharmacy

Text Message and Social Media Invitation

ਦੱਖਣ ਏਸ਼ੀਅਨ ਕਮਿਊਨਿਟੀ ਅੰਦਰ ਸਿੰਗਲ ਲੀਡ ਈਸੀਜੀ ਦੀ ਵਰਤੋਂ ਨਾਲ ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰਿਨਿੰਗ

ਜੇ ਤੁਸੀਂ 18 ਸਾਲ ਜਾਂ ਵੱਧ ਉਮਰ ਦੇ ਹੋ, ਤਾਂ ਤੁਸੀਂ ਦਿਲ ਦੀ ਮੁਫ਼ਤ ਜਾਂਚ ਕਰਾਉਣ ਦੇ ਯੋਗ ਹੋ ਸਕਦੇ ਹੋ. ਜੇ ਤੁਸੀਂ ਆਪਣੇ ਦਿਲ ਦੀ ਬਿਮਾਰੀ ਦੀ ਜਾਂਚ ਕਰਵਾਉਣਾ ਚਾਹੋ, ਤਾਂ ਗੁਰਦੁਆਰੇ ਦੇ ਅੰਦਰ 11 ਤੋਂ 24 ਨਵੰਬਰ 2019 ਦਰਮਿਆਨ ਸਾਡੇ ਸਟੈਂਡ 'ਤੇ ਆਓ।. ਵਧੇਰੇ ਜਾਣਕਾਰੀ ਲਈ, ਕਿਰਪਾ ਕਰਕੇ ਗੁਰਦੁਆਰੇ ਅੰਦਰੋਂ ਇੱਕ ਪੜ੍ਹਿਕਾ ਲਓ ਜਾਂ www.msp.ac.uk/saaf.

Appendix 48 Homepage contents of the website for atrial fibrillation screening within a South Asian community

Atrial Fibrillation Research Study

If you **are aged 18 years** or over you may be eligible for a free heart check!

What is Atrial Fibrillation (AF)?

AF is the most common kind of irregular heart rhythm which means the heart has to work harder. Many people have this condition without knowing, placing them at increased risk of stroke and heart disease.

Why is the study being done?

This study is conducted in conjunction with the Atrial Fibrillation Association and aims to find out if trained pharmacy students can successfully use mobile and painless electrocardiogram (ECG) devices to accurately detect AF in individuals of South Asian origin. In order to encourage all individuals from the local community to participate, we are carrying out the screening at the Guru Nanak Darbar Gurdwara, Gravesend and have selected a research team fluent in Punjabi.

Mobile ECG test

Why should I get my heart beat checked?

If you are diagnosed with AF or another heart condition, you and your doctor will be able to decide on how to treat it. Your test results and views will also enable our study to determine how best to deliver and measure future screening programmes for AF amongst the individuals of South Asian origin.

University of Kent

How can I get involved?

First check that you are eligible to participate:

- Are you an adult aged 18 or over?
- Do you **NOT** have a pacemaker or cardiac defibrillator?
- Do you **NOT** have a terminal illness (e.g. cancer with life expectancy under 1 month)?

If you have answered **yes** to all the questions, then feel free to approach us at the stand within the temple between the **11th and 24th of November 2019**.

If you would like more information, please review the Patient Information Leaflet online [link to be added] or grab one at our stand.

Contact Details

For all queries regarding this study, please do not hesitate to contact:

The Pharmacists Detecting Atrial Fibrillation (PDAF) Study Team

Email: afstudy@kent.ac.uk

Tel: 01634 202935

Should you have any concerns, worries or complaints about the study, please contact:

Dr Trudy Thomas

Email: t.thomas@kent.ac.uk

Tel: 01634 88 8909.

For more information about AF, please visit:

www.afa.org.uk or www.afa-international.org or contact the AF Association:

AF Association®
Unit 6B
Essex House
Cromwell Business Park
Chipping Norton
OX7 5SR
+44(0)1789 867502
info@afa.org.uk

THANK YOU FOR TAKING PART

ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਜਾਗਰੂਕਤਾ ਸੰਬੰਧੀ ਪ੍ਰਾਜੈਕਟ

ਜੇ ਤੁਸੀਂ 18 ਸਾਲ ਜਾਂ ਵੱਧ ਉਮਰ ਦੇ ਹੋ, ਤਾਂ ਤੁਸੀਂ ਦਿਲ ਦੀ ਮੁਫ਼ਤ ਜਾਂਚ ਕਰਵਾਉਣ ਲਈ ਯੋਗ ਹੋ ਸਕਦੇ ਹੋ!

ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ (ਏਐੱਫ) ਕੀ ਹੈ?

ਏਐਫ ਇਹ ਦਿਲ ਦੀ ਆਮ ਕਿਸਮ ਦੀ ਅਨਿਯਮਿਤ ਧੜਕਨ ਹੈ ਜਿਸਦਾ ਭਾਵ ਹੈ ਕਿ ਦਿਲ ਨੂੰ ਜ਼ਿਆਦਾ ਕੰਮ ਕਰਨਾ ਪੈਂਦਾ ਹੈ। ਬਹੁਤ ਸਾਰੇ ਲੋਕੀ ਇਸ ਤੋਂ ਪੀੜਤ ਹੁੰਦੇ ਹਨ, ਪਰ ਉਹ ਇਸ ਤੋਂ ਅਜਾਣ ਹੁੰਦੇ ਹਨ, ਇਸ ਨਾਲ ਸਟ੍ਰੋਕ ਅਤੇ ਦਿਲ ਦੀ ਬਿਮਾਰੀ ਦਾ ਖਤਰਾ ਵੱਧ ਜਾਂਦਾ ਹੈ।

ਅਧਿਐਨ ਕਿਉਂ ਕੀਤਾ ਜਾ ਰਿਹਾ ਹੈ?

ਇਸ ਅਧਿਐਨ ਦਾ ਉਦੇਸ਼ ਇਹ ਪਤਾ ਕਰਨਾ ਹੇ ਕਿ ਸਿਖਿਅਤ ਫਾਰਮੇਸੀ ਵਿਦਿਆਰਥੀ ਦੱਖਣੀ ਏਸ਼ੀਆ ਦੇ ਮੂਲ ਵਿਅਕਤੀਗਤ ਲੋਕਾਂ ਦੀ ਸਹੀ ਏਐਫ ਪਛਾਣ ਕਰਨ ਲਈ ਸਫ਼ਲਤਾ ਨਾਲ ਮੋਬਾਇਲ ਅਤੇ ਦਰਦ ਰਹਿਤ ਇਲੈਕਟ੍ਰੋਕਾਰਡੀਅਗਰਾਮ (ਈਸੀਜੀ) ਯੰਤਰਾਂ ਦਾ ਇਸਤੇਮਾਲ ਕਰ ਸਕਦੇ ਹਨ ਜਾਂ ਨਹੀਂ। ਸਥਾਨਕ ਭਾਈਚਾਰੇ ਦੇ ਸਾਰੇ ਵਿਅਕਤੀਆਂ ਨੂੰ ਭਾਗ ਲੈਣ ਲਈ ਉਤਸਾਹਿਤ ਕਰਨ ਲਈ, ਅਸੀਂ ਗੁਰੁ ਨਾਨਕ ਦਰਬਾਰ ਗੁਰਦੁਆਰਾ ਗਰੈਵਸੈਂਡ ਵਿਖੇ ਸਕ੍ਰੀਨਿੰਗ ਕਰ ਰਹੇ ਹਾਂ ਅਤੇ ਪੰਜਾਬੀ ਬੋਲਣ ਵਾਲੀ ਇਕ ਖੋਜੀ ਟੀਮ ਦੀ ਚੋਣ ਕੀਤੀ ਹੈ।

ਮੈਨੂੰ ਆਪਣੇ ਦਿਲ ਦੀ ਧੜਕਨ ਦੀ ਜਾਂਚ ਕਿਉਂ ਕਰਨੀ ਚਾਹੀਦੀ ਹੈ?

ਜੇਕਰ ਤੁਹਾਨੂੰ ਏਐਫ ਜਾਂ ਕਿਸੇ ਹੋਰ ਦਿਲ ਦੀ ਬਿਮਾਰੀ ਦਾ ਪਤਾ ਲਗਦਾ ਹੈ, ਤਾਂ ਤੁਸੀਂ ਅਤੇ ਤੁਹਾਡਾ ਡਾਕਟਰ ਇਸ ਬਾਰੇ ਫ਼ੈਸਲਾ ਕਰਨ ਦੇ ਯੋਗ ਹੋ ਸਕਦੇ ਹੋ ਕਿ ਇਸਦਾ ਇਲਾਜ ਕਿਵੇਂ ਕਰਨਾ ਹੈ। ਤੁਹਾਡੇ ਟੈਸਟ ਦੇ ਨਤੀਜੇ ਅਤੇ ਪ੍ਰਾਪਤ ਵਿਚਾਰਾਂ ਰਾਹੀਂ ਦੱਖਣ ਏਸ਼ੀਅਨ ਮੂਲ ਦੇ ਵਿਅਕਤੀਗਤ ਲੋਕਾਂ ਵਿਚਕਾਰ ਏਐਫ ਲਈ ਭਵਿਖ ਦੇ ਸਕ੍ਰੀਨਿੰਗ ਪ੍ਰੋਗਰਾਮ ਨੂੰ ਕਿਵੇਂ ਬਿਹਤਰ ਢੰਗ ਨਾਲ ਪੇਸ਼ ਕਰਨ ਅਤੇ ਮਾਪਣ ਲਈ ਸਾਡੇ ਅਧਿਐਨ ਨੂੰ ਯੋਗ ਬਣਾਉਣ ਵਿਚ ਮਦਦ ਹੋਵੇਗੀ।

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ਮੈਂ ਕਿਵੇਂ ਸ਼ਾਮਲ ਹੋ ਸਕਦਾ/ਸਕਦੀ ਹਾਂ?

ਪਹਿਲਾਂ ਇਹ ਪਤਾ ਕਰੋ ਕਿ ਤੁਸੀਂ ਹਿੱਸਾ ਲੈਣ ਦੇ ਯੋਗ ਹੋ:

- ਕੀ ਤੁਸੀਂ 18 ਸਾਲ ਜਾਂ ਵੱਧ ਉਮਰ ਦੇ ਬਾਲਗ਼ ਹੋ?
- ਜੇਕਰ ਤੁਸੀਂ ਪੇਸਮੇਕਰ ਜਾਂ ਕਾਰਡੀਅਕ ਡੀਫਿਬ੍ਰਿਲੇਟਰ ਦੀ ਵਰਤੋਂ **ਨਹੀਂ** ਕਰਦੇ ਹੋ, ਤਾਂ ਹਿੱਸਾ ਲੈ ਸਕਦੇ ਹੋ।
- ਕੀ ਤੁਹਾਡੀ ਜ਼ਿੰਦਗੀ ਗੰਭੀਰ ਬਿਮਾਰੀ ਕਾਰਣ ਅਖੀਰੀ ਮੋੜ ਤੇ ਤਾਂ ਨਹੀਂ ਹੈ? (ਮਿਸਾਲ ਲਈ ਕੈਂਸਰ ਵਜੋਂ ਇਕ ਮਹੀਨੇ ਤਕ ਜੀਉਣ ਦੀ ਉਮੀਦ)

ਜੇ ਤੁਸੀਂ ਸਾਰੇ ਪ੍ਰਸ਼ਨਾਂ ਦਾ ਜਵਾਬ ਹਾਂ ਵਿਚ ਦਿੱਤਾ ਹੈ, ਤਾਂ ਫਿਰ **11 ਤੋਂ 24 ਨਵੰਬਰ 2019** ਦੇ ਵਿਚਾਲੇ ਗੁਰਘਰ ਅੰਦਰ ਸਾਡੇ ਸਟੈਂਡ 'ਤੇ ਆਕੇ ਸਾਨੂੰ ਮਿਲੋ।

ਜੇ ਤੁਸੀਂ ਹੋਰ ਜਾਣਕਾਰੀ ਲੈਣੀ ਚਾਹੁੰਦੇ ਹੋ, ਤਾਂ ਕਿਰਪਾ ਕਰਕੇ ਆੱਨਲਾਈਨ 'ਤੇ ਮਰੀਜ ਬਾਰੇ ਜਾਣਕਾਰੀ ਦਿੰਦੀ ਪਤ੍ਰਿਕਾ ਪੜ੍ਹੋ (ਲਿੰਕ ਸ਼ਾਮਿਲ ਕਰੋ) ਜਾਂ ਸਾਡੇ ਸਟੈਂਡ ਤੋਂ ਇਕ ਪਤ੍ਰਿਕਾ ਲਵੋ।

ਸੰਪਰਕ ਕਰਨ ਦੇ ਵੇਰਵੇ

ਇਸ ਅਧਿਐਨ ਦੇ ਸੰਬੰਧ ਵਿਚ ਸਾਰੇ ਹੀ ਸਵਾਲਾਂ ਲਈ ਬਿਨਾਂ ਸੰਕੋਚ ਸੰਪਰਕ ਕਰੋ:

ਮਿਸਟਰ ਵਿਲਸ ਸੇਵਿਕਾਸ (Mr Vilius Savickas)

ਈਮੇਲ: afstudy@kent.ac.uk

ਟੈਲੀਫ਼ੋਨ: 01634 202935

ਜੇ ਤੋਹਾਨੂੰ ਅਧਿਐਨ ਬਾਰੇ ਕੋਈ ਚਿੰਤਾਵਾਂ ਜਾਂ ਸ਼ਿਕਾਇਤਾਂ ਹਨ, ਤਾਂ ਕਿਰਪਾ ਕਰਕੇ ਸੰਪਰਕ ਕਰੋ:

ਡਾ. ਟਰੂਡੀ ਥੋਮਸ (Dr Trudy Thomas)

ਈਮੇਲ:t.thomas@kent.ac.uk

ਟੈਲੀਫ਼ੋਨ: 01634 88 8909.'ਤੇ ਸੰਪਰਕ ਕਰੋ।

ਏਐਫ਼ ਬਾਰੇ ਹੋਰ ਵਧੇਰੇ ਜਾਣਕਾਰੀ ਲਈ, ਕ੍ਰਿਪਾ ਕਰਕੇ ਵੈਬਸਾਈਟ ਦੇਖੋ: www.afa.org.uk ਜਾਂ www.afa-international.org ਜਾਂ ਦ ਏਐਫ਼ ਅਸੋਸ਼ੀਏਸ਼ਨ (The AF Association) ਨਾਲ ਹੇਠ ਦਿੱਤੇ ਪਤੇ ਤੇ ਸੰਪਰਕ ਕਰੋ:

AF Association®
Unit 6B
Essex House
Cromwell Business Park
Chipping Norton
OX7 5SR
+44(0)1789 867502
info@afa.org.uk

AF Association
www.afa.org.uk

ਭਾਗ ਲੈਣ ਲਈ ਤੁਹਾਡਾ ਧੰਨਵਾਦ

University of Kent

Appendix 49 Participant information leaflet for atrial fibrillation screening within a South Asian community

medway school of pharmacy

PARTICIPANT INFORMATION LEAFLET

Title of Project: Atrial Fibrillation Screening using Single-lead ECG within a South Asian Community

Name of Researcher (s): Mr Vilius Savickas, Dr Sukvinder Bhamra, Dr Adrian Stewart, Dr Emma Veale, Dr Sarah Corlett, Prof Alistair Mathie, MPharm Undergraduates

If you are 18 years or over and interested in taking part in this study, you must understand why the study is being done and what it involves. Please take time to read the following information. Ask if anything is not clear or if you would like more information. Take time to decide if you want to take part or not.

