Developing a new measure of health-related quality of life for individuals with atrial fibrillation: a mixed method study.

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Acknowledgments

Dedicated in loving memory of my Father, [redacted]

And my Grandmother, [redacted].

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Declarations

I, Sarah Elizabeth Horan, confirm that the work presented in this thesis is my own.

Where information has been derived from other sources, I confirm this has been indicated in the thesis.

Abbreviations

AAD	Anti-arrhythmic Drug
AF	Atrial Fibrillation
AF PROM	A newly developed disease-specific HRQoL questionnaire
AFA	Atrial Fibrillation Association
AFEQT	The AF Effect on QualiTy of life Survey (Spertus et al, 2011)
AFQLQ	A disease-specific HRQoL questionnaire (Yamashita, 2003)
AFQoL	A disease-specific HRQoL questionnaire (Arribas et al, 2010)
AFSymp	Atrial Fibrillation Symptom Questionnaire
AV Node	Atrioventricular Node
BDI	Beck Depression Inventory
CA	Catheter Ablation
CBT	Cognitive Behavioural Therapy
CFA	Confirmatory Factor Analysis
COSMIN	COnsensus-based Standards for the selection of health status Measurement INstruments
CTT	Classical Test Theory
CVI	Content validity index
DoH	Department of Health
ECG	Electrocardiogram
EFA	Exploratory Factor Analysis
EMA	European Medicines Agency
EP	Electrophysiology
ESC	European Society of Cardiology
HCP	Health Care Professional
HRQoL	Health-Related Quality of Life
IAF	Interview with AF participant
IHCP	Interview with Health Care Professional
INR	International Normalised Ratio
IRoC	Interview with Relative or Carer
IRT	Item Response Theory
KMO index	Kaiser-Mayer-Olkin index
NHS	National Health Service
NICE	National Institute of Clinical Excellence
NOAC	Non-Vitamin K Antagonist Oral Anticoagulant (also referenced as Novel Oral Anticoagulants)
ONS	Office for National Statistics
PAF	Paroxysmal AF
PCA	Principal Component Analysis
PPM	Permanent Pacemaker
PROM	Patient-Reported Outcome Measure
PwAF	Participant/Person/People with AF
QLAF	A disease-specific HRQoL questionnaire (Braganca et al, 2010)
QoL	Quality of Life

RCT	Randomised Controlled Trial
RoC	Relative or Carer
SA Node	Sinoatrial Node
SD	Standard Deviation
SE	Standard Error
SF-36	Medical Outcomes Study 36-Item Short Form Survey
STAI	The State-Trait Anxiety Inventory
TIA	Transient ischemic attack (mini stroke)
TOE	Transesophageal echocardiogram
TTE	Transthoracic echocardiogram
UK	United Kingdom
VKA	Vitamin K antagonists
WHO	World Health Organisation
WHOQOL Group.	World Health Organisation Quality of Life Group
WHOQOL-BREF	World Health Organisation Quality of Life Group BREF

Developing a new measure of health-related quality of life for individuals with atrial fibrillation: a mixed method study.

Abstract

Background: Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting around 2% of the population. AF Symptoms, increased risk of stroke, along with anxiety about illness course, potential complications and adverse treatments effects can have a clear detrimental effect on patients' Health Related Quality of Life (HRQoL). A literature review revealed inadequacies in the methods used to develop extant HRQoL measures, most of which have had limited patient involvement in their development which potentially limits validity.
Aim: The aim of the PhD research project was to develop a novel and AF-specific HRQoL measure with greater emphasis on patient involvement throughout development; and to conduct preliminary testing of the instrument's psychometric characteristics.
Methods: The development of an AF-specific HRQoL measure involved several interrelated study phases. The first item generation stage used a series of focus groups (k=8) made up from patients with paroxysmal (n=7), persistent (n=9) and asymptomatic (n=5) AF; relatives of those with AF (n=3) and healthcare professionals (n=7). Item selection and assessment of face and content validity was assessed by a series of reviews by health care professionals (n=6), patients (n=2), academics (n=3) and patient organisation leads (n=1); individual interviews with patients with AF (n=15) and healthy controls (n=3). Transcripts from the focus group, interviews, and panel meetings were thematically analysed to derive AF PROM domains. Items were generated to reflect these domains. Preliminary validation of AF PROM was based on survey completion by participants with paroxysmal (n=46), persistent (n=22) and asymptomatic (n=9) AF and healthy controls (n=29) recruited from Barts Health NHS Trust and the AF Association website. Completion of AF PROMs, a generic QoL measure (WHOQOL-BREF) and an AF symptom questionnaire allowed the factor structure of AF PROM to be evaluated using Principle Component Analysis (PCA), internal consistency was evaluated using Cronbach's alpha, and convergent and discriminant validity using Pearson's correlation coefficient.
Findings: Item generation and selection phases identified five domains of HRQoL affected by AF, which formed a 28-item scale. From the five themes identified in the qualitative phase, PCA identified five different underlying components. Internal consistency of individual components ranged from α = .779 (component five) to α = .942 (component one). Initial results support the convergent and discriminant validity of AF PROM (AF PROM and generic QoL measure [r= .624; p< 0.00]) (AF PROM and symptom measure [r=-.734; p< 0.00]).
Conclusion: The AF PROM scale appears to be a psychometrically sound instrument of HRQoL. Following these preliminary validation stages, further work in a larger population is recommended and planned prior to wider use