Why is the study being done?
Atrial fibrillation (AF) is a heart condition, which results in an irregular and sometimes very fast heart beat. If you develop AF it means that your heart may not be working properly. However, if AF is detected early, the treatment can prevent serious complications such as heart failure and stroke. This study aims to find out if trained pharmacy students can successfully use mobile and painless electrocardiogram (ECG) devices to accurately detect AF in individuals of South Asian origin. In order to encourage all individuals from the local community to participate, we are carrying out the screening at the Guru Nanak Darbar (Gurdwara) and have intentionally selected a research team fluent in Punjabi.

Do I have to take part?
No. It is up to you to decide whether or not to take part. Even if you agree to take part, you can change your mind at any time without giving any reason. If you decide not to take part in the study, your medical care will not be affected in any way.

If I do take part, what would I have to do and what would be done to me?
If you do take part, you will be offered a free heart beat check with a pharmacy student under the supervision of a clinical pharmacist. Before the check, you will be asked to confirm your eligibility and sign a consent form. The test will be carried out at a desk within the Gurdwara using a small, painless ECG device. During the check you will be asked to hold two fingers of each hand on two metal pads to record an ECG trace over 30 seconds as shown in the picture below. The student will also ask you a few questions about your lifestyle, past medical history and any medicines you may be taking.

Mobile ECG test

If you are found to have a possible AF or if the test is inconclusive, the student will give you a letter advising to make an appointment at your doctor's surgery to either confirm or reject this provisional diagnosis. You will also be given an optional feedback questionnaire and a form to record any outcomes of your appointment at the surgery, which you may wish to send back to the University using a pre-paid envelope provided.

AFA AFAssociation www.afa.org.uk

University of Kent

Are there any risks if I take part?
This study is not associated with any significant risks. In the unlikely event where you feel uncomfortable during the appointment, you can stop at any time. Since we are carrying out the test within the Gurdwara, there is a chance that people may see you be tested. However, we can guarantee your personal information and results will be protected as described below.

Are there any benefits if I take part?
You will have your heart beat checked to confirm that it is normal. If you are diagnosed with AF or another heart condition as a result of the test, you and your doctor will be able to decide on how to treat it. Your test results and views will also enable our study to determine how best to deliver and measure future screening programmes for AF amongst the individuals of South Asian origin.

Will anyone know that I've taken part?
We will not tell anyone that you have taken part in the study. Your doctor will not be informed about the result of the test unless you share the letter given to you with the surgery.

What will happen to the results?
All data collected as part of the study will be kept strictly confidential and stored securely at the Medway School of Pharmacy for 5 years in line with the Data Protection Act 2018 and the European Union General Data Protection Regulation. All data except the consent form you sign before the appointment will be anonymised by assigning you a unique number. This data will be used in future reports and publications however it will not be possible to identify you. If you wish receive information about study findings, please email afstudy@kent.ac.uk. More information about the University's use of personal data can be found here: https://research.kent.ac.uk/researchservices/wp-content/uploads/sites/51/2018/05/GDPR-Privacy-Notice-Research.pdf.

Who is organising and funding the study?
The study is carried out by researchers at the Medway School of Pharmacy (University of Kent) in conjunction with the AF Association as part of their MPharm and PhD research projects. It is funded by the Medway School of Pharmacy and the University of Kent.

Who should I contact if I want to know more about the study?
The PDAF Study Team by email: afstudy@kent.ac.uk or by phone: 01634 202935 or by post: Medway School of Pharmacy, Anson Building, Central Avenue, Chatham, ME4 4TB.

Who should I contact if I have any concerns about the study or the way it has been conducted?
If you have concerns about this study, please contact Dr Trudy Thomas, Senior Lecturer by email t.thomas@kent.ac.uk or by phone/post as listed above.

For more information about AF, please visit: www.afa.org.uk or www.afa-international.org or contact the AF Association: 01789 867502 or info@afa.org.uk.

Thank you for taking time to consider taking part in this study.

This project has been looked at and approved by the
Medway School of Pharmacy Research Ethics Committee

medway school of pharmacy

ਭਾਗ ਲੈਣ ਵਾਲੇ ਲਈ ਜਾਣਕਾਰੀ ਪਤ੍ਰਿਕਾ

ਪ੍ਰੋਜੈਕਟ ਦਾ ਸਿਰਲੇਖ: ਇਕ ਦੱਖਣ ਏਸ਼ੀਅਨ ਕਮਿਊਨਿਟੀ ਅੰਦਰ ਸਿੰਗਲ ਲੀਡ ਈਸੀਜੀ ਦੀ ਵਰਤੋਂ ਨਾਲ ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰਿਨਿੰਗ

ਖੋਜਕਾਰ(ਰਾਂ) ਦਾ(ਦੇ) ਨਾਮ: ਵਿਲੀਅਸ ਸਵੀਕਾਸ, ਡਾ. ਸੁਕਵਿੰਦਰ ਭਮਰਾ, ਡਾ. ਅਡੀਰੀਅਨ ਸਟਯੂਏਟ, ਡਾ. ਐਮਾ ਵੇਲ੍ਹ, ਡਾ. ਸ਼ੇਰ੍ਹਾ ਕੋਰਲਟ, ਪ੍ਰੋਫ਼ੈਸਰ ਐਲੀਸਟਰ ਮੈਥੀ, ਐਮਫਾਰਮ ਅਨਡਰਗ੍ਰੈਜੂਏਟ

ਜੇ ਤੁਸੀਂ 18 ਸਾਲ ਜਾਂ ਇਸ ਤੋਂ ਵੱਧ ਉਮਰ ਦੇ ਹੋ ਅਤੇ ਇਸ ਅਧਿਐਨ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਵਿਚ ਦਿਲਚਸਪ ਹੋ, ਤਾਂ ਤੁਹਾਨੂੰ ਇਹ ਸਮਝਣਾ ਚਾਹੀਦਾ ਹੈ ਕਿ ਅਧਿਐਨ ਕਿਉਂ ਕੀਤਾ ਜਾ ਰਿਹਾ ਹੈ ਅਤੇ ਇਸ ਵਿਚ ਕੀ ਸ਼ਾਮਲ ਹੈ। ਕ੍ਰਿਪਾ ਕਰਕੇ ਹੇਠਾਂ ਦਿੱਤੀ ਜਾਣਕਾਰੀ ਪੜ੍ਹਨ ਲਈ ਸਮਾਂ ਕਢੋ। ਕੁੱਝ ਸਪਸ਼ਟ ਨਹੀਂ ਹੈ ਜਾਂ ਤੁਸੀਂ ਵਧੇਰੇ ਜਾਣਕਾਰੀ ਚਾਹੁੰਦੇ ਹੋ, ਤਾਂ ਇਸ ਬਾਰੇ ਪੁੱਛੋ।

ਅਧਿਐਨ ਕਿਉਂ ਕੀਤਾ ਜਾ ਰਿਹਾ ਹੈ?
ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ (ਏਐਫ) ਦਿਲ ਦੀ ਉਹ ਸਥਿਤੀ ਹੈ ਜਿਸ ਦੇ ਨਤੀਜੇ ਵਜੋਂ ਦਿਲ ਦੀ ਧੜਕਨ ਅਨਿਯਮਿਤ ਅਤੇ ਕਈ ਵਾਰ ਬਹੁਤ ਤੇਜ਼ ਹੋ ਜਾਂਦੀ ਹੈ। ਜੇ ਤੁਹਾਡੇ ਵਿਚ ਏਐਫ਼ ਦਾ ਵਿਕਾਸ ਹੋਇਆ ਹੈ, ਤਾਂ ਇਸ ਦਾ ਭਾਵ ਹੋ ਸਕਦਾ ਹੈ ਕਿ ਤੁਹਾਡਾ ਦਿਲ ਸਹੀ ਢੰਗ ਨਾਲ ਕੰਮ ਨਹੀਂ ਕਰ ਰਿਹਾ। ਹਾਲਾਂਕਿ ਏਐਫ਼ ਦਾ ਜੇ ਜਲਦੀ ਪਤਾ ਲੱਗ ਜਾਂਦਾ ਹੈ, ਤਾਂ ਇਲਾਜ ਰਾਹੀਂ ਗੰਭੀਰ ਜਟਿਲਤਾਵਾਂ ਨੂੰ ਰੋਕਿਆ ਜਾ ਸਕਦਾ ਹੈ ਜਿਵੇਂ ਕਿ ਦਿਲ ਦੀ ਧੜਕਨ ਦਾ ਰੁਕ ਜਾਣਾ ਜਾਂ ਸਟ੍ਰੋਕ। ਇਸ ਅਧਿਐਨ ਦਾ ਉਦੇਸ਼ ਇਹ ਪਤਾ ਕਰਨਾ ਹੈ ਕਿ ਸਿਖਿਅਤ ਫ਼ਾਰਮੇਸੀ ਵਿਦਿਆਰਥੀ ਦੱਖਣੀ ਏਸ਼ੀਆ ਦੇ ਮੂਲ ਵਿਅਕਤੀਆਂ ਦੀ ਏਐਫ ਦੀ ਸਹੀ ਪਛਾਣ ਕਰਨ ਲਈ ਸਫ਼ਲਤਾ ਨਾਲ ਮੋਬਾਇਲ ਅਤੇ ਦਰਦ ਰਹਿਤ ਇਲੈਕਟ੍ਰੋਕਾਰਡੀਅਗਰਾਮ (ਈਸੀਜੀ) ਯੰਤਰਾਂ ਦਾ ਇਸਤੇਮਾਲ ਕਰ ਸਕਦੇ ਹਨ ਜਾਂ ਨਹੀਂ।ਸਥਾਨਕ ਭਾਈਚਾਰੇ ਤੋਂ ਸਾਰੇ ਵਿਅਕਤੀਆਂ ਨੂੰ ਭਾਗ ਲੈਣ ਲਈ ਉਤਸਾਹਿਤ ਕਰਨ ਲਈ, ਅਸੀਂ ਗੁਰੁ ਨਾਨਕ ਦਰਬਾਰ (ਗੁਰਦੁਆਰਾ) ਵਿਖੇ ਸਕ੍ਰਿਨਿੰਗ ਕਰ ਰਹੇ ਹਾਂ ਅਤੇ ਵਿਸ਼ੇਸ਼ ਤੌਰ 'ਤੇ ਪੰਜਾਬੀ ਬੋਲਣ ਵਾਲੀ ਇਕ ਖੋਜੀ ਟੀਮ ਨੂੰ ਚੁਣਿਆ ਹੈ।

ਕੀ ਮੈਨੂੰ ਭਾਗ ਲੈਣ ਦੀ ਲੋੜ ਹੈ?
ਨਹੀਂ। ਇਹ ਫ਼ੈਸਲਾ ਕਰਨਾ ਤੁਹਾਡੀ ਜ਼ਿਮੇਵਾਰੀ ਹੈ ਕਿ ਤੁਸੀਂ ਹਿੱਸਾ ਲੈਣਾ ਹੈ ਜਾਂ ਨਹੀਂ। ਭਾਵੇਂ ਤੁਸੀਂ ਹਿੱਸਾ ਲੈਣ ਲਈ ਸਹਿਮਤ ਹੋ, ਤੁਸੀਂ ਕਿਸੇ ਵੀ ਕਾਰਨ ਤੋਂ ਬਗੈਰ ਕਿਸੇ ਵੀ ਸਮੇਂ ਆਪਣਾ ਮਨ ਬਦਲ ਸਕਦੇ ਹੋ। ਜੇ ਤੁਸੀਂ ਅਧਿਐਨ ਵਿਚ ਹਿੱਸਾ ਨਾ ਲੈਣ ਦਾ ਫ਼ੈਸਲਾ ਕਰਦੇ ਹੋ, ਤਾਂ ਤੁਹਾਡੀ ਡਾਕਟਰੀ ਦੇਖਭਾਲ ਕਿਸੇ ਵੀ ਤਰ੍ਹਾਂ ਪ੍ਰਭਾਵਿਤ ਨਹੀਂ ਹੋਵੇਗੀ।

ਜੇ ਮੈਂ ਭਾਗ ਲੈਂਦਾ ਹਾਂ, ਤਾਂ ਮੈਨੂੰ ਕੀ ਕਰਨਾ ਪਵੇਗਾ ਅਤੇ ਮੇਰੇ ਨਾਲ ਕੀ ਕੀਤਾ ਜਾਵੇਗਾ?
ਜੇ ਤੁਸੀਂ ਹਿੱਸਾ ਲੈਂਦੇ ਹੋ, ਤਾਂ ਤੁਹਾਨੂੰ ਫ਼ਾਰਮਾਸਿਸਟ ਦੀ ਨਿਗਰਾਨੀ ਹੇਠ ਇੱਕ ਫ਼ਾਰਮੇਸੀ ਵਿਦਿਆਰਥੀ ਨਾਲ ਦਿਲ ਦੀ ਧੜਕਨ ਦੀ ਮੁਫ਼ਤ ਜਾਂਚ ਕਰਨ ਦੀ ਪੇਸ਼ਕਸ਼ ਕੀਤੀ ਜਾਵੇਗੀ। ਜਾਂਚ ਤੋਂ ਪਹਿਲਾਂ, ਤੁਹਾਨੂੰ ਆਪਣੀ ਯੋਗਤਾ ਦੀ ਪੁਸ਼ਟੀ ਕਰਨ ਅਤੇ ਇੱਕ ਸਹਿਮਤੀ ਫ਼ਾਰਮ ਤੇ ਹਸਤਾਖਰ ਕਰਨ ਲਈ ਕਿਹਾ ਜਾਵੇਗਾ। ਇਹ ਜਾਂਚ ਇੱਕ ਛੋਟੇ ਜਿਹੇ ਪੀੜਹੀਣ ਈਸੀਜੀ ਯੰਤਰ ਨਾਲ ਗੁਰਦੁਆਰੇ ਵਿਚ ਇੱਕ ਡੈਸਕ 'ਤੇ ਕੀਤੀ ਜਾਵੇਗੀ। ਜਾਂਚ ਦੇ ਦੌਰਾਨ ਤੁਹਾਨੂੰ ਦੋ ਮੈਟਲ ਦੇ ਪੈਡ 'ਤੇ ਦੋ ਹੱਥਾਂ ਦੀਆਂ ਦੋ ਉਂਗਲਾਂ ਰੱਖਣ ਲਈ ਕਿਹਾ ਜਾਵੇਗਾ ਤਾਂ ਕਿ ਈਸੀਜੀ ਟਰੇਸ ਨੂੰ 30 ਸਕਿੰਟਾਂ ਤਕ ਰਿਕਾਰਡ ਕੀਤਾ ਜਾ ਸਕੇ ਜਿਵੇਂ ਕਿ ਹੇਠ ਦਿੱਤੇ ਫ਼ੋਟੋ ਵਿਚ ਦਿਖਾਇਆ ਗਿਆ ਹੈ। ਵਿਦਿਆਰਥੀ ਤੁਹਾਨੂੰ ਆਪਣੀ ਜੀਵਨਸ਼ੈਲੀ, ਪਿਛਲੇ ਡਾਕਟਰੀ ਇਤਿਹਾਸ ਅਤੇ ਜੋ ਵੀ ਦਵਾਈਆਂ ਲੈ ਰਹੇ ਹੋ ਬਾਰੇ ਕੁੱਝ ਸਵਾਲ ਪੁੱਛੇਗਾ।