Chapter 1: Clinical Background

This thesis will discuss the process of development of a Patient Reported Outcome Measure (PROM) for patients with Atrial Fibrillation (AF). This chapter will provide the reader with an initial understanding of the medical background of AF and its management. This will allow the reader to gain necessary understanding of this condition prior to discussion of the impact of AF on health-related quality of life (HRQoL), which will be discussed in later chapters.

1.1 Clinical Background: Introduction

Atrial Fibrillation (AF) is a tachyarrhythmia of the atria (The National Collaborating Centre for Chronic Conditions, 2006) involving the uncoordinated activation of the atria leading to deterioration of the mechanical function. AF is the most common arrhythmia, affecting 1-2% of the general population (Go et al., 2001; Savelieva and Camm, 2008; Zoni-Berisso et al., 2014). An estimated 33.5 million individuals had AF in 2010 globally (Chugh et al., 2014). The prevalence of AF is noted to increase with age (Reardon and Camm, 1996; Go et al., 2001), affecting 5% of those over the age of 65 and 10% of individuals over the age of 80 (Lip and TelloMontoliu, 2006). Recent studies indicate that the prevalence of AF in the general adult population of Europe ranges from 1.9% in England, Iceland and Italy to 2.3% in Germany and 2.9% in Sweden (Zoni-Berisso et al., 2014). It accounts for one third of all patients hospitalised for arrhythmias (Fuster et al., 2006).

It has been widely documented that AF affects health-related quality of life (HRQoL) (Van de Berg et al., 2001; Sanoski, 2009; Spertus et al., 2011). HRQoL in individuals with AF has been shown to be reduced when compared to those individuals without AF (and also without other cardiovascular conditions), and it also has been shown to be a significant risk factor for strokes and other medical conditions which may further reduce HRQoL (Wolf et al., 1991; Hannon et al., 2009). Although some patients may be asymptomatic, some studies have found an improvement of HRQoL after treatment for AF has taken place (Yamamoto et al., 2014).

In the United States of America (USA), the United Kingdom (UK) and other European nations, there has been growing attention and activity in measuring patient outcomes in a way that reflects and captures the patient's perspective in various settings such as healthcare systems, clinical practice and research (Nelson et al., 2015). Many Patient Reported Outcome Measures (PROMs) collect information such as symptoms, mental health, physical function and socialisation. Such information may be used by healthcare providers to indicate the cost effectiveness of treatments instead of relying solely on morbidity and mortality indicators, which can be used to make quality

improvements (Nelson et al., 2015). Furthermore, data on treatment outcomes and progress of conditions may be of interest to patients and clinicians when choosing treatments and healthcare providers (Nelson et al., 2015).

There are many hundreds of PROMs, and their development predates the use of this umbrella term. In 2009 the National Health Service (NHS) introduced four PROMs to measure changes in patients' self-reported health status following elective surgical interventions. Although these were initially for procedures such as hip replacements, varicose veins and inguinal hernia repairs (NHS choices, 2013), the information derived proved so beneficial that it led to a focus on the use of PROMs to measure the outcomes of other treatments, particularly for long-term conditions where the focus of treatment is on symptomatic control rather than cure (Doward et al., 2010).

Increasingly, attention has been focused on the importance of measuring the effectiveness of care for long-term conditions, and in ensuring that measures are relevant to patients' needs and experiences. The combination of improved living standards and success in combating many diseases has led to increased life expectancy and improved health in the world's industrialised societies. Low fertility rates have accentuated the effects of these changes on demographic structure, increasing the proportion of older persons to one-third or more of the population of Western Europe and North America. In 2012, 1.4 million people over the age of 85 where living in the UK, and this is expected to rise to over 3.6 million by 2037 (Office for National Statistics 2014). This demographic change is associated with an increased risk of other diseases associated with older age such as diabetes and AF. In England, 15 million people experience at least one long-term condition, accounting for 70% of the NHS's budget (Department of Health, 2013). This increased burden on the NHS is expected to rise; there is, therefore, an urgent need for policy-makers to provide clinicians with guidance on appropriate and cost-effective treatments to ensure patients receive the best patient-centred care (Heeringa et al., 2006). As well as enabling more detailed and accurate understanding of the burden of disease attributable to AF, a tool for measuring HRQoL specifically developed for this patient group will allow clearer quantification of the harms and benefits of the treatments for this condition, which can include costly and invasive procedures such as catheter ablation.

1.2 Medical Background

1.2.1 The Heart

The heart is a muscular organ located in the middle and slightly to the left of the thorax. The heart is made up of four chambers: the left atrium the left ventricle, the right atrium and right ventricle. The left and right side of the heart are separated by the septum. The atrium and ventricles work together to pump blood around the body to supply the body with essential oxygen and nutrients and also to help transport the removal of waste products within the cardiovascular system. The heart is a muscle, and the oxygen and nutrients it requires to function are supplied by the coronary arteries (Figure 1.1) and associated blood vessels that surround it. Any blockage or reduction in the size of these vessels reduces blood flow to the heart. Occlusion or sudden reduction of coronary artery blood flow is termed acute coronary syndrome.

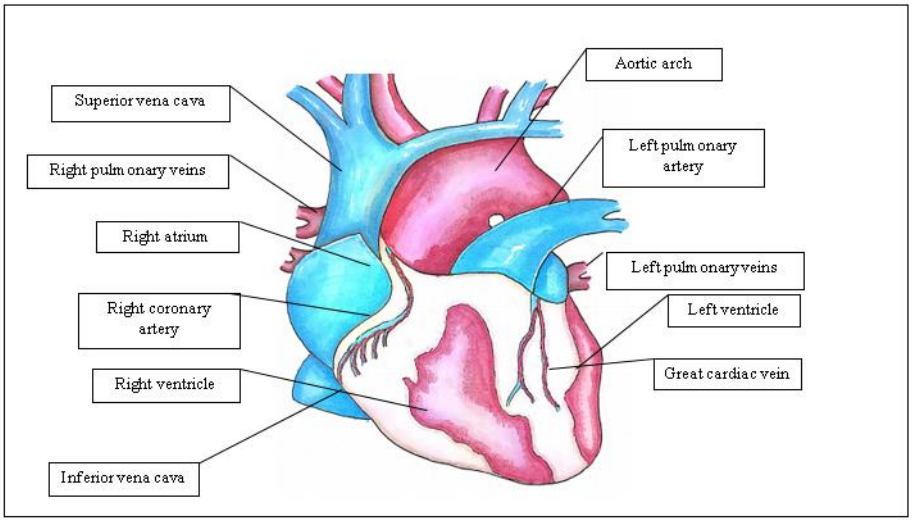


Figure 1.1: Heart Diagram: Coronary arteries and veins.

The heart is made up of three layers and the cells which make up these layers have different properties. The outside layer, called the pericardium, is a fibrous sac that covers the heart. The middle layer, the myocardium, is made up of cardiac muscle tissue which enables the heart to contract and therefore work as a pump. The endocardium is the innermost layer; it is made up of layers which include a conductive tissue layer and nerves and fibres.

1.2.2 Cardiac Cycle

The right side of the heart is involved in pumping the pulmonary circulation (relating to the lungs). Deoxygenated blood is pumped from the right atrium via the tricuspid valve into the right ventricle;

the ventricle then pumps the blood via the pulmonary valve into the pulmonary artery, which drives blood to the lungs. There it loses the carbon dioxide and gains oxygen becoming oxygenated blood.

The left side of the heart is involved in pumping the circulatory system. The oxygenated blood passes through the pulmonary veins into the left atrium and is pumped into the left ventricle via the mitral valve. The left ventricle then pumps the blood around the rest of the body via the aortic valve and the aorta. Body tissues are delivered oxygenated blood and nutrients via this blood system, exchanging oxygenated blood for deoxygenated blood. This is delivered back to the right atrium via the superior and inferior vena cava returning to the pulmonary circulation system. In a healthy heart, this process is repeated 60-100 times a minute.

As described above, the heart is made up of different tissues, one of which has the property of being electrically conductive. This electrical conduction system stimulates the cardiac muscle to contract and pump blood around the body. The cardiac pumping cycle is initiated by the heart's natural pacemaker, which is a small bundle of specialised cells located in the top right side of the heart called the SA Node. These electrical signals travel down the electrical pathway of the heart, which in a healthy heart causes the heart to contract in a coordinated way and therefore pump blood effectively around the body.