ਮੋਬਾਈਲ ਈਸੀਜੀ ਜਾਂਚ

ਸੰਭਵ ਤੌਰ 'ਤੇ ਜੇ ਤੁਹਾਨੂੰ ਏਐਫ਼ ਹੈ ਜਾਂ ਜਾਂਚ ਤੋਂ ਕੁੱਝ ਅਨਿਸ਼ਚਿਤ ਹੈ, ਤਾਂ ਤੁਹਾਨੂੰ ਇੱਕ ਚਿੱਠੀ ਦਿੱਤੀ ਜਾਵੇਗੀ ਜੋ ਕਿ ਇਸ ਤਬਾਦਲੇ ਦੀ ਪੁਸ਼ਟੀ ਜਾਂ ਅਸ਼ਵਿਕਾਰ ਕਰਨ ਲਈ ਤੁਹਾਡੇ ਡਾਕਟਰ ਦੀ ਸਰਜਰੀ ਲਈ ਅਪਾਇੰਟਮੈਂਟ ਬਣਾਉਣ ਦੀ ਸਲਾਹ ਬਾਰੇ ਹੋਵੇਗੀ। ਤੁਹਾਨੂੰ ਇੱਕ ਵਿਕਲਪਿਕ ਫ਼ੀਡਬੈਕ ਪ੍ਰਸ਼ਨਾਵਲੀ ਅਤੇ ਸਰਜਰੀ ਵਿਚ ਆਪਣੀ ਅਪਾਇੰਟਮੈਂਟ ਦੇ ਕਿਸੇ ਵੀ ਨਤੀਜੇ ਨੂੰ ਰਿਕਾਰਡ ਕਰਨ ਲਈ ਇੱਕ ਫ਼ਾਰਮ ਵੀ ਦਿੱਤਾ ਜਾਵੇਗਾ, ਜਿਸ ਨੂੰ ਤੁਸੀਂ ਪ੍ਰਦਾਨ ਕੀਤੇ ਗਏ ਪ੍ਰੀ-ਪੇਡ ਲਿਫ਼ਾਫ਼ੇ ਦੀ ਵਰਤੋਂ ਕਰਕੇ ਯੂਨਿਵਰਸਿਟੀ ਨੂੰ ਵਾਪਸ ਭੇਜ ਸਕਦੇ ਹੋ।

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ਜੇ ਮੈਂ ਹਿੱਸਾ ਲੈਂਦਾ ਹਾਂ, ਤਾਂ ਕੀ ਕੋਈ ਖ਼ਤਰਾ ਹੈ?
ਇਹ ਅਧਿਐਨ ਕਿਸੇ ਵੀ ਮਹੱਵਪੂਰਣ ਖ਼ਤਰੇ ਨਾਲ ਜੁੜਿਆ ਨਹੀਂ ਹੈ। ਅਸੰਭਵ ਘਟਨਾ ਵਿਚ ਜਿੱਥੇ ਤੁਸੀਂ ਅਪਾਇੰਟਮੰਟ ਦੌਰਾਨ ਬੇਆਰਾਮੀ ਮਹਿਸੂਸ ਕਰਦੇ ਹੋ, ਤਾਂ ਤੁਸੀਂ ਕਿਸੇ ਵੀ ਸਮੇਂ ਹਿੱਸਾ ਲੈਣਾ ਬੰਦ ਕਰ ਸਕਦੇ ਹੋ। ਅਸੀਂ ਜਾਂਚ ਗੁਰਦੁਆਰੇ ਦੇ ਅੰਦਰ ਕਰ ਰਹੇ ਹਾਂ ਇਸ ਕਾਰਣ ਹੋ ਸਕਦਾ ਹੈ ਕਿ ਤੁਹਾਡੀ ਹੁੰਦੀ ਜਾਂਚ ਨੂੰ ਲੋਕੀ ਦੇਖ ਸਕਦੇ ਹਨ। ਹਾਲਾਂਕਿ ਅਸੀਂ ਤੁਹਾਨੂੰ ਇਹ ਵਿਸ਼ਵਾਸ ਦੇ ਸਕਦੇ ਹਾਂ ਕਿ ਤੁਹਾਡੀ ਵਿਅਕਤੀਗਤ ਜਾਣਕਾਰੀ ਅਤੇ ਨਤੀਜੇ ਹੇਠਾਂ ਦਿੱਤੇ ਅਨੁਸਾਰ ਸੁਰਖ਼ਿਅਤ ਕੀਤੇ ਜਾਣਗੇ।

ਮੇਰੇ ਹਿੱਸਾ ਲੈਣ ਨਾਲ ਕੀ ਕੋਈ ਫ਼ਾਇਦਾ ਹੈ?
ਤੁਸੀਂ ਆਪਣੇ ਦਿਲ ਦੀ ਧੜਕਨ ਦੀ ਜਾਂਚ ਇਹ ਯਕੀਨੀ ਕਰਨ ਲਈ ਕਰਾਵੋਗੇ ਕਿ ਇਹ ਆਮ ਹੈ। ਜਾਂਚ ਦੇ ਨਤੀਜੇ ਵਜੋਂ ਜੇ ਤੁਹਾਨੂੰ ਏਐਫ਼ ਜਾਂ ਕਿਸੇ ਹੋਰ ਦਿਲ ਦੀ ਸਥਿਤੀ ਦਾ ਪਤਾ ਲਗਾਇਆ ਜਾਂਦਾ ਹੈ, ਤਾਂ ਤੁਸੀਂ ਅਤੇ ਤੁਹਾਡਾ ਡਾਕਟਰ ਇਸ ਬਾਰੇ ਫ਼ੈਸਲਾ ਕਰਨ ਦੇ ਯੋਗ ਹੋ ਸਕਦੇ ਹੋ ਕਿ ਇਹਦਾ ਇਲਾਜ ਕਿਵੇਂ ਕਰਨਾ ਹੈ। ਤੁਹਾਡੀ ਜਾਂਚ ਦੇ ਨਤੀਜੇ ਅਤੇ ਵਿਚਾਰਾਂ ਰਾਹੀਂ ਦੱਖਣ ਏਸ਼ੀਅਨ ਮੂਲ ਦੇ ਵਿਅਕਤੀਆਂ ਵਿਚਕਾਰ ਏਐਫ਼ ਲਈ ਭਵਿਖ ਦੇ ਸਕ੍ਰਿਨਿੰਗ ਪ੍ਰੋਗਰਾਮਾਂ ਨੂੰ ਕਿਵੇਂ ਬਿਹਤਰ ਢੰਗ ਨਾਲ ਪੇਸ਼ ਕਰਨ ਅਤੇ ਮਾਪਣ ਲਈ ਸਾਡੇ ਅਧਿਐਨ ਨੂੰ ਯੋਗ ਬਣਾਇਆ ਜਾਵੇਗਾ।

ਕੀ ਕਿਸੇ ਨੂੰ ਪਤਾ ਹੋਵੇਗਾ ਕਿ ਮੈਂ ਭਾਗ ਲਿਆ ਹੈ?
ਅਸੀਂ ਕਿਸੇ ਨੂੰ ਨਹੀਂ ਦਸਾਂਗੇ ਕਿ ਤੁਸੀਂ ਅਧਿਐਨ ਵਿਚ ਹਿੱਸਾ ਲਿਆ ਹੈ। ਤੁਹਾਡੇ ਡਾਕਟਰ ਨੂੰ ਜਾਂਚ ਦੇ ਨਤੀਜਿਆਂ ਬਾਰੇ ਸੂਚਿਤ ਨਹੀਂ ਕੀਤਾ ਜਾਵੇਗਾ ਜੱਦੋਂ ਤੱਕ ਤੁਸੀਂ ਸਰਜਰੀ ਨਾਲ ਦਿੱਤੇ ਪੱਤਰ ਨੂੰ ਨਹੀਂ ਸਾਂਝਾ ਕਰਦੇ ਹੋ।

ਨਤੀਜਿਆਂ ਦਾ ਕੀ ਹੋਵੇਗਾ?
ਅਧਿਐਨ ਦੇ ਹਿੱਸੇ ਦੇ ਰੂਪ ਵਿੱਚ ਇਕੱਤਰ ਕੀਤੇ ਗਏ ਸਾਰੇ ਡੇਟਾ ਨੂੰ ਰਾਖਵੇਂ ਰੂਪ ਵਿਚ ਗੁਪਤ ਰੱਖਿਆ ਜਾਵੇਗਾ ਅਤੇ ਡੇਟਾ ਪ੍ਰੋਟੈਕਸਨ ਐਕਟ 2018 ਅਤੇ ਯੂਰਪੀ ਯੂਨੀਅਨ ਜਨਰਲ ਡੇਟਾ ਪ੍ਰੋਟੈਕਸਨ ਰੈਗੂਲੇਸ਼ਨ ਦੇ ਅਨੁਸਾਰ 5 ਸਾਲਾਂ ਲਈ ਮੀਡਵੇ ਸਕੂਲ ਆੱਫ਼ ਫ਼ਾਰਮੇਸੀ ਵਿੱਚ ਸੁੱਰਖਿਅਤ ਢੰਗ ਨਾਲ ਰੱਖਿਆ ਜਾਵੇਗਾ। ਮੁਲਾਕਾਤ ਤੋਂ ਪਹਿਲਾਂ ਤੁਹਾਡੇ ਦੁਆਰਾ ਹਸਤਾਖਰ ਕੀਤੇ ਗਏ ਸਹਿਮਤੀ ਨੂੰ ਛੱਡ ਕੇ ਸਾਰੀ ਡੇਟਾ ਤੁਹਾਨੂੰ ਇੱਕ ਵਿਲਖਣ ਨੰਬਰ ਦੇ ਕੇ ਅਗਿਆਤ ਕਰ ਦਿੱਤੀ ਜਾਵੇਗੀ। ਇਹ ਡੇਟਾ ਭੱਵਿਖ ਦੀਆਂ ਰਿਪੋਰਟਾਂ ਅਤੇ ਪ੍ਰਕਾਸ਼ਨਾਂ ਵਿੱਚ ਵਰਤੀ ਜਾਵੇਗੀ, ਪਰੰਤੂ ਇਸ ਨਾਲ ਤੁਹਾਨੂੰ ਪਛਾਣਨਾ ਸੰਭਵ ਨਹੀਂ ਹੋਵੇਗਾ। ਜੇ ਤੁਸੀਂ ਅਧਿਐਨ ਦੇ ਨਤੀਜਿਆਂ ਬਾਰੇ ਜਾਣਕਾਰੀ ਪ੍ਰਾਪਤ ਕਰਨਾ ਚਾਹੁੰਦੇ ਹੋ, ਤਾਂ ਕਿਰਪਾ ਕਰਕੇ afstudy@kent.ac.uk ਤੇ ਈਮੇਲ ਕਰੋ। ਯੂਨੀਵਰਸਿਟੀ ਦੇ ਨਿਜੀ ਡੇਟਾ ਦੀ ਵਰਤੋਂ ਬਾਰੇ ਹੋਰ ਜਾਣਕਾਰੀ ਇਥੇ ਮਿਲ ਸਕਦੀ ਹੈ: https://research.kent.ac.uk/researchservices/wp-content/uploads/sites/51/2018/05/GDPR-Privacy-Notice-Research.pdf.

ਅਧਿਐਨ ਲਈ ਕੌਣ ਪ੍ਰਬੰਧ ਅਤੇ ਫ਼ੰਡਿੰਗ ਕਰ ਰਿਹਾ ਹੈ?
ਖੋਜ ਦਾ ਅਧਿਐਨ ਮੀਡਵੇ ਸਕੂਲ ਆੱਫ਼ ਫ਼ਾਰਮੇਸੀ (ਯੂਨੀਵਰਸਿਟੀ ਆੱਫ਼ ਕੈਨਟ) ਦੇ ਖੋਜਕਰਤਾਵਾਂ ਦੁਆਰਾ ਕੀਤਾ ਜਾਂਦਾ ਹੈ ਜੋ ਉਹਨਾਂ ਦੇ ਐਮਫ਼ੱਾਰਮ ਅਤੇ ਪੀਐਚਡੀ ਖੋਜ ਪ੍ਰਾਜੈਕਟਾਂ ਦੇ ਹਿੱਸੇ ਵਜੋਂ ਕੀਤਾ ਜਾਂਦਾ ਹੈ। ਇਸ ਨੂੰ ਮੀਡਵੇ ਸਕੂਲ ਆੱਫ਼ ਫ਼ਾਰਮੇਮੀ ਅਤੇ ਯੂਨੀਵਰਸਿਟੀ ਆੱਫ਼ ਕੈਨਟ ਦੁਆਰਾ ਫ਼ੰਡ ਕੀਤਾ ਜਾਂਦਾ ਹੈ।

ਜੇ ਮੈਂ ਅਧਿਐਨ ਬਾਰੇ ਹੋਰ ਜਾਣਨਾ ਚਾਹੁੰਦਾ ਹਾਂ, ਤਾਂ ਮੈਨੂੰ ਕਿਸ ਨਾਲ ਸੰਪਰਕ ਕਰਨਾ ਚਾਹੀਦਾ ਹੈ?
ਵਿਲਿਅਸ ਸਵੀਕਾਸ ਨੂੰ ਈਮੇਲ afstudy@kent.ac.uk ਦੁਆਰਾ ਜਾਂ ਫ਼ੋਨ 01634 202935 ਰਾਹੀਂ ਜਾਂ ਡਾਕ ਰਾਹੀਂ Medway School of Pharmacy, Anson Building, Central Avenue, Chatham, ME4 4TB ਸੰਪਰਕ ਕਰੋ।

ਜੇ ਮੈਨੂੰ ਅਧਿਐਨ ਜਾਂ ਜਿਸ ਤਰੀਕੇ ਨਾਲ ਜਾਂਚ ਕੀਤੀ ਗਈ ਹੈ ਬਾਰੇ ਕੋਈ ਚਿੰਤਾਵਾਂ ਹੋਣ, ਤਾਂ ਮੈਨੂੰ ਕਿਸ ਨਾਲ ਸੰਪਰਕ ਕਰਨਾ ਚਾਹੀਦਾ ਹੈ?
ਜੇ ਤੁਹਾਨੂੰ ਇਸ ਅਧਿਐਨ ਬਾਰੇ ਚਿੰਤਾਵਾਂ ਹਨ, ਤਾਂ ਕ੍ਰਿਪਾ ਕਰਕੇ ਡਾ. ਟਰੂਡੀ ਥੱਾਮਸ ਸੀਨੀਅਰ ਲੈਕਚਰਰ ਨਾਲ ਈਮੇਲ t.thomas@kent.ac.uk ਰਾਹੀਂ ਜਾਂ ਉਪਰ ਦਿੱਤੇ ਫ਼ੋਨ/ਡਾਕ ਰਾਹੀਂ ਸੰਪਰਕ ਕਰੋ।

ਏਐਫ਼ ਬਾਰੇ ਹੋਰ ਵਧੇਰੇ ਜਾਣਕਾਰੀ ਲਈ, ਕ੍ਰਿਪਾ ਕਰਕੇ ਵੈਬਸਾਈਟ ਦੇਖੋ: www.afa.org.uk **ਜਾਂ** www.afa-international.org **ਜਾਂ ਦ ਏਐਫ਼ ਅਸੋਸ਼ੀਏਸ਼ਨ** (The AF Association) **ਨਾਲ ਟੈਲੀਫ਼ੋਨ ਨੰਬਰ:** 01789 867502 **'ਤੇ ਜਾਂ** info@afa.org.uk **ਨਾਲ ਸੰਪਰਕ ਕਰੋ।.**

ਅਧਿਐਨ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਸੋਚਣ ਬਾਰੇ ਸਮਾਂ ਦੇਣ ਲਈ ਤੁਹਾਡਾ ਧੰਨਵਾਦ।

This project has been looked at and approved by the Medway School of Pharmacy Research Ethics Committee

Appendix 50 Consent form for participants of atrial fibrillation screening within a South Asian community

medway school of pharmacy

CONSENT FORM FOR ATRIAL FIBRILLATION SCREENING

Atrial Fibrillation Screening using Single-lead ECG within a South Asian Community

Name of researcher: The PDAF Study Team (afstudy@kent.ac.uk)
Participant's UPIN:

I have read and understand the **information provided** for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	Initial Here
I have read the **eligibility criteria** and can confirm that I am eligible to participate in this study.	Initial Here
I understand that my **participation is voluntary** and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. If I decide to withdraw, any data collected up to the point of withdrawal will be retained.	Initial Here
I understand that any **personal information** collected during the study will be anonymised and remain confidential.	Initial Here
I understand that data collected during the study may be used in **publications and reports**, but that these will be anonymised and not traceable to me.	Initial Here
I agree to participate in the **atrial fibrillation screening study**.	Initial Here

Name of Participant (Print)	Signature	Date

Name of person taking consent	Signature	Date

(if different from the researcher) Where possible, this is normally signed and dated in presence of the participant.