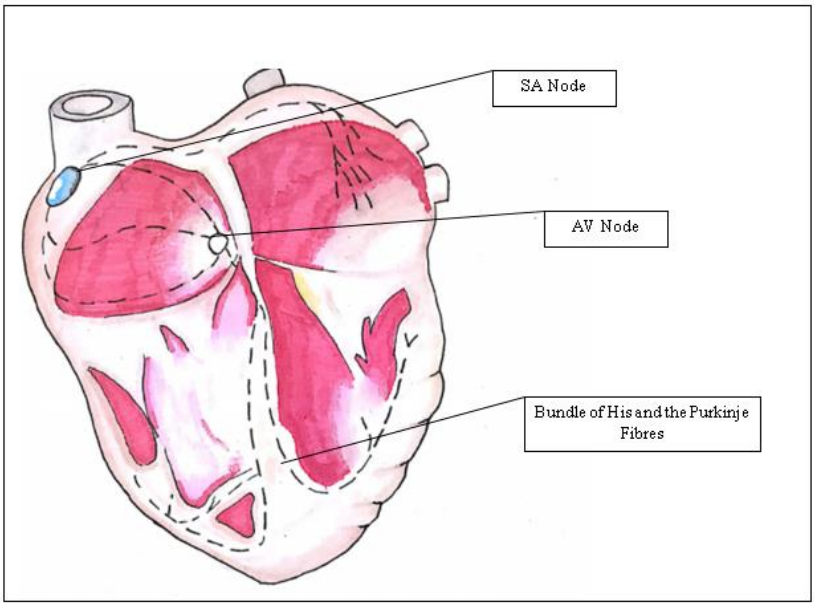


Figure 1.2: Heart Diagram: Electrical conductive system.

The electrical signal commences at the SA node (shown in Figure 1.2), and as the signal travels it causes the atria to contract and pump the blood into the ventricles. As the electrical signal reaches the AV node (shown in Figure 1.2), there is a slight delay and this delay gives the atria extra time to

pump the blood into the ventricles. The electrical signal then travels down the Bundle of His and the Purkinje Fibres (shown in Figure 1.2), causing the cardiac muscle tissue in the ventricles to contract, which causes the ventricles to pump the blood around the body.

There are four different valves in the heart, and during the cardiac cycle there are a number of different pressure and volume changes which initiate the opening and closing of different valves in the appropriate sequence.

1.2.3 Atrial Fibrillation

Atrial fibrillation is a tachyarrhythmia of the atria (The National Collaborating Centre for Chronic Conditions, 2006) involving the uncoordinated activation of the atria and is followed by a deterioration of the mechanical function (NICE, 2006).

It appears that the irregular electrical activity originates from the pulmonary veins surrounding the atria, particularly in paroxysmal AF. Because electrical activity is not originating from the SA node (seen in Figure 1.2) as in a normal heart, uncoordinated electrical activity causes the atria to fibrillate. This additional uncoordinated electrical activity floods the AV node with extra electrical signals. Although the AV node does not allow every signal to pass (as it requires time to repolarise), a higher number of electrical signals will pass through. This increases the rate at which the ventricle pumps (from 100 to 175 beats per minute), causing ventricles to pump less effectively as there is less time for the blood to flow from the atria to the ventricles.

As the atria are not pumping the blood into the ventricles effectively, there is a risk of a pooling of blood which can mean blood becomes stagnant. This increases the risk of clotting in the atria and therefore ultimately increases the risk of stroke.

1.3 Epidemiology

AF is the most common arrhythmia, affecting around 1-2% of the population (Savelieva and Camm, 2008; Go et al., 2001; Zoni-Berisso et al., 2014) with worldwide prevalence estimated to be 33.5 million in 2010 (Chugh et al., 2014). Some researchers suggest the prevalence of AF has doubled in the last ten years (Zoni-Berisso et al., 2014). Various studies have explored the prevalence of AF in America and Western Europe. The Framingham study, for example, which has informed prevalence figures for the United States, reported that incidence of AF increased with age (Reardon and Camm, 1996; Go et al., 2001), rising to 10% in individuals over the age of 80 (Lip and TelloMontoliu, 2006).

Other studies such as the Rotterdam study provided prevalence figures for European countries presenting (age-adjusted) prevalence of 17.8% in patients over the age of 85 but only 0.7% prevalence in those aged between 55 and 59 (Heeringa et al., 2006). Researchers report that 46,000 new cases are identified each year in the UK (Iqbal et al., 2005) and prevalence figures for the UK from studies such as the ECHOES study indicate higher prevalence in the older population (8.0%) compared to younger patients aged 45-54 (0.2%); they also report a higher prevalence in men compared to women (Davis et al., 2012).

The prevalence of AF identified from primary care diagnostic recordings was 1.48% of the population of England in 2011/12 (Quality and Outcomes Framework, 2013). However, the National Institute of Health and Care and Excellence (NICE) (2014) suggests that reported prevalence figures may underestimate the true prevalence of AF. This is supported by the SAFE study, which noted a 0.5% increase in prevalence when opportunistic screening is used (Hobbs et al., 2005). Recent NICE (2014) guidance suggests that the true prevalence of AF in England is likely to be 2.0% of the population, which is similar to the 1.9% estimated by Zoni-Berisso et al. (2014).

Incidence in Europe ranges from 0.21 to 0.41 per thousand people per year (Zoni-Berisso et al., 2014). The incidence is predicted to increase due to the widespread demographic changes that are leading to an increasingly ageing population (Go et al., 2001; Fuster et al., 2006). It is therefore estimated that the number of individuals in 2030 with AF will be 14–17 million in Europe (Zoni-Berisso et al., 2014).