Lead researcher	Signature	Date

AF Association www.afa.org.uk University of Kent

medway school of pharmacy

ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰਿਨਿੰਗ ਲਈ ਮਨਜ਼ੂਰੀ ਫ਼ੱਰਮ

ਦੱਖਣ ਏਸ਼ੀਅਨ ਕਮਿਊਨਿਟੀ ਅੰਦਰ ਸਿੰਗਲ ਲੀਡ ਈਸੀਜੀ ਦੀ ਵਰਤੋਂ ਨਾਲ ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰਿਨਿੰਗ

ਖੋਜਕਾਰ ਦਾ ਨਾਮ: ਵਿਲੀਅਸ ਸਵੀਕਾਸ (afstudy@kent.ac.uk)
ਭਾਗੀਦਾਰ ਦੀ ਯੂਪੀਨ (UPIN)

ਮੈਂ ਉਪਰ ਦਿੱਤੇ ਅਧਿਐਨ ਲਈ ਦਿੱਤੀ ਜਾਣਕਾਰੀ ਨੂੰ ਪੜ੍ਹ ਅਤੇ ਸਮਝ ਲਿਆ ਹੈ। ਮੈਨੂੰ ਜਾਣਕਾਰੀ ਬਾਰੇ ਵਿਚਾਰ ਕਰਨ ਅਤੇ ਸਵਾਲ ਪੁੱਛਣ ਦਾ ਮੌਕਾ ਮਿਲਿਆ ਅਤੇ ਇਨ੍ਹਾਂ ਦੇ ਤਸੱਲੀਬਖਸ ਜਵਾਬ ਪ੍ਰਾਪਤ ਹੋਏ ਹਨ। ਮੈਂ ਪਾਤਰਤਾ ਦੇ ਮਾਪਦੰਡ ਨੂੰ ਪੜ੍ਹ ਲਿਆ ਹੈ ਅਤੇ ਇਹ ਪੁਸ਼ਟੀ ਕਰ ਸਕਦਾ ਹਾਂ ਕਿ ਮੈਂ ਇਸ ਅਧਿਐਨ ਵਿੱਚ ਹਿੱਸਾ ਲੈਣ ਦੇ ਯੋਗ ਹਾਂ। ਮੈਂ ਸਮਝਦਾ/ਸਮਝਦੀ ਹਾਂ ਕਿ ਮੇਰੀ ਸਮੂਲੀਅਤ ਸਵੈ-ਇਛੱਕ ਹੈ ਅਤੇ ਕਿਸੇ ਵੀ ਸਮੇਂ ਬਿਨਾਂ ਕਾਰਣ ਦਸੇ, ਬਿਨਾਂ ਕਿਸੇ ਡਾਕਟਰੀ ਦੇਖਭਾਲ ਜਾਂ ਕਾਨੂੰਨੀ ਹੱਕਾਂ ਨੂੰ ਪ੍ਰਭਾਵਿਤ ਕੀਤੇ ਬਿਨਾਂ ਇਹ ਅਧਿਐਨ ਛੱਡਣ ਲਈ ਆਜ਼ਾਦ ਹਾਂ। ਜੇ ਮੈਂ ਅਧਿਐਨ ਛੱਡਣ ਦਾ ਫ਼ੈਸਲਾ ਕਰ ਲਿਆ ਹੈ, ਤਾਂ ਛੱਡਣ ਤੱਕ ਮੇਰੇ ਸੰਬੰਧੀ ਜਿਹੜੀ ਵੀ ਜਾਣਕਾਰੀ ਪ੍ਰਾਪਤ ਹੋਈ ਹੈ ਉਹ ਕਾਇਮ ਰੱਖੀ ਜਾਵੇਗੀ।	Initial Here
ਮੈਂ ਸਮਝਦਾ/ਸਮਝਦੀ ਹਾਂ ਕਿ ਅਧਿਐਨ ਦੌਰਾਨ ਇਕੱਠੀ ਕੀਤੀ ਗਈ ਕੋਈ ਵੀ ਨਿੱਜੀ ਜਾਣਕਾਰੀ ਗੁਮਨਾਮ ਹੋਵੇਗੀ ਅਤੇ ਗੁਪਤ ਰੱਖੀ ਜਾਵੇਗੀ।	Initial Here
ਮੈਂ ਸਮਝਦਾ/ਸਮਝਦੀ ਹਾਂ ਕਿ ਅਧਿਐਨ ਸਮੇਂ ਇਕੱਤਰ ਕੀਤੀ ਗਈ ਡੇਟਾ ਦੀ ਵਰਤੋਂ ਪ੍ਰਕਾਸ਼ਨਾਂ ਅਤੇ ਰਿਪੋਰਟਾਂ ਵਿੱਚ ਕੀਤੀ ਜਾ ਸਕਦੀ ਹੈ, ਪਰ ਇਹ ਨਾਮਾਂਕਿਤ ਨਹੀਂ ਹੋਵੇਗੀ ਅਤੇ ਮੇਰੇ ਲਈ ਖੋਜਣਯੋਗ ਨਹੀਂ ਹੋਵੇਗੀ। ਮੈਂ ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰਿਨਿੰਗ ਅਧਿਐਨ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਸਹਿਮਤ ਹਾਂ।	Initial Here

ਭਾਗ ਲੈਣ ਵਾਲੇ ਦਾ ਨਾਮ (ਲਿਖਤ) ਹਸਤਾਖਰ ਮਿਤੀ

ਸਹਿਮਤੀ ਲੈ ਰਹੇ ਵਿਅਕਤੀ ਦਾ ਨ।ਮ ਹਸਤਾਖਰ ਮਿਤੀ

(ਜੇ ਖੋਜਕਾਰ ਤੋਂ ਵੱਖਰੀ ਹੈ) ਜਿਵੇਂ ਵੀ ਸੰਭਵ ਹੋਵੇ, ਇਹ ਆਮ ਤੌਰ 'ਤੇ ਭਾਗੀਦਾਰ ਦੀ ਹਾਜਰੀ ਤੇ ਹਸਤਾਖਰ ਅਤੇ ਮਿਤੀ ਕੀਤੀ ਜਾਂਦੀ ਹੈ

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ਮੁੱਖ ਖੋਜਕਾਰ ਹਸਤਾਖਰ ਮਿਤੀ

Appendix 51 Case report form for atrial fibrillation screening within a South Asian community

medway school of pharmacy

Atrial Fibrillation Screening using Single-lead ECG

within a South Asian Community

CASE REPORT FORM

Date of Visit:	(dd/mm/yyyy)
Name of Researcher:	
Time at the Start:	(hours:minutes)
Time at the End:	(hours:minutes)
Participant's UPIN	S T
Language used during the appointment	☐English ☐Punjabi ☐Other (please specify)_____

Participant's Eligibility

All boxes must be ticked before enrolling the participant. **Consult the pharmacist if in doubt.**

☐ Adult aged ≥ 18
☐ Sufficient mental capacity to provide written informed consent
☐ **Not** fitted with a pacemaker or a cardiac defibrillator
☐ **No** severe co-existing medical condition (e.g. terminal illness with life expectancy under 1 month).

Screening Results

Do they have a hearing aid?	Yes (switch off)	No
Number of ECG's Recorded:		
Quality of the ECG:	☐ Excellent ☐ Acceptable	☐ Poor ☐ Unreadable
Kardia Mobile® ECG Result	☐ Normal ☐ Possible AF	☐ Unclassified ☐ Unreadable
Provisional diagnosis on the letter	☐ Normal ☐ Possible AF	☐ Unclassified ☐ Unreadable

Comments (e.g. results if more than one ECG is recorded)

University of Kent

About You (Demographic Data)

To be filled in by the participant with the help of a researcher if needed

What is your gender?	☐ **Male**	☐ **Female**
What is your ethnicity?	☐ Asian/Asian British/Indian ☐ Asian/Asian British/Pakistani ☐ Asian/Asian British/Bangladeshi ☐ Other (please specify) _____	
What is your country of birth?		
How old are you?		

Do you have or have you ever had any of the following conditions?	**Yes**	**No**	**Don't know**
High blood pressure			
High cholesterol			
Heart muscle disease also known as failure			
Heart disease causing chest pain also known as angina			
Diabetes			
Peripheral arterial disease (painful muscle cramping in the hips, thighs or calves when walking, climbing stairs or exercising)			
Stroke or transient ischaemic attack			
Clot in the body (not the veins of the lungs)			
Heart attack			

Do you take or use any medicines? (please list the names below)

Do you smoke?	**Yes**	**No**
Do you drink alcohol?	**Yes**	**No**
What is your height?		
What is your weight?		

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ਦੱਖਣ ਏਸ਼ੀਅਨ ਕਮਿਊਨਿਟੀ ਅੰਦਰ ਸਿੰਗਲ ਲੀਡ ਈਸੀਜੀ ਦੀ ਵਰਤੋਂ ਨਾਲ ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰਿਨਿੰਗ

ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰੀਨਿੰਕੇਸ ਰਿਪੋਰਟ ਫ਼ਾੱਰਮ

ਮੁਲਾਕਾਤ ਦੀ ਤਾਰੀਖ:	(dd/mm/yyyy)
ਖੋਜਕਾਰ ਦਾ ਨਾਮ:	
ਸ਼ੁਰੂ ਕਰਨ ਵੇਲੇ ਸਮਾਂ	(hours:minutes)
ਅੰਤ ਹੋਣ ਵੇਲੇ ਸਮਾਂ	(hours:minutes)
ਭਾਗੀਦਾਰ ਦੀ ਯੂਪੀਨ (UPIN)	S T

ਭਾਗੀਦਾਰ ਦੀ ਯੋਗਤਾ

ਭਾਗੀਦਾਰ ਦਾ ਨਾਮਦਰਜ ਕਰਨ ਤੋਂ ਪਹਿਲਾਂ ਸਾਰੇ ਬਕਸੇ ਨਿਸ਼ਾਨ ਕੀਤੇ ਜਾਣੇ ਚਾਹੀਦੇ ਹਨ। ਜੇਕਰ ਸ਼ਕ ਹੈ, **ਤਾਂ ਫ਼ਾਰਮਾਸਿਸਟ ਨਾਲ ਸੰਪਰਕ ਕਰੋ।**

- ☐ ਬਾਲਗ ਉਮਰ ≥ 18
- ☐ ਲਿਖਤੀ ਸੂਚਿਤ ਸਹਿਮਤੀ ਪ੍ਰਦਾਨ ਕਰਨ ਲਈ ਲੋੜੀਂਦੀ ਦਿਮਾਗੀ ਕੁਸ਼ਲਤਾ
- ☐ ਪੇਸਮੇਕਰ ਜਾਂ ਕਾਰਡੀਅਕ ਡੀਫਿਬ੍ਰਿਲਿਟਰ ਦੀ ਵਰਤੋਂ ਤਾਂ **ਨਹੀਂ** ਕਰਦੇ
- ☐ ਕੋਈ ਗੰਭੀਰ ਸਹਿ-ਮੌਜੂਦਾ ਡਾਕਟਰੀ ਹਾਲਤ ਤਾਂ **ਨਹੀਂ** (ਜਿਵੇਂ ਕਿ ਇੱਕ ਮਹੀਨੇ ਤੋਂ ਘੱਟ ਜਿਂਦਗੀ ਵਾਲੀ ਗਂਭੀਰ ਬਿਮਾਰੀ)

ਸਕ੍ਰੀਨਿੰਗ ਨਤੀਜੇ

ਕੀ ਉਹਨਾਂ ਕੋਲ ਸੁਣਨ ਸਹਾਇਤਾ ਹੈ?	ਹਾਂ (ਸਵਿਚ ਬੰਦ ਕਰੋ)	ਨਹੀਂ
ਈਸੀਜੀ ਦੇ ਰਿਕਾਰਡਾਂ ਦੀ ਗਿਣਤੀ:		
ਈਸੀਜੀ ਦੀ ਗੁਣਵੰਤਾ:	☐ ਵਧਿਆ ☐ ਸਵੀਕਾਰਯੋਗ	☐ ਘੱਟਿਆ ☐ ਪੜਨਯੋਗ ਨਹੀਂ
ਕਾਰਡੀਆ ਮੋਬਾਈਲ® ਈਸੀਜੀ ਨਤੀਜੇ	☐ ਆਮ ☐ ਸੰਭਵ ਏਐਫ	☐ ਗੈਰ ਵਰਣਿਤ ☐ ਪੜਨਯੋਗ ਨਹੀਂ
ਚਿੱਠੀ 'ਤੇ ਆਰਜੀ ਨਿਦਾਨ	☐ ਆਮ ☐ ਸੰਭਵ ਏਐਫ	☐ ਗੈਰ ਵਰਣਿਤ ☐ ਪੜਨਯੋਗ ਨਹੀਂ
ਟਿੱਪਣੀਆਂ (ਜਿਵੇਂ ਕਿ ਨਤੀਜੇ ਜੇਕਰ ਇਕ ਤੋਂ ਵੱਧ ਈਸੀਜੀ ਕੀਤੀਆਂ ਦਾ ਰਿਕਾਰਡ ਹੈ)		

University of Kent

ਤੁਹਾਡੇ ਬਾਰੇ (ਜਨਗਣਨਾ ਡੇਟਾ)

ਜੇਕਰ ਲੋੜ ਪਵੇ, ਤਾਂ ਇੱਕ ਖੋਜਕਰਤਾ ਦੀ ਮਦਦ ਨਾਲ ਭਾਗੀਦਾਰ ਦੁਆਰਾ ਭਰਿਆ ਜਾਏ

ਤੁਹਾਡਾ ਲਿੰਗ ਕੀ ਹੈ?	☐ **ਮਰਦ**	☐ **ਔਰਤ**
ਤੁਹਾਡੀ ਨਸਲ ਕੀ ਹੈ?	☐ ਏਸ਼ੀਆਈ/ਏਸ਼ੀਅਨ ਬ੍ਰਿਟਿਸ਼/ਇੰਡੀਅਨ ☐ ਏਸ਼ੀਆਈ/ਏਸ਼ੀਅਨ ਬ੍ਰਿਟਿਸ਼/ਪਾਕਿਸਤਾਨੀ ☐ ਏਸ਼ੀਆਈ ਏਸ਼ੀਅਨ ਬ੍ਰਿਟਿਸ਼/ਬੰਗਲਾਦੇਸ਼ੀ ☐ ਹੋਰ (ਕਿਰਪਾ ਕਰਕੇ ਨਿਸ਼ਚਿਤ ਕਰੋ) _____	
ਤੁਹਾਡਾ ਜਨਮ ਕਿਹੜੇ ਮੁਲਕ ਵਿਚ ਹੋਇਆ?		
ਤੁਹਾਡੀ ਉਮਰ ਕੀ ਹੈ?		