Much has been published describing the prevalence of AF in the Caucasian population, but less research has examined prevalence among other ethnic groups (Alonso et al., 2009; Camm et al., 2010). Although prevalence data is known to vary between countries, with data from regions such as Africa and Asia being limited, it is suggested that prevalence may be underestimated in both developing and developed countries (Rahman et al., 2014; Lim et al., 2016). Although the recent focus on examining prevalence of AF in developing countries may lead to an increase in worldwide prevalence figures, prevalence is anticipated to further rise because of an ageing population, increasing healthcare awareness and opportunistic screening (Chugh et al., 2014).

1.4 Mortality

There are four main studies which provide findings derived from long-term follow-up of patients with AF. The Manitoba Follow-Up Study, which followed 3,983 participants over 44 years, found that the total mortality rate increased 1.31 fold (Krahn et al., 1995). The Framingham Heart Study, which

involved 5,000 patients followed up over 40 years, examined survival rates in individuals with AF; it demonstrated that total mortality rate increased 1.4 fold in patients with AF (Benjamin et al., 1998). The Renfrew/Paisley study observed 15,406 patients over 20 years in West Scotland (Stewart et al., 2002) and revealed that during this period, 0.5% of the total male population (n=35, total male n=6999) had AF that involved an episode of hospitalisation or led to death. Similarly, 0.5% (n=42, total women=8307) of women patients during this time had AF that involved an episode of hospitalisation or led to death (Stewart et al., 2002). The Marshfield Epidemiologic Study Area, which involved a four-year follow up, found that the risk of death increased 2.4 fold in patients with AF or atrial flutter (Vidaillet et al., 2002).

The higher mortality rate in this population is in part because AF is strongly associated with risk of stroke and heart failure (Bordignon et al., 2012). The risk of stroke is increased further because hypertension is more common in patients with AF compared to other atrial arrhythmias (Mareedu et al., 2010). The risk of stroke is doubled in patients with AF and the risk of heart failure is tripled, even when individuals have no other comorbidities compared to a control group (Andersson et al., 2014). There has also been found to be a 40% increase in mortality with patients who have had a myocardial infarction (MI) as well as AF (Jabre et al., 2011). There is currently great interest in treatments and outcomes for patients with AF, with an international multicentre study (GARFIELD: Global Anticoagulant Registry in the Field) involving 55,000 people currently underway (Kakkar et al., 2012).

Although AF has been shown to increase mortality, anticoagulation significantly reduces this risk (Liew et al., 2014). Updated NICE (2014) guidelines and recent European Society of Cardiology (ESC) guidelines (Kirchhof et al., 2016) have stressed the importance of screening through the CHA2DS2-VASc scoring system and of ensuring adequate anticoagulation. Several non-vitamin K antagonist oral anticoagulants (NOACs) have been developed and found to have similar efficacy as warfarin in reducing the risk of stroke. One systematic review further suggests that although warfarin has the advantage of having been used for years and is able to be reversed if needed, NOACs provide patients with a choice of treatments and may be viewed as less inconvenient than vitamin K antagonists such as warfarin (Hicks et al., 2016).

1.5 Aetiology

According to major studies such as the Framingham Heart Study, the incidence of AF doubles every ten years after the age of 50 (Munger et al., 2014), with the prevalence increasing from 0.5% of the population below 60 years old to more than 10% of the population above 80 years old. The

association of increasing incidence of AF with increasing age is likely to be because AF in the majority of people is a vascular disease related to hypertension, atherosclerosis and other cardiovascular risk factors (Chugh et al., 2014), which are strongly associated with ageing (Khand et al., 2000; Cordina and Mead, 2006). There is also a genetic element: in 2004, the Framingham Heart Study investigators described an increased risk of AF in offspring in whom at least one parent had AF, even after accounting for established AF risk factors (Lubitz et al., 2010), and further genetic studies have established a number of common genetic variants associated with AF risk (Lubitz et al., 2010; Calkins et al., 2017).

Associations are found between other medical conditions such as hyperthyroidism, electrolyte disturbances such as hypokalaemia and hyponatremia, lung disease, asthma, diabetes and sleep apnoea (Camm et al., 2010; Calkins et al., 2017). Additionally, some dietary factors may affect the development of AF: individuals who have an excessive alcohol intake may be more likely to develop AF (sometimes referred to as having a 'holiday heart'); illicit stimulant drugs and excessive caffeine intake from coffee and energy drinks is also thought to have an effect on AF (Camm et al., 2010).

Idiopathic AF is where there is no identifiable reversible cause. A wide range of prevalence findings have been reported, dependent largely upon the condition definition and criteria used by the researchers (Nieuwlaat et al., 2005; Nabauer et al., 2009; Weijs et al., 2012; Wyse et al., 2014). Recent ESC guidelines highlight the need for systematic research to be carried out to define AF type and pathophysiology.