ਕੀ ਤੁਹਾਨੂੰ ਹੁਣ ਦੇ ਸਮੇਂ ਜਾਂ ਇਸ ਤੋਂ ਪਹਿਲਾਂ ਕਦੇ ਹੇਠ ਲਿਖਿਆਂ ਬਿਮਾਰੀਆਂ ਹਨ/ਸੀ?	**ਹਾਂ**	**ਨਹੀਂ**	**ਨਹੀਂ ਜਾਣਦੇ**
ਹਾਈ ਬਲੱਡ ਪ੍ਰੈਸ਼ਰ			
ਹਾਈ ਕੋਲੇਸਟ੍ਰੋਲ			
ਦਿਲ ਦੀ ਮਾਸਪੇਸੀ ਦੀ ਬਿਮਾਰੀ ਨੂੰ ਵੀ ਅਸਫ਼ਲਤਾ ਵਜੋਂ ਜਾਣਿਆ ਜਾਂਦਾ ਹੈ			
ਛਾਤੀ ਦੇ ਦਰਦ ਵਜੋਂ ਹੁੰਦੀ ਦਿਲ ਦੀ ਬਿਮਾਰੀ ਵੀ ਐਨਜਾਈਨਾ ਤੌਰ 'ਤੇ ਜਾਣੂ ਹੈ			
ਡਾਇਬੀਟੀਜ਼			
ਪੈਰੀਫਿਨਲ ਧਮਨੀ ਰੋਗ (ਤੁਰਨ, ਪੌੜੀਆਂ ਚੜ੍ਹਨ ਜਾਂ ਕਸਰਤ ਕਰਨ ਵੇਲੇ ਕੁੱਲ੍ਹੇ, ਪੱਟ ਜਾਂ ਲਤਾਂ ਵਿੱਚ ਦਰਦਨਾਕ ਨਾੜ ਦਾ ਚੜ੍ਹਨਾ)			
ਸਟ੍ਰੋਕ ਜਾਂ ਅਸਥਾਈ ਹਮਲਾ			
ਸਰੀਰ ਵਿਚ ਕਲੌਟ (ਫ਼ੇਫੜਿਆਂ ਦੀ ਨਾੜੀ ਨਹੀਂ)			
ਦਿਲ ਦਾ ਦੌਰਾ			

ਕੀ ਤੁਸੀਂ ਕੋਈ ਦਵਾਈਆਂ ਲੈਂਦੇ ਜਾਂ ਵਰਤਦੇ ਹੋ? (ਕਿਰਪਾ ਕਰਕੇ ਹੇਠਾਂ ਦਵਾਈਆਂ ਦੇ ਨਾਮ ਦੀ ਸੂਚੀ ਬਣਾਓ)

ਕੀ ਤੁਸੀਂ ਧੂਮਰਪਾਨ ਕਰਦੇ ਹੋ?	ਹਾਂ	ਨਹੀਂ
ਕੀ ਤੁਸੀਂ ਸ਼ਰਾਬ ਪੀਂਦੇ ਹੋ?	ਹਾਂ	ਨਹੀਂ
ਤੁਹਾਡੀ ਉਚਾਈ ਕੀ ਹੈ?		
ਤੁਹਾਡਾ ਭਾਰ ਕੀ ਹੈ?		

University of Kent

Appendix 52 Provisional diagnosis letter for atrial fibrillation screening within a South Asian community

medway school of pharmacy

Atrial Fibrillation Screening using Single-lead ECG

within a South Asian Community

LETTER OF PROVISIONAL DIAGNOSIS

Date:

Dear Doctor

Patient's full name: Date of birth:

This person's heart rhythm has been checked using AliveCor Kardia Mobile® single-lead ECG device as part of a research study conducted by the Medway School of Pharmacy (University of Kent) in conjunction with the Atrial Fibrillation Association. Please find a copy of the ECG trace(s) enclosed.

The monitor detected:

☐ Normal (no irregularity detected) – no further intervention is required.

☐ Possible Atrial Fibrillation – consider requesting a 12-lead ECG.

☐ Unclassified trace (inconclusive result) – consider requesting a 12-lead ECG.

☐ Unreadable trace – consider requesting a 12-lead ECG.

Kardia Mobile® is named in European Society of Cardiology guidelines as suitable for AF screening and has NICE and FDA approval. This device has demonstrated a high degree of accuracy in studies versus 12-lead ECG. The automated software has an overall accuracy of 97% and sensitivity of 98% using 12-lead ECG as a reference. Please see AliveCor.com/en for more information. According to the recent ESC guideline, a 30 second ECG trace showing AF is sufficient to consider treatment.[1]

For more information about the study, visit our website www.msp.ac.uk/saaf or contact us by email: afstudy@kent.ac.uk or by phone: 01634 202935; by post: Medway School of Pharmacy, Anson Building, Central Avenue, Chatham, ME4 4TB. Or for more information about AF, please visit: www.afa.org.uk or www.afa-international.org or contact the AF Association: 01789 867502 or info@afa.org.uk.

Thank you very much for your collaboration.

1. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37(38):2893-962. doi: 10.1093/eurheartj/ehw210.

AF Association www.afa.org.uk

University of Kent

medway school of pharmacy

ਦੱਖਣ ਏਸ਼ੀਅਨ ਕਮਿਊਨਿਟੀ ਦੇ ਅੰਦਰ ਸਿੰਗਲ ਲੀਡ ਈਸੀਜੀ ਦੀ ਵਰਤੋਂ ਨਾਲ

ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰਿਨਿੰਗ

ਆਰਜ਼ੀ ਨਿਦਾਨ ਦਾ ਖਤ

ਮਿਤੀ:

ਪਿਆਰੇ ਡਾਕਟਰ

ਮਰੀਜ਼ ਦਾ ਪੂਰਾ ਨਾਮ: ਜਨਮ ਤਾਰੀਖ:

ਮੀਡਵੇ ਸਕੂਲ ਆੱਫ਼ ਫਾਰਮੇਸੀ (ਯੂਨਿਵਰਸਿਟੀ ਆੱਫ਼ ਕੈਨਟ) ਦੁਆਰਾ ਕਰਵਾਏ ਗਏ ਖੋਜ ਅਧਿਐਨ ਦੇ ਹਿੱਸੇ ਦੇ ਰੂਪ ਵਿਚ ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਅਸੋਸ਼ੀਏਸ਼ਨ ਦੇ ਨਾਲ ਮਿਲਕੇ ਇਸ ਵਿਅਕਤੀ ਦੇ ਦਿਲ ਦੀ ਧੜਕਨ ਦੀ ਜਾਂਚ ਅਲਿਵਕੋਰ ਕਾਰਡੀਆ ਮੋਬਾਈਲ® ਸਿੰਗਲ ਲੀਡ ਈਸੀਜੀ ਡਿਵਾਈਸ (ਯੰਤਰ) ਦੀ ਵਰਤੋਂ ਕਰਕੇ ਕੀਤੀ ਗਈ ਹੈ। ਕ੍ਰਿਪਾ ਕਰਕੇ ਈਸੀਜੀ ਟਰੇਸ ਦੀ ਇਕ ਕਾਪੀ ਦੇਖੋ।

ਮੌਨੀਟਰ ਤੋਂ ਪਤਾ ਲਗਾ ਹੈ ਕਿ:

☐ ਆਮ (ਅਨਿਯਮਿਤਤਾ ਨਹੀਂ ਲੱਭੀਆਂ) – ਅੱਗੇ ਕੋਈ ਹੋਰ ਜਾਂਚ ਦੀ ਲੋੜ ਨਹੀਂ ਹੈ।

☐ ਸੰਭਵ ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ – 12-ਲੀਡ ਈਸੀਜੀ ਕਰਾਉਣ ਦੀ ਬੈਨਤੀ ਕਰਨ ਬਾਰੇ ਵਿਚਾਰ ਕਰੋ।

☐ ਅੱਚੁਕਵਾਂ ਟਰੇਸ – 12-ਲੀਡ ਈਸੀਜੀ ਕਰਾਉਣ ਦੀ ਬੈਨਤੀ ਕਰਨ ਬਾਰੇ ਵਿਚਾਰ ਕਰੋ।

ਕਾਰਡੀਆ ਮੋਬਾਈਲ® ਨੂੰ ਯੂਰੋਪੀਅਨ ਸੁਸਾਇਟੀ ਆੱਫ਼ ਕਾਰਡੀਅਲੋਜੀ ਮਾਰਗਦਰਸ਼ਨਾਂ ਵਿਚ ਨਾਮਜ਼ਦ ਕੀਤਾ ਗਿਆ ਹੈ ਕਿਉਂਕਿ ਇਹ ਏਐਫ ਸਕ੍ਰਿਨਿੰਗ ਲਈ ਢੁੱਕਵਾਂ ਹੈ ਅਤੇ ਨਾਈਸ ਅਤੇ ਐਫ਼ਡੀਏ ਵਲੋਂ ਮਨਜੂਰੀ ਪ੍ਰਾਪਤ ਹੈ। ਇਸ ਡਿਵਾਈਸ ਨੇ 12 ਲੀਡ ਈਸੀਜੀ ਬਨਾਮ ਸਿਖਿਆ ਲਈ ਉਚ ਪੱਧਰੀ ਸੂਧਤਾ ਦਾ ਪ੍ਰਦਰਸ਼ਨ ਕੀਤਾ ਹੈ। ਇਕ ਹਵਾਲੇ ਦੀ ਤੌਰ 'ਤੇ 12 ਲੀਡ ਈਸੀਜੀ ਦੀ ਵਰਤੋਂ ਨਾਲ ਆਟੋਮੇਟਿਡ ਸੋਫਟਵੇਅਰ ਰਾਹੀਂ 97% ਦੀ ਕੁਲ ਸੰਪੂਰਨਤਾ ਅਤੇ 98% ਦੀ ਸੰਵੇਦਨਸ਼ੀਲਤਾ ਪ੍ਰਾਪਤ ਹੈ। ਹੋਰ ਜਾਣਕਾਰੀ ਲਈ ਕਿਰਪਾ ਕਰਕੇ AliveCOR.com/en ਦੇਖੋ। ਹਾਲ ਹੀ ਵਿਚ ਈਸੀਜੀ ਦੇ ਦਿਸ਼ਾ-ਨਿਰਦੇਸ਼ ਅਨੁਸਾਰ ਏਐਫ਼ ਦੇ ਇਲਾਜ ਨੂੰ ਸਮਝਣ ਲਈ 30 ਸਕਿੰਟਾਂ ਦਾ ਇੱਕ ਈਸੀਜੀ ਕਾਫ਼ੀ ਹੈ। .[1]

ਅਧਿਐਨ ਬਾਰੇ ਵਧੇਰੇ ਜਾਣਕਾਰੀ ਲਈ ਸਾਡੀ ਵੈਬਸਾਈਟ www.msp.ac.uk/saaf 'ਤੇ ਜਾਉ ਜਾਂ ਮਿਸਟਰ ਵਿਲਿਅਸ ਸਵਿਕਾਸ ਨਾਲ ਈਮੇਲ afstudy@kent.ac.uk ਰਾਹੀਂ ਜਾਂ ਫ਼ੋਨ 01634 202935 ਦੁਆਰਾ ਜਾਂ ਡਾਕ ਦੁਆਰਾ: Medway School of Pharmacy, Anson Building, Central Avenue, Chatham, ME4 4TB ਪਤੇ 'ਤੇ ਸੰਪਰਕ ਕਰੋ। ਏਐਫ਼ ਬਾਰੇ ਹੋਰ ਵਧੇਰੇ ਜਾਣਕਾਰੀ ਲਈ, ਕ੍ਰਿਪਾ ਕਰਕੇ ਵੈਬਸਾਈਟ ਦੇਖੋ: www.afa.org.uk ਜਾਂ www.afa-international.org ਜਾਂ ਦ ਏਐਫ਼ ਅਸੋਸ਼ੀਏਸ਼ਨ (The AF Association) ਨਾਲ ਟੈਲੀਫ਼ੋਨ ਨੰਬਰ: 01789 867502 'ਤੇ ਜਾਂ info@afa.org.uk ਨਾਲ ਸੰਪਰਕ ਕਰੋ।.

ਤੁਹਾਡੇ ਸਹਿਯੋਗ ਲਈ ਬਹੁਤ ਧੰਨਵਾਦ।

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1. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37(38):2893-962. doi: 10.1093/eurheartj/ehw210.

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Appendix 53 Follow-up outcomes form for atrial fibrillation screening within a South Asian community

medway school of pharmacy

Atrial Fibrillation Screening using Single-lead ECG

within a South Asian Community

FOLLOW-UP OUTCOMES FORM

Participant's UPIN (to be completed by the researcher): | S | T | | | |

Dear Participant,

Thank you very much for taking part in our study. We would be grateful if you could take a few minutes to complete the following form after your appointment at the doctor's surgery. Please note some of the options presented below may not be relevant in your case. Try and complete the form to the best of your ability. Once completed, please post the form using the pre-paid envelope provided.

Which of the following investigations did you have at the surgery?	**Yes**	**No**	**Don't know**
12-lead ECG			
24-hour ECG			
7-day ECG			
Echocardiography (ultrasound)			
Blood tests			
Other (please specify):			
Were you diagnosed with any of the following conditions during or after your appointment?			
Atrial fibrillation			
Heart block			
Ectopic beats (additional heart beats)			
Hight blood pressure			
Heart failure			
Other (please specify):			
Were you started on any of the following medicines during your or after appointment?			
Warfarin			
Apixaban			
Rivaroxaban			
Dabigatran			
Beta blocker, such as bisoprolol			
Angiotensin converting enzyme inhibitor, such as ramipril			
Cholesterol lowering tablet, such as atorvastatin			
Diuretic or water tablet, such as furosemide			
Other (please specify):			

If you have any questions or concerns about this form, please contact The PDAF Study Team by email: afstudy@kent.ac.uk or by phone: 01634 202935; by post: Medway School of Pharmacy, Anson Building, Central Avenue, Chatham, ME4 4TB. For more information about AF, please visit: www.afa.org.uk or www.afa-international.org or contact the AF Association: 01789 867502 or info@afa.org.uk.