Documented evidence suggests that 'Atrial Fibrillation begets Atrial Fibrillation' (Wijffels et al., 1995): often paroxysmal atrial fibrillation (PAF) evolves to persistent or permanent AF and this is thought to be due atrial remodelling. Naccarelli and Allessie (2006) suggest that if sinus rhythm is maintained for as long as possible then this may slow the remodelling of the atria, hence the desire that sinus rhythm is achieved as soon as possible with an appropriate treatment. However, the absence of clinical effect with therapies such as the atrial defibrillator suggest that 'reverse re-modelling' may not be an effect seen in humans. Furthermore, the progression from PAF to persistent AF has been shown not to be universal in all patients with many patients developing persistent AF as their first manifestation (Campbell et al., 2014).

1.6 Classification of Atrial Fibrillation

Initial episodes of AF may be symptomatic or asymptomatic, making it difficult to define when onset of the condition occurs. It is generally accepted that there are four classifications of AF:

- Asymptomatic Atrial Fibrillation (AF)
- Paroxysmal Atrial Fibrillation (AF)
- Persistent Atrial Fibrillation (AF)
- Longstanding persistent (sometimes referred as Permanent) Atrial Fibrillation (AF)

The classifications of AF are described in Table 1.1 below**.**

Table 1.1: Classifications of AF	
Asymptomatic or Silent Atrial Fibrillation (AF)	Patients may be unaware of having episodes of AF. AF may be diagnosed whilst being routinely tested or having tests for another medical condition. Asymptomatic AF can be paroxysmal, persistent, long standing persistent or permanent AF.
Paroxysmal Atrial Fibrillation (AF)	Recurrent episodes that self-terminate within seven days without any treatment.
Persistent Atrial Fibrillation (AF)	Recurrent episodes that last longer than seven days, or that are terminated (either by a pharmacological approach or by electrical means).
Longstanding persistent (sometimes referred as Permanent) Atrial Fibrillation (AF)	A continuous episode that lasts for more than one year. This type of AF does not self-terminate. Treatment may have been attempted previously but has been unsuccessful.
(Source: AF Association, 2011)	

1.7 Diagnosis

1.7.1 Symptoms

Although some individuals with AF may be asymptomatic and only diagnosed by a routine check-up, the most typical symptoms associated with AF include breathlessness, palpations, dizziness, chest pain and tiredness (NICE, 2014). These symptoms are not unique to AF and therefore may be confused with other long-term conditions (by the patient and even by medical staff). Some individuals may attribute these symptoms to reducing fitness levels or old age. Although they may not sound

serious at first, when the symptoms begin to affect a person's HRQoL and their ability to carry out day-to-day activities, it can be very difficult for them to manage without treatment. This can lead to a loss of independence for the individual and also a sense of reliance on family or friends who may have other underlying conditions, which may have an effect on the relatives or carers who live with and look after them. A major factor in the management of AF is the control of symptoms and improving and sustaining a good HRQoL for individuals.

1.7.2 Diagnosis

The pathway of diagnosis may be variable and may depend on whether a person has been asymptomatic or symptomatic of their AF. For example, a person may be asymptomatic and diagnosed by opportunistic screening in the course of a routine health check; alternatively, a person may present with symptoms to their pharmacist, GP or to an Accident and Emergency Department. Updated guidelines such as those issued by ESC and NICE (2014) recommend that a pulse check and an electrocardiogram (ECG) be taken in those who are older or are suspected of having AF. It is recommended to provide documented evidence of AF in the form of an ECG rhythm strip with a pattern of AF (NICE, 2014; Kirchhof et al., 2016; Calkins et al., 2017). However, difficulty capturing AF can arise due to sporadic episodes especially in those who are asymptomatic of PAF. This may mean longer monitoring periods are needed which can involve the use of an ambulatory Holter monitor for a period of time such as 24 hours, 72 hours or seven days. New advances in technology (such as single lead monitors, blood pressure cuff machines, hand-held mobile devices and implantable devices) allow longer periods of screening to increase detection rates. Once diagnosed by confirmation of ECG, blood tests may be used to identify a cause of AF (such as sepsis or thyroid problems) (Kirchhof et al., 2016). The person may be referred to an electrophysiologist or a cardiologist for further management advice.

1.7.3 ECG

An ECG is the main form of diagnosis; it measures the electrical activity and the rhythm of the heart. AF is generally characterised on an ECG as an irregular rhythm, where there are variable R-R intervals because the atria contract irregularly. There also may be no P waves on the ECG before the QRS complex. This can be seen on the ECG in Figure 1.3.

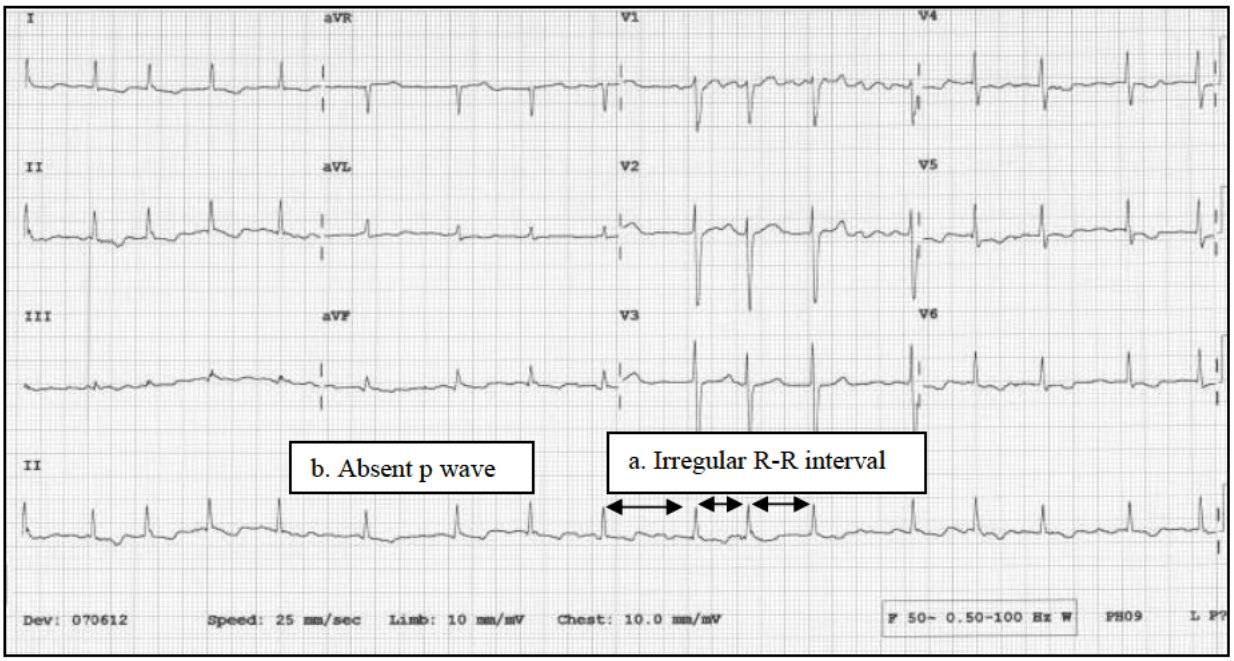


Figure 1.3: 12 lead ECG of a 71-year-old female (showing AF. Rate 98 bpm).

The ECG can also show if there are any structural abnormalities which would indicate the need for further investigations. It is important to gain an understanding of the management of the AF pathway that patients experience and how this may influence their HRQoL. A brief overview of the management will be covered, including the effect these may have on HRQoL.

1.8 Management of AF

Guidelines informing current AF clinical care, such as NICE (2014), ESC, the catheter and surgical Ablation of AF consensus statement (Calkins et al., 2017) and those produced by the American College of Cardiology and American Heart Association (January et al.,2014) are informed by evidence and clinical expertise.

Although the most recent literature may not influence the current care pathways, they have the potential to influence future care pathways and further research. For example, 'A Focus on Atrial Fibrillation in Scotland', a report produced by the Cross-Party Group Inquiry (2018), highlighted the need for further work in AF management and assessing the risk of stroke in those with AF. This has led to collaborations within Scotland which have great potential to impact future care.

1.8.1 Current Clinical Guidelines

Stroke risk assessment, assessing the need for anticoagulant to reduce stroke risk, and rate and rhythm control are priorities in current European and United Kingdom guidelines even after catheter ablation in some individuals (NICE, 2014; Kirchhof et al., 2016; Calkins et al., 2017). To aid clinical decisions regarding long-term management of AF, NICE guidelines (2014) recommend that cardiac function be assessed using a transthoracic echocardiograph (TTE). The presence of structural heart disease may influence treatment preference (NICE, 2014). If the results of the TTE are unclear, a transoesophageal echocardiography (TOE) is recommended.

1.9 Stroke

1.9.1 Stroke Risk

The Framingham Heart Study which commenced in 1948 found that AF increases the risk of stroke (Reardon and Camm, 1996). It is therefore important that patients with an increased risk of stroke take anticoagulants to reduce the risk. Strokes and transient ischaemic attack (TIA, sometimes referred to as a 'mini stroke') can have a significant effect on patients' HRQoL. Preventative measures can make a large difference. Practitioners involved in the care of patients with AF use the CHA_2DS_2-VASc scoring system to determine risk of stroke.

Table 1.2 (below) shows details of the CHA_2DS_2-VASc scoring system, which was developed for patients with AF to identify patients at risk of stroke. Patients with AF have their risk factors totalled up and if a patient has a score of 2 or more they are advised to commence oral anticoagulation. If a patient has a score of 1 or more, they may previously have been recommended aspirin or an oral anticoagulant (as of 2014, oral anticoagulation is preferred). If a patient has a score of 0 then their risk is considered minimal and they would not be recommended for anticoagulation treatment.