AFA AFAssociation www.afa.org.uk University of Kent

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ਦੱਖਣ ਏਸ਼ੀਅਨ ਕਮਿਊਨਿਟੀ ਦੇ ਗੁਰਦੁਆਰੇ ਅੰਦਰ ਸਿੰਗਲ ਲੀਡ (lead) ਈਸੀਜੀ ਦੀ ਵਰਤੋਂ ਨਾਲ

ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰੀਨਿੰਗ

ਨਤੀਜਿਆਂ ਦੀ ਪੈਰਵੀ ਸੰਬੰਧੀ ਫ਼ਾਰਮ

ਭਾਗ ਲੈਣ ਵਾਲੇ ਦਾ ਯੂਪੀਨ (UPIN) (ਖੋਜਕਾਰ ਦੁਆਰਾ ਪੂਰਾ ਕੀਤਾ ਜਾਣਾ ਚਾਹੀਦਾ ਹੈ) :

S	T			

ਪਿਆਰੇ ਭਾਗੀਦਾਰ,

ਸਾਡੇ ਅਧਿਐਨ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਤੁਹਾਡਾ ਬਹੁਤ ਧੰਨਵਾਦ। ਜੇ ਤੁਸੀਂ ਡਾਕਟਰ ਦੀ ਸਰਜਰੀ ਦੀ ਆਪਣੀ ਮੁਲਾਕਾਤ ਤੋਂ ਬਾਅਦ ਹੇਠ ਦਿੱਤੇ ਫ਼ਾਰਮ ਨੂੰ ਪੂਰਾ ਕਰਨ ਲਈ ਕੁਝ ਮਿੰਟ ਦੇ ਸਕਦੇ ਹੋ, ਤਾਂ ਅਸੀਂ ਧੰਨਵਾਦੀ ਹੋਵਾਂਗੇ। ਕਿਰਪਾ ਕਰਕੇ ਧਿਆਨ ਦਿਓ ਕਿ ਹੇਠਾਂ ਦਿੱਤੇ ਗਏ ਕੁੱਝ ਵਿਕਲਪ ਤੁਹਾਡੇ ਮਾਮਲੇ ਵਿੱਚ ਸੰਬੰਧਿਤ ਨਹੀਂ ਹੋ ਸਕਦੇ ਹਨ। ਆਪਣੀ ਕਾਬਲੀਅਤ ਦੇ ਸਭ ਤੋਂ ਵਧੀਆ ਤਰੀਕੇ ਮੁਤਾਬਕ ਫ਼ਾਰਮ ਪੂਰਾ ਕਰਨ ਦੀ ਕੋਸ਼ਿਸ਼ ਕਰੋ। ਇੱਕ ਵਾਰ ਪੂਰਾ ਹੋਣ 'ਤੇ ਕਿਰਪਾ ਕਰਕੇ ਟਿਕਟ ਲਾਏ ਹੋਏ (ਪ੍ਰੀ-ਪੇਡ) ਲਿਫ਼ਾਫ਼ੇ ਦੀ ਵਰਤੋਂ ਕਰਕੇ ਫ਼ਾਰਮ ਨੂੰ ਡਾਕ ਰਾਹੀਂ ਭੇਜੋ।

ਸਰਜਰੀ ਵਿਚ ਹੇਠ ਲਿਖੀਆਂ ਵਿਚੋਂ ਕਿਹੜੀਆਂ ਜਾਂਚਾਂ ਕੀਤੀਆਂ ਗਈਆਂ ਹਨ?	ਹਾਂ	ਨਹੀਂ	ਨਹੀਂ ਜਾਣਦੇ
12-lead ECG			
24-hour ECG			
7-day ECG			
Echocardiography (ultrasound)			
Blood tests			
ਹੋਰ (ਕ੍ਰਿਪਾ ਕਰਕੇ ਸਪਸ਼ਟ ਕਰੋ):			
ਕੀ ਤੁਹਾਡੀ ਮੁਲਾਕਾਤ ਦੌਰਾਨ ਜਾਂ ਬਾਅਦ ਵਿੱਚ ਹੇਠ ਲਿਖੀ ਕਿਸੇ ਵੀ ਹਾਲਾਤ ਦਾ ਨਿਦਾਨ ਕੀਤਾ ਗਿਆ ਸੀ?			
Atrial fibrillation			
Heart block			
Ectopic beats (additional heart beats)			
Hight blood pressure			
Heart failure			
ਹੋਰ (ਕ੍ਰਿਪਾ ਕਰਕੇ ਸਪਸ਼ਟ ਕਰੋ):			
ਕੀ ਤੁਸੀਂ ਆਪਣੀ ਮੁਲਾਕਾਤ ਦੇ ਸਮੇਂ ਦੌਰਾਨ ਜਾਂ ਬਾਅਦ ਵਿੱਚ ਹੇਠ ਲਿਖੀਆਂ ਦਵਾਈਆਂ ਵਿੱਚੋਂ ਕਿਸੇ ਦੀ ਸ਼ੁਰੂਆਤ ਕੀਤੀ ਸੀ?			
Warfarin			
Apixaban			
Rivaroxaban			
Dabigatran			
Beta blocker, such as bisoprolol			
Angiotensin converting enzyme inhibitor, such as ramipril			
Cholesterol lowering tablet, such as atorvastatin			
Diuretic or water tablet, such as furosemide			
ਹੋਰ (ਕ੍ਰਿਪਾ ਕਰਕੇ ਸਪਸ਼ਟ ਕਰੋ):			

ਜੇ ਤੁਹਾਡੇ ਕੋਲ ਇਸ ਫ਼ਾਰਮ ਬਾਰੇ ਕੋਈ ਪ੍ਰਸ਼ਨ ਜਾਂ ਚਿੰਤਾਵਾਂ ਹਨ, ਤਾਂ ਕਿਰਪਾ ਕਰਕੇ ਦ ਪੀਡੀਏਐਫ਼ ਸੱਟਡੀ ਟੀਮ (The PDAF Study Team) **ਨਾਲ ਈਮੇਲ** afstudy@kent.ac.uk **ਜਾਂ ਫ਼ੋਨ:** 01634 202935; **ਡਾਕ ਰਾਹੀਂ:** Medway School of Pharmacy, Anson Building, Central Avenue, Chatham, ME4 4TB **'ਤੇ ਸੰਪਰਕ ਕਰੋ। ਏਐਫ਼ ਬਾਰੇ ਹੋਰ ਵਧੇਰੇ ਜਾਣਕਾਰੀ ਲਈ, ਕ੍ਰਿਪਾ ਕਰਕੇ ਵੈਬਸਾਈਟ ਦੇਖੋ:** www.afa.org.uk **ਜਾਂ** www.afa-international.org **ਜਾਂ ਦ ਏਐਫ਼ ਅਸੋਸ਼ੀਏਸ਼ਨ** (The AF Association) **ਨਾਲ ਟੈਲੀਫ਼ੋਨ ਨੰਬਰ:** 01789 867502 **'ਤੇ ਜਾਂ** info@afa.org.uk **ਨਾਲ ਸੰਪਰਕ ਕਰੋ।**

Appendix 54 Participant feedback questionnaire for atrial fibrillation screening within a South Asian community

medway school of pharmacy

Atrial Fibrillation Screening using Single-lead ECG

within a South Asian Community

PARTICIPANT FEEDBACK QUESTIONNAIRE

Please complete this questionnaire to tell us about your appointment with the pharmacy student (researcher) who helped to record your ECG.

Your feedback will enable us to identify areas that may need improvement and may help develop future health screening initiatives. Your opinions are therefore very valuable.

There are no right or wrong answers. We are interested in your honest views.

By taking part you are giving your consent for your answers to be used as described in the participant information leaflet, that you received before having your appointment. It is important for you to know that your doctor's surgery will not know whether you have participated in the questionnaire or not, and that taking part will not affect your future care in any way.

For all queries regarding this study, please do not hesitate to contact:

The PDAF Study Team

Tel: 01634 202935; Email: afstudy@kent.ac.uk

For more information about AF, please visit: www.afa.org.uk or www.afa-international.org or contact the AF Association: 01789 867502 or info@afa.org.uk.

Instructions: Please answer all the questions on the following pages. Please tick or mark the box that best reflects your level of agreement. Please **indicate one response only** for each statement.

We think that it will take you about **5 minutes** to complete this questionnaire.

Thank you

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Date of Visit:	_____ [dd/mm/yyyy]

1. Your Gurdwara facilitated this study to support the early detection and diagnosis of atrial fibrillation. From your experience of it, how important was the screening for you? ☐ **Very Important** ☐ **Important** ☐ **Not Important**

2. Were you aware of this condition before you were screened? ☐ **Yes** ☐ **No**

3. Were you aware of any of the health risks associated with this condition, before you were screened? ☐ **Yes** ☐ **No**

4. How satisfied were you with the information provided before the appointment? ☐ **Very Satisfied** ☐ **Satisfied** ☐ **Neither satisfied nor dissatisfied** ☐ **Dissatisfied** ☐ **Very Dissatisfied**

5. Did the researcher clearly explain what was involved in having an ECG? ☐ **Yes** ☐ **No**

6. Afterwards did the researcher clearly explain the results of the test to you? ☐ **Yes** ☐ **No**

7. How satisfied were you with the information provided after the appointment? ☐ **Very Satisfied** ☐ **Satisfied** ☐ **Neither satisfied nor dissatisfied** ☐ **Dissatisfied** ☐ **Very Dissatisfied**

8. Please rate how well you thought the researcher carried out the tests: ☐ **Very Good** ☐ **Good** ☐ **Poor** ☐ **Very Poor**

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9. Did the researcher make you feel at ease? ☐ **Yes** ☐ **No**

10. How satisfied were you with the length of the appointment?

☐ **Very Satisfied** ☐ **Satisfied** ☐ **Neither satisfied nor dissatisfied**
☐ **Dissatisfied** ☐ **Very Dissatisfied**

11. Overall how satisfied were you with the service that you received?

☐ **Very Satisfied** ☐ **Satisfied** ☐ **Neither satisfied nor dissatisfied**
☐ **Dissatisfied** ☐ **Very Dissatisfied**

12. If the test was offered to you again next year, would you have it done?

☐ **Yes** ☐ **No**

13. Was there anything you particularly **LIKED** about the service?

☐ **Yes** ☐ **No**

If you particularly liked something about the service please tell us what it was and what was good about this?

14. Was there anything that you particularly **DISLIKED** about the service?

☐ **Yes** ☐ **No**

If you particularly disliked something, please tell us about this.

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15. Would you be happy for **other screening tests** to be delivered at the Gurdwara in the future? ☐ **Yes** ☐ **No**

What other screening tests would you like to receive?

16. In your opinion, what are the key barriers for individuals of South Asian origin to engage in health screening initiatives? (tick as many as may apply)

☐ **Language barrier** ☐ **Cultural norms** ☐ **Religious beliefs**
☐ **Costs** ☐ **Lack of health education** ☐ **Other** (please specify below):

Please specify/discuss any other barriers to engagement here:

17. Please add any further comments that may help us to **improve** this proposed AF screening strategy.

Further comments:

Thank you for taking the time to complete this questionnaire.

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ਦੱਖਣ ਏਸ਼ੀਅਨ ਕਮਿਊਨਿਟੀ ਦੇ ਅੰਦਰ ਸਿੰਗਲ ਲੀਡ ਈਸੀਜੀ ਦੀ ਵਰਤੋਂ ਨਾਲ

ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਸਕ੍ਰਿਨਿੰਗ

ਭਾਗੀਦਾਰ ਦੇ ਵਿਚਾਰ ਪ੍ਰਾਪਤ ਕਰਨ ਸੰਬੰਧੀ ਪ੍ਰਸ਼ਨਾਵਲੀ

ਫ਼ਾਰਮੈਸੀ ਵਿਦਿਆਰਥੀ (ਖੋਜਕਾਰ) ਜਿਸਨੇ ਤੁਹਾਡੇ ਈਸੀਜੀ ਨੂੰ ਰਿਕਾਰਡ ਕਰਨ ਵਿਚ ਮਦਦ ਕੀਤੀ ਉਸ ਨਾਲ ਤੁਹਾਡੀ ਮੁਲਾਕਾਤ ਬਾਰੇ ਸਾਨੂੰ ਦੱਸਣ ਲਈ ਇਹ ਪ੍ਰਸ਼ਨਾਵਲੀ ਭਰੋ।

ਤੁਹਾਡੇ ਪ੍ਰਤੀਕਰਮ ਰਾਹੀਂ ਅਸੀਂ ਉਨ੍ਹਾਂ ਖ਼ੇਤਰਾਂ ਦੀ ਪਛਾਣ ਕਰਨ ਦੇ ਯੋਗ ਹੋਵਾਂਗੇ ਜਿਨ੍ਹਾਂ ਨੂੰ ਸੁਧਾਰ ਦੀ ਜਰੂਰਤ ਹੋ ਸਕਦੀ ਹੈ ਅਤੇ ਇਸ ਨਾਲ ਭੱਵਿਖ ਵਿਚ ਸਿਹਤ ਜਾਂਚ ਕਰਨ ਦੀਆਂ ਪਹਿਲਕਦਮੀਆਂ ਨੂੰ ਵਿਕਸਿਤ ਕਰਨ ਵਿਚ ਮਦਦ ਹੋ ਮਕਦੀ ਹੈ। ਤੁਹਾਡੇ ਵਿਚਾਰ ਇਸ ਲਈ ਬਹੁਤ ਕੀਮਤੀ ਹਨ।

ਕੋਈ ਸਹੀ ਜਾਂ ਗ਼ਲਤ ਜਵਾਬ ਨਹੀਂ ਹੈ। ਅਸੀਂ ਤੁਹਾਡੇ ਈਮਾਨਦਾਰ ਵਿਚਾਰਾਂ ਵਿੱਚ ਦਿਲਚਸਪੀ ਰੱਖਦੇ ਹਾਂ।

ਹਿੱਸਾ ਲੈ ਕੇ ਤੁਸੀਂ ਆਪਣੇ ਜਵਾਬਾਂ ਦੀ ਵਰਤੋਂ ਕਰਨ ਲਈ ਸਹਿਮਤੀ ਦਿੰਦੇ ਹੋ ਜਿਵੇਂ ਭਾਗੀਦਾਰ ਲਈ ਜਾਣਕਾਰੀ ਦਿੰਦੇ ਪਰਚੇ ਵਿਚ ਦੱਸਿਆ ਗਿਆ ਹੈ ਜੋ ਕਿ ਤੁਹਾਡੀ ਮੁਲਾਕਾਤ ਤੋਂ ਪਹਿਲਾਂ ਤੁਸੀਂ ਪ੍ਰਾਪਤ ਕੀਤੀ ਸੀ। ਤੁਹਾਡੇ ਲਈ ਇਹ ਜਾਣਨਾ ਮਹੱਤਵਪੂਰਨ ਹੈ ਕਿ ਤੁਹਾਡੇ ਡਾਕਟਰ ਦੀ ਸਰਜਰੀ ਨੂੰ ਇਹ ਜਾਣਕਾਰੀ ਨਹੀਂ ਦਿੱਤੀ ਜਾਵੇਗੀ ਕਿ ਤੁਸੀਂ ਪ੍ਰਸ਼ਨਾਵਲੀ ਵਿਚ ਹਿੱਸਾ ਲਿਆ ਹੈ ਜਾਂ ਨਹੀਂ ਅਤੇ ਹਿੱਸਾ ਲੈਣ ਵਜੋਂ ਤੁਹਾਡੀ ਭੱਵਿਖੀ ਦੇਖਭਾਲ ਪ੍ਰਭਾਵਤ ਨਹੀਂ ਹੋਵੇਗੀ।

ਇਸ ਅਧਿਐਨ ਦੇ ਸੰਬੰਧ ਵਿਚ ਸਾਰੇ ਸਵਾਲਾਂ ਲਈ ਕਿਰਪਾ ਕਰਕੇ ਬਿਨਾਂ ਸੰਕੋਚ ਸੰਪਰਕ ਕਰੋ:

ਮਿਸਟਰ ਵਿਲੀਅਸ ਸਵੀਕਿਆਸ

ਟੈਲੀਫ਼ੋਨ: 01634 202935

ਈਮੇਲ afstudy@kent.ac.uk

'ਤੇ ਸੰਪਰਕ ਕਰੋ। ਏਐਫ਼ ਬਾਰੇ ਹੋਰ ਵਧੇਰੇ ਜਾਣਕਾਰੀ ਲਈ, ਕ੍ਰਿਪਾ ਕਰਕੇ ਵੈਬਸਾਈਟ ਦੇਖੋ: www.afa.org.uk ਜਾਂ www.afa-international.org ਜਾਂ ਦ ਏਐਫ਼ ਅਸੋਸ਼ੀਏਸ਼ਨ (The AF Association) ਨਾਲ ਟੈਲੀਫ਼ੋਨ ਨੰਬਰ: 01789 867502 'ਤੇ ਜਾਂ info@afa.org.uk ਨਾਲ ਸੰਪਰਕ ਕਰੋ।

ਨਿਰਦੇਸ਼: ਕਿਰਪਾ ਕਰਕੇ ਹੇਠਾਂ ਦਿੱਤੇ ਪੰਨਿਆ 'ਤੇ ਸਾਰੇ ਪ੍ਰਸ਼ਨਾਂ ਦੇ ਉਤੱਰ ਦਿਓ। ਕਿਰਪਾ ਕਰਕੇ ਉਸ ਬੱਾਕਸ 'ਤੇ ਸਹੀ ਜਾਂ ਟਿਕ ਦਾ ਨਿਸ਼ਾਨ ਲਾਓ ਜੋ ਤੁਹਾਡੇ ਸਮਝੌਤੇ ਦੇ ਪੱਧਰ ਨੂੰ ਬਿਹਤਰ ਦਰਸਾਉਂਦਾ ਹੈ। ਕਿਰਪਾ ਕਰਕੇ **ਸਿਰਫ਼ ਹਰ ਕਥਨ ਲਈ ਇੱਕ ਹੀ ਜਵਾਬ ਦਿਉ।**

ਸਾਡੀ ਸੋਚ ਅਨੁਸਾਰ ਇਹ ਪ੍ਰਸ਼ਨਾਵਲੀ ਨੂੰ ਪੂਰਾ ਕਰਨ ਵਿੱਚ ਤੁਹਾਨੂੰ **5 ਮਿੰਟ** ਲੱਗਣਗੇ।

ਤੁਹਾਡਾ ਧੰਨਵਾਦ।

ਮੁਲਾਕਾਤ ਦੀ ਤਾਰੀਖ	_____ ਤਾਰੀਖ/ਮਹੀਨਾ/ਸਾਲ

1. ਤੁਹਾਡੇ ਗੁਰਦੁਆਰੇ ਨੇ ਅਟ੍ਰਿਅਲ ਫਿਬ੍ਰਿਲਿਸ਼ਨ ਦੀ ਸ਼ੁਰੂਆਤੀ ਪਛਾਣ ਅਤੇ ਨਿਦਾਨ ਦਾ ਸਮਰਥਨ ਕਰਨ ਲਈ ਇਸ ਅਧਿਐਨ ਦੀ ਸਹੂਲਤ ਦਿੱਤੀ ਹੈ। ਇਸਦੇ ਆਪਣੇ ਅਨੁਭਵ ਤੋਂ ਤੁਹਾਡੇ ਲਈ ਸਕ੍ਰਿਨਿੰਗ ਕਿੰਨੀ ਮਹੱਤਵਪੂਰਨ ਸੀ?

   ☐ ਬਹੁਤ ਹੀ ਮਹੱਤਵਪੂਰਨ ☐ ਮਹੱਤਵਪੂਰਨ

   ☐ ਮਹੱਤਵਪੂਰਨ ਨਹੀਂ

2. ਤੁਹਾਨੂੰ ਸਕ੍ਰਿਨਿੰਗ ਤੋਂ ਪਹਿਲਾਂ ਸਿਹਤ ਦੀ ਸਥਿਤੀ ਬਾਰੇ ਪਤਾ ਸੀ?

   ☐ ਹਾਂ ☐ ਨਹੀਂ

3. ਤੁਹਾਨੂੰ ਸਕ੍ਰੀਨ ਕੀਤਾ ਇਸ ਤੋਂ ਪਹਿਲਾਂ, ਕੀ ਤੁਸੀਂ ਇਸ ਬਿਮਾਰੀ ਨਾਲ ਜੁੜੇ ਕਿਸੇ ਵੀ ਸਿਹਤ ਦੇ ਖ਼ਤਰੇ ਤੋਂ ਜਾਣੂ ਸੀ?

   ☐ ਹਾਂ ☐ ਨਹੀਂ

4. ਅਪਾਇੰਟਮੈਂਟ ਤੋਂ ਪਹਿਲਾਂ ਦਿੱਤੀ ਜਾਣਕਾਰੀ ਨਾਲ ਤੁਸੀਂ ਕਿੰਨੇ ਸੰਤੁਸ਼ਟ ਸੀ?

   ☐ ਬਹੁਤ ਸੰਤੁਸ਼ਟ ☐ ਸੰਤੁਸ਼ਟ ☐ ਨਾਂ ਸੰਤੁਸ਼ਟ ਨਾਂ ਅਸੰਤੁਸ਼ਟ

   ☐ ਅਸੰਤੁਸ਼ਟ ☐ ਬਹੁਤ ਅਸੰਤੁਸ਼ਟ

5. ਕੀ ਖੋਜਕਰਤਾ ਨੇ ਸਪਸ਼ਟ ਤੌਰ 'ਤੇ ਇਹ ਸਪੱਸ਼ਟ ਕੀਤਾ ਕਿ ਈਸੀਜੀ ਕਰਨ ਵਿਚ ਸ਼ਾਮਲ ਕੀ ਹੈ?

   ☐ ਹਾਂ ☐ ਨਹੀਂ

6. ਬਾਅਦ ਵਿਚ ਖੋਜਕਾਰ ਨੇ ਟੈਸਟ ਦੇ ਨਤੀਜਿਆਂ ਨੂੰ ਸਪੱਸ਼ਟ ਕੀਤਾ ਹੈ?

   ☐ ਹਾਂ ☐ ਨਹੀਂ

7. ਅਪਾਇੰਟਮੈਂਟ ਤੋਂ ਬਾਅਦ ਦਿੱਤੀ ਗਈ ਜਾਣਕਾਰੀ ਨਾਲ ਤੁਸੀਂ ਕਿੰਨੇ ਸੰਤੁਸ਼ਟ ਸੀ?

   ☐ ਬਹੁਤ ਸੰਤੁਸ਼ਟ ☐ ਸੰਤੁਸ਼ਟ ☐ ਨਾਂ ਸੰਤੁਸ਼ਟ ਨਾਂ ਅਸੰਤੁਸ਼ਟ

   ☐ ਅਸੰਤੁਸ਼ਟ ☐ ਬਹੁਤ ਅਸੰਤੁਸ਼ਟ

8. ਕਿਰਪਾ ਕਰਕੇ ਦਸੋ ਕਿ ਖ਼ੋਜਕਰਤਾ ਦੁਆਰਾ ਕੀਤੀ ਜਾਂਚ ਬਾਰੇ ਤੁਹਾਡਾ ਵਿਚਾਰ ਕੀ ਹੈ:

☐ ਬਹੁਤ ਚੰਗਾ ☐ ਚੰਗਾ ☐ ਮਾੜਾ ☐ ਬਹੁਤ ਮਾੜਾ

9. ਕੀ ਖ਼ੋਜਕਰਤਾ ਨੇ ਤੁਹਾਨੂੰ ਆਸਾਨੀ ਜਿਹਾ ਮਹਿਸੂਸ ਕਰਾਇਆ? ☐ ਹਾਂ ☐ ਨਹੀਂ

10. ਮੁਲਾਕਾਤ ਦੇ ਪੂਰੇ ਸਮੇਂ ਤੋਂ ਤੁਸੀਂ ਕਿੰਨੇ ਸੰਤੁਸ਼ਟ ਸਨ?

☐ ਬਹੁਤ ਸੰਤੁਸ਼ਟ ☐ ਸੰਤੁਸ਼ਟ ☐ ਨਾਂ ਸੰਤੁਸ਼ਟ ਨਾਂ ਅਸੰਤੁਸ਼ਟ

☐ ਅਸੰਤੁਸ਼ਟ ☐ ਬਹੁਤ ਅਸੰਤੁਸ਼ਟ

11. ਤੁਸੀਂ ਪ੍ਰਾਪਤ ਕੀਤੀ ਗਈ ਸੇਵਾ ਨਾਲ ਪੂਰੀ ਤਰਾਂ ਕਿੰਨੇ ਸੰਤੁਸ਼ਟ ਹੋ?

☐ ਬਹੁਤ ਸੰਤੁਸ਼ਟ ☐ ਸੰਤੁਸ਼ਟ ☐ ਨਾਂ ਸੰਤੁਸ਼ਟ ਨਾਂ ਅਸੰਤੁਸ਼ਟ

☐ ਅਸੰਤੁਸ਼ਟ ☐ ਬਹੁਤ ਅਸੰਤੁਸ਼ਟ

12. ਜੇ ਅਗਲੇ ਸਾਲ ਤੁਹਾਨੂੰ ਟੈਸਟ ਦੀ ਪੇਸ਼ਕਸ਼ ਕੀਤੀ ਗਈ, ਤਾਂ ਕੀ ਤੁਸੀਂ ਇਹ ਕਰਵਾਉਂਗੇ?

☐ ਹਾਂ ☐ ਨਹੀਂ

13. ਕੀ ਤੁਹਾਨੂੰ ਸੇਵਾ ਦੀ ਕੋਈ ਅਜਿਹੀ ਖਾਸ ਗੱਲ ਚੰਗੀ ਲਗੀ?

☐ ਹਾਂ ☐ ਨਹੀਂ

ਜੇਕਰ ਤੁਹਾਨੂੰ ਸੇਵਾ ਬਾਰੇ ਕੋਈ ਖ਼ਾਸ ਗੱਲ ਅਛੀ ਲੱਗੀ, ਤਾਂ ਕਿਰਪਾ ਕਰਕੇ ਸਾਨੂੰ ਇਸ ਬਾਰੇ ਦਸੋ ਅਤੇ ਇਸ ਵਿਚ ਇਹੋ ਜਿਹਾ ਕੀ ਚੰਗਾ ਸੀ?

14. ਕੀ ਤੁਹਾਨੂੰ ਸੇਵਾ ਦੀ ਕੋਈ ਅਜਿਹੀ ਖਾਸ ਗੱਲ **ਚੰਗੀ ਨਹੀਂ ਲਗੀ**?

☐ ਹਾਂ ☐ ਨਹੀਂ

ਜੇਕਰ ਤੁਹਾਨੂੰ ਵਿਸ਼ੇਸ਼ ਤੌਰ 'ਤੇ ਕੁੱਝ ਅਛਾ ਨਹੀਂ ਲਗਾ, ਤਾਂ ਕਿਰਪਾ ਕਰਕੇ ਸਾਨੂੰ ਇਸ ਬਾਰੇ ਦਸੋ।

15. ਕੀ ਤੁਸੀਂ ਭੱਵਿਖ ਵਿਚ ਗੁਰਦੁਆਰੇ ਵਿਚ ਪੇਸ਼ ਕੀਤੀ ਜਾਣ ਵਾਲੀਆਂ ਸਕ੍ਰਿਨਿੰਗ ਟੈਸਟਾਂ ਕਰਵਾਉਣ ਲਈ ਰਾਜੀ ਹੋਵੋਗੇ?

☐ ਹਾਂ ☐ ਨਹੀਂ

ਤੁਸੀਂ ਹੋਰ ਕਿਹੜੀਆਂ ਸਕ੍ਰਿਨਿੰਗ ਟੇਸਟ ਕਰਾਉਣ ਬਾਰੇ ਸੋਚਦੇ ਹੋ?

16. ਤੁਹਾਡੇ ਵਿਚਾਰ ਅਨੁਸਾਰ, ਦੱਖਣ ਏਸ਼ੀਅਨ ਮੂਲ ਦੇ ਵਿਅਕਤੀਆਂ ਲਈ ਸਿਹਤ ਜਾਂਚ ਕਾਰਜਾਂ ਵਿਚ ਰੁਕਾਵਟ ਪਾਉਣ ਲਈ ਮੁੱਖ ਰੁਕਾਵਟਾਂ ਕੀ ਹਨ? (ਲਾਗੂ ਹੁੰਦੇ ਸਾਰੇਆਂ ਤੇ ਨਿਸ਼ਾਨ ਲਾਓ

☐ ਭਾਸ਼ਾ ਰੁਕਾਵਟ ☐ ਸਭਿਆਚਾਰਕ ਨਿਯਮ ☐ ਧਾਰਮਿਕ ਸ਼ਰਧਾ

☐ ਲਾਗਤ ☐ ਸਿਹਤ ਸਿੱਖਿਆ ਦੀ ਘਾਟ ☐ ਹੋਰ (ਕਿਰਪਾ ਕਰਕੇ ਹੋਠਾਂ ਦੱਸੋ)

ਕਿਰਪਾ ਕਰਕੇ ਸ਼ਾਸਲ ਹੋਣ ਵਿਚ ਆਉਂਦੀਆਂ ਹੋਰ ਰੁਕਾਵਟਾਂ ਬਾਰੇ ਇਥੇ ਸਪਸ਼ਟ ਕਰੋ/ਦਸੋ:

17. ਕਿਰਪਾ ਕਰਕੇ ਕੋਈ ਹੋਰ ਟਿੱਪਣੀ ਸ਼ਾਮਲ ਕਰੋ ਜੋ ਕਿ ਸਾਨੂੰ ਇਸ ਪ੍ਰਸਤਾਵਿਤ ਏਐਫ ਸਕ੍ਰਿਨਿੰਗ ਰਣਨੀਤੀ ਵਿੱਚ ਸੁਧਾਰ ਕਰਨ ਲਈ ਮਦਦ ਕਰ ਸਕਦੀ ਹੈ।

ਹੋਰ ਟਿੱਪਣੀਆਂ:

ਇਸ ਪ੍ਰਸ਼ਨਾਵਲੀ ਨੂੰ ਪੂਰਾ ਕਰਨ ਲਈ ਸਮਾਂ ਦੇਣ ਲਈ ਤੁਹਾਡਾ ਧੰਨਵਾਦ।

Appendix 55 Input parameters for the economic model of atrial fibrillation screening within a South Asian community

Table S4 Input parameters for the PSA of the Markov cost-effectiveness model evaluating the AF screening strategy within the South Asian community of individuals aged ≥ 18 years using Kardia Mobile® devices.

Abbreviations: AF – atrial fibrillation; ECG – electrocardiogram; PSA – probabilistic sensitivity analysis.

Cost Parameter		**Base Case (£)**	**Range in PSA (£)**		**References**
			Lower	Upper	
3-monthly AF screening costs/participant		261.54	130.77	392.31	NICE (2014b); NICE (2015); Welton *et al.* (2017); NHS Improvement (2017); AliveCor (2019c); NHS Employers (2019)
*Cost of single-lead ECG screening**		*0.58*	-	-	AliveCor (2019c); NHS Employers (2019)
*Cost of new diagnosis***		*102.85*	-	-	NICE (2015); Welton *et al.* (2017); NHS Improvement (2017)
Cost of oral anticoagulant therapy		*158.11*	-	-	NICE (2014b)
Cost of ischaemic stroke		3,395.08	1,697.54	5,092.62	
Cost of major bleed		325.73	162.87	488.60	
Transition Probabilities		**Base Case**	**Range in PSA**		**References**
			Lower	Upper	
Ischaemic stroke from stable AF	No screening	0.0184	0.0173	0.0196	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Gunarathne *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); George *et al.* (2017); Office for National Statistics (2018c)
	Screening	0.0127	0.0117	0.0137	
Major bleed from stable AF	No screening	0.0022	0.0018	0.0026	
	Screening	0.0025	0.0021	0.0029	
Death from stable AF	No screening	0.0109	0.0101	0.0118	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride
	Screening	0.0082	0.0074	0.0090	

					(1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Bhopal *et al.* (2018); Office for National Statistics (2018c)
Death from ischaemic stroke	No screening	0.0575	0.0427	0.0723	Wild & Mckeigue (1997); Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Gunarathne *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Jacobs *et al.* (2018); Office for National Statistics (2018c)
	Screening	0.0431	0.0276	0.0587	
Death from major bleed	No screening	0.0164	-0.0068	0.0397	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Eikelboom *et al.* (2006); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2018c)
	Screening	0.0123	-0.0065	0.0311	

Utilities	**Base Case**	**Range in PSA**		**References**
		Lower	Upper	
Stable AF	0.8430	0.7587	0.9273	Jacobs *et al.* (2018)
Post-ischaemic stroke	0.4490	0.3610	0.5370	
Post-major bleed	0.6660	0.5355	0.7965	

Table S5 Input parameters for the PSA of the Markov cost-effectiveness model evaluating the AF screening strategy within the South Asian community of individuals aged ≥ 65 years using Kardia Mobile® devices.

Abbreviations: AF – atrial fibrillation; ECG – electrocardiogram; PSA – probabilistic sensitivity analysis.

Cost Parameter		**Base Case (£)**	**Range in PSA (£)**		**References**
			Lower	Upper	
3-monthly AF screening costs/participant		223.52	111.76	335.28	NICE (2014b); NICE (2015); Welton *et al.* (2017); NHS Improvement (2017); AliveCor (2019c); NHS Employers (2019)
*Cost of single-lead ECG screening**		*0.58*	-	-	AliveCor (2019c); NHS Employers (2019)
*Cost of new diagnosis***		*64.82*	-	-	NICE (2015); Welton *et al.* (2017); NHS Improvement (2017)
Cost of oral anticoagulant therapy		*158.11*	-	-	NICE (2014b)
Cost of ischaemic stroke		3,395.08	1,697.54	5,092.62	
Cost of major bleed		325.73	162.87	488.60	
Transition Probabilities		**Base Case**	**Range in PSA**		**References**
			Lower	Upper	
Ischaemic stroke from stable AF	No screening	0.0184	0.0153	0.0216	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Gunarathne *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); George *et al.* (2017); Office for National Statistics (2018c)
	Screening	0.0150	0.0121	0.0179	
Major bleed from stable AF	No screening	0.0022	0.0011	0.0033	
	Screening	0.0035	0.0021	0.0048	
Death from stable AF	No screening	0.0396	0.0349	0.0442	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Granger *et al.*
	Screening	0.0362	0.0318	0.0407	

					(2011); Patel *et al.* (2011); Bhopal *et al.* (2018); Office for National Statistics (2017b); Office for National Statistics (2018c)
Death from ischaemic stroke	No screening	0.2078	0.1381	0.2776	Wild & Mckeigue (1997); Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Connolly *et al.* (2009); Gunarathne *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Jacobs *et al.* (2018); Office for National Statistics (2017b); Office for National Statistics (2018c)
	Screening	0.1904	0.1159	0.2648	
Death from major bleed	No screening	0.0593	-0.0480	0.1667	Petersen *et al.* (1989); Connolly *et al.* (1991); Mcbride (1991); Ezekowitz *et al.* (1992); EAFT Study Group (1993); Eikelboom *et al.* (2006); Connolly *et al.* (2009); Granger *et al.* (2011); Patel *et al.* (2011); Office for National Statistics (2017b); Office for National Statistics (2018c)
	Screening	0.0543	-0.0304	0.1391	

Utilities	**Base Case**	**Range in PSA**		**References**
		Lower	Upper	
Stable AF	0.8430	0.7587	0.9273	Jacobs *et al.* (2018)
Post-ischaemic stroke	0.4490	0.3610	0.5370	
Post-major bleed	0.6660	0.5355	0.7965	

*The cost of screening per participating British Indian individual of appropriate age in England and Wales (Office for National Statistics 2018c) included the clinical pharmacist's

supervisory time (7 min/appointment) and the acquisition cost of Kardia Mobile® devices (The AHSN Network 2019a).

**The cost of a 'new' AF diagnosis was based on the prevalence of previously undiagnosed AF (1.0% and 1.5% amongst those aged ≥ 18 and ≥ 65 years, respectively) determined by the cardiologist's interpretation of single-lead ECG and the sensitivity of the index test for the identification of AF. It took into account the cost of 12-lead ECG procedures and associated GP interpretations following the initial referral as well as the cost of GP and cardiologist's appointments for 'new' AF diagnoses (10 minutes each). It also considered the hypothetical costs of extra 12-lead ECGs and GP interpretations which would have been incurred due to false positive AF and 'Unclassified'/'Unreadable'/'Sinus Tachycardia' diagnoses resulting from the device's algorithm.

Appendix 56 Topic guide for individual interviews with general practitioners

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General practitioners' perspectives on UK atrial fibrillation screening programme: a qualitative study

SEMI-STRUCTURED INTERVIEW TOPIC GUIDE

Date of Interview: _____

Participant's UPIN: _____

Introduction	1. Welcome and thank you for taking part
	2. Purpose of the interview
	3. Duration
	4. Consent form
	5. Data reporting (confidentiality)
	6. Reimbursement

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Questions	Probes/Follow-ups	Comments
1. How important is it to screen patients for AF?	Benefits Impact for general practices Impact for health economy Risks of not screening	
2. Despite the underlying evidence and international recommendations, UK does not have a national AF screening programme. What do you think are the key barriers to routine AF screening in primary care? Would you support such an initiative in the future?	Time Workload/practice capacity Remuneration/funding Training/education/support Professional confidence/competence Knowledge relating to AF diagnosis/ management Infrastructure Environment/workspace Complexity of the healthcare system Problems with follow-up Communication issues Lack of leadership	
3. Are you or your practice involved in any AF screening initiatives locally, regionally or nationally? If so, what do you think enables such programmes? What prevents them from being implemented more effectively? If you're not involved, are you aware of any such initiatives? What prevents you from becoming more involved and what could change that?	See Question 2 above. 'Detect, Protect, Perfect' initiative by the Academic Health Science Networks in England Digital Health & Care Institute initiative in Scotland The One Stop AF Clinic in Llanelli, Wales Northern Ireland Chest Heart & Stroke 'It's time to talk about AF' initiative Concerns? Solutions? Do you feel well-informed about these initiatives?	

	Do you feel supported in delivering such initiatives? How much support has been provided?	
4. What do you think is the most optimal AF screening strategy? Should we screen everyone or just certain groups of individuals?	Systematic population screening (e.g. screening everyone over a certain age) Systematic targeted screening (only screening at-risk individuals) Systematic opportunistic screening (screening random individuals during another consultation) Target group for screening (e.g. based on comorbidities, age, location) Combination with other services, e.g. blood pressure or diabetes screening, seasonal influenza vaccinations, medication reviews One-stop screening-anticoagulation clinics	
5. What is the most suitable environment for AF screening?	General practice surgeries Community pharmacies Public locations	
6. In your opinion, who should deliver AF screening in primary care?	GPs Nurses Pharmacists Healthcare assistants Opticians Administrators/receptionists Multidisciplinary team Self-screening at home	

7. The introduction of modern technology has transformed the AF screening process. What are your views on the uptake and use of new technology, such as single-lead ECG devices, in the screening of AF? Do you use them in your practice?	Single-lead ECG devices Modified blood pressure monitors Mobile phone applications using photoplethysmography (PPG) Strengths? Limitations? Comparison with pulse palpation Comparison with 12-lead ECG Convenience Non-invasiveness Anxiety-free tests Reassurance Prompt result Inbuilt algorithm Ability to detect other cardiovascular conditions with ECG Educational potential Diagnostic accuracy/reliability	
8. Patients and the public are largely unaware of AF or the risks associated with it. How can we improve their awareness?	Leaflets Posters Health campaigns (Social) media National organisations/charities Community groups	
9. Is there anything else you would like to state or add?		

Appendix 57 Email invitation for general practitioners participating in individual interviews

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General practitioners' perspectives on UK atrial fibrillation screening programme: a qualitative study

EMAIL INVITATION TO A SEMI-STRUCTURED INTERVIEW

Subject: GP Perspectives on UK Atrial Fibrillation Screening Programme: a Qualitative Study

Dear Colleague,

You have received this email because your general practice surgery or group of surgeries has been selected for participation in the qualitative study aimed at ascertaining the general practitioners' (GPs') views about the UK atrial fibrillation (AF) screening programme. This study is conducted by researchers at the Medway School of Pharmacy (University of Kent) and has been approved by the Medway School of Pharmacy Research Ethics Committee.

We would like to request your assistance in distributing this invitation and information enclosed to any qualified GPs within your organisation. This email will be followed by two reminder emails one week apart.

All qualified GPs who are registered with the General Medical Council are eligible to participate in the study by attending a short telephone interview with one of the researchers at the time convenient for them. During this interview, participants will have an opportunity to provide their perspective on AF screening initiatives, which may ultimately contribute to the development of a future national AF screening programme. The time taken to participate will be reimbursed with a £50 Amazon voucher.

For more information about the study, please read the participant information sheet and the consent form attached to this email. If you or prospective participants have any questions or require further information about the study or the interview, please do not hesitate to get in touch with me using any of the contact details below.

Any prospective participants who wish to take part, should reply to this email with the following information:

Name and surname:
GMC registration number:
Preferred contact details (telephone/email/postal address):
Preferred date(s) and time(s) of the interview:

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Thank you very much for your time and consideration.

Yours sincerely,

Vilius Savickas | MRPharmS, PGDipGPP, FHEA, MClinRes

PhD Candidate and Graduate Teaching Assistant | Faculty of Sciences (University of Kent)

Medway School of Pharmacy | Universities of Greenwich and Kent at Medway, Anson Building, Central Avenue, Chatham Maritime, Chatham, Kent, ME4 4TB

Tel: +44 (0)1634202935 (ext. 2960) | **E-mail:** v.savickas@kent.ac.uk

Appendix 58 Participant information leaflet for general practitioners participating in individual interviews

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PARTICIPANT INFORMATION LEAFLET

Title of Project: General practitioners' perspectives on UK atrial fibrillation screening programme: a qualitative study

Name of Researcher (s): Mr Vilius Savickas, Dr Sarah Corlett, Dr Sukvinder Bhamra, Dr Emma Veale, Prof Alistair Mathie

If you are a qualified GP registered with the General Medical Council and are interested in taking part in this study, please take time to read the following information, so that you understand why the study is being done and what it involves. Ask if anything is not clear or if you would like more information. Take time to decide if you want to take part or not.

Why is the study being done?
Atrial fibrillation (AF) is a growing public health concern and a preventable cause of stroke, which results in a yearly bill of £2.2 billion. Unfortunately, as many as 30% of all AF cases remain undiagnosed, and despite international recommendations, the UK is yet to establish a national AF screening programme. Several qualitative studies involving patients and healthcare professionals showed that the implementation of AF screening programmes in primary care may be limited by increased workload or the lack of funding. However, no UK-based qualitative studies to date involved GPs, who are central to the design, commissioning and delivery of new services in primary care. This study aims to explore the views of GPs across the UK in relation to AF screening initiatives focusing on the facilitators and barriers to their development and implementation.

Do I have to take part?
No. It is up to you to decide whether or not to take part. Even if you agree to take part, you can change your mind at any time without giving any reason.

If I do take part, what would I have to do and what would be done to me?
If you do take part, you will be invited to undergo a 20-40-minute telephone interview with one of the researchers at the time convenient for you. If you agree to take part, you will be asked to sign a consent form. During the interview the researcher will ask you a series of questions regarding your current involvement in AF screening initiatives (if any), any perceived enablers and barriers to such initiatives, the possible design of future screening programmes and the use of novel technology. They may also use a number of follow-up questions to probe into your answers and will make notes accordingly.

Are there any risks if I take part?
This study is not associated with any significant risks. In an unlikely event where you feel distressed or otherwise uncomfortable during the interview, you will be able to stop at any time.

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Are there any benefits if I take part?
Your time taken to participate in the interview will be reimbursed with a £50 Amazon voucher. Your participation will also help to generate qualitative evidence in support of the future AF screening initiatives in the UK and/or abroad.

Will anyone know that I've taken part?
We will not tell anyone that you have taken part in the study.

What will happen to the results?
Your interview will be digitally audio-recorded. Your responses and interviewer's notes will be summarised in the comments section of the interview topic guide. After we interview another 14-19 GPs, these data will be analysed to derive the key themes and draw conclusions. All data collected as part of the study will be kept strictly confidential and stored securely at the Medway School of Pharmacy for 5 years in line with the Data Protection Act 2018 and the European Union General Data Protection Regulation. All data except the consent form and audio recording will be anonymised by assigning you a unique number. This data will be used in future reports and publications however it will not be possible to identify you. If you wish receive information about the study findings, please email v.savickas@kent.ac.uk. More information about the University's use of personal data can be found here: https://research.kent.ac.uk/researchservices/wp-content/uploads/sites/51/2018/05/GDPR-Privacy-Notice-Research.pdf

Who is organising and funding the study?
The study is carried out by researchers at the Medway School of Pharmacy (University of Kent) as part of a PhD research project. It is funded by the UK Clinical Pharmacy Congress Award and the Faculty of Science Research Funding, University of Kent.

Who should I contact if I want to know more about the study?
Vilius Savickas, PhD Candidate, by email: v.savickas@kent.ac.uk or by telephone: 01634 202935 or by post: Medway School of Pharmacy, Anson Building, Central Avenue, Chatham, ME4 4TB.

Who should I contact if I have any concerns about the study or the way it has been conducted?
If you have concerns about this study, please contact Dr Trudy Thomas, Senior Lecturer by email t.thomas@kent.ac.uk or by phone/post as listed above.

Thank you for taking time to consider taking part in this study.

This project has been looked at and approved by the
Medway School of Pharmacy Research Ethics Committee

University of Kent

Appendix 59 Consent form for general practitioners participating in individual interviews

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CONSENT FORM FOR SEMI-STRUCTURED INTERVIEW

General practitioners' perspectives on UK atrial fibrillation screening programme: a qualitative study

Name of researcher: Vilius Savickas (v.savickas@kent.ac.uk)

I have read and understand the **information provided** for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	Initial Here
I have read the **eligibility criteria** and can confirm that I am eligible to participate in this study.	Initial Here
I understand that my **participation is voluntary** and that I am free to withdraw at any time, without giving any reason. If I decide to withdraw, any data collected up to the point of withdrawal will be retained.	Initial Here
I understand that any **personal information** collected during the study will be anonymised and remain confidential.	Initial Here
I understand that data collected during the study may be used in **publications and reports**, but that these will be anonymised and not traceable to me.	Initial Here
I agree to participate in a **semi-structured interview and the study concerned**.	Initial Here

Name of Participant (Print)	Signature	Date

Name of person taking consent	Signature	Date

(if different from the researcher) Where possible, this is normally signed and dated in presence of the participant.

Lead researcher	Signature	Date

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