Table 1.2 CHA_2DS_2-VASc Scoring System

Risk Factor	**Score**
Congestive Heart Failure / LV dysfunction	1
Hypertension	1
Age 75 and above	2
Diabetes Mellitus	1
Prior Stroke/TIA/Thrombo-embolism	2
Vascular Disease	1
Age 65-74	1
Sex Category (i.e. Female sex)	1
Maximum score	**10**

1.9.2 Stroke Prevention

Evidence from several Randomised Controlled Trials (RCTs) has shown that aspirin has little if any benefit in reducing the risk of thromboembolic events in patients with AF who are at moderate to high risk of stroke when compared to anticoagulants such as warfarin (Deshpande and Wann, 2016). This has led to the removal of the use of aspirin for effective stroke prevention from UK, European and Japanese guidelines (NICE, 2014; Kirchhof et al., 2016). Other antiplatelet medications do not reduce the risk of stroke.

The choice of anticoagulant treatment depends on several factors, including liver function tests, patient suitability and patient choice. The most commonly used oral anticoagulant (Vitamin K antagonist [VKA]) is warfarin. Warfarin dose is influenced by the results of a blood test (usually a finger prick test) called the International Normalised Ratio (INR). This blood test indicates how long it takes the blood to clot. Patients are usually given a target therapeutic INR. For patients with AF this target is usually between 2 and 3. The frequency with which this test is repeated depends on INR stability and patient compliance. Dietary restrictions may be placed upon the patient as many foods and drinks (such as green leafy vegetables and cranberry juice) interact with warfarin, causing the INR to change as a result. When a patient is initially commenced on warfarin they may be required to take this blood test every day or weekly, but this frequency usually decreases as time progresses.

More recently, alternatives to VKAs called non-vitamin K antagonist oral anticoagulants (NOACs) which include rivaroxaban, dabigatran and apixaban have been developed and licensed for stroke risk reduction in AF (NICE, 2014; Steffel et al., 2018). Recent European guidelines (ESC) have recommended using NOACs instead of VKAs unless there is a low risk of stroke or there are contraindications to taking these medications. NOACs will not be suitable for some individuals; this includes those with mechanical valves and those with kidney problems. Although NOACs have several advantages over VKAs, including fewer dietary interactions, consistent dosing and not requiring regular blood tests, less is known about their long-term effects and their safety. Another disadvantage of NOACs is due to the impact of a short half-life; as there is no need for regular blood testing, compliance cannot be assessed and if compliance is poor this could lead to stroke. It should be noted that some NOACs still have no reversal agent and therefore in the event of serious bleeding, admission to hospital would be essential.

For those patients who are unable to take oral anticoagulation medication, a left atrial appendage occlusion may be more suitable. Although some patients may prefer this method, this is a costly invasive procedure, the funding of which has been recently restricted and therefore only available for

a limited few throughout the UK. Further research is recommended comparing this approach to NOACs (Kirchhof et al., 2016).

1.10 Anticoagulation and Health-Related Quality of Life (HRQoL)

Qualitative literature exploring adherence to warfarin identified factors which may influence the degree of negative impact of warfarin on HRQoL (Dantas et al., 2004; Prins et al., 2009; Kneeland and Fang, 2010). Such literature suggests that factors such as associated side effects, restrictions on activities, diet, essential regular hospital appointments and the amount of information given to patients may influence the degree of impact on HRQoL (Prins et al., 2009; Kneeland and Fang, 2010). Although the literature portrays the negative impact of such inconveniences on HRQoL from vitamin K antagonists (VKAs), some researchers argue that this negative impact may be less than described (Smith et al., 2010). This argument is supported by the results of the Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) study, which compared HRQoL scores in patients on warfarin and aspirin (which has fewer of the inconveniences associated with warfarin) and found no significant differences between the HRQoL scores in these two groups (Lancaster et al., 1991). More recently, there has been growing attention on NOACs and their impact on HRQoL, with the results of the Randomized Evaluation of Long-term anticoagulant therapY (RE-LY) lending further support to this argument. This study, which compared the HRQoL scores of patients on warfarin with those on a NOAC (Dabigatran), found no significant difference (Monz et al., 2013). However, the findings from another study suggest that NOACs have a less negative impact on HRQoL compared to warfarin, with those on warfarin self-reporting higher levels of depression and anxiety compared to those on NOACs (Balci et al., 2016). However, as there is still uncertainty regarding the use of NOACs the authors acknowledge these results may have been influenced by clinicians preferring to prescribe NOACs to healthier participants with fewer comorbidities who may be better able to respond to side effects (Balci et al., 2016). Although the impact on HRQoL is important to consider, adherence to the prescribed anticoagulant therapy is essential to reduce the risk of stroke, and compliance may be influenced by patient preference. Some studies suggest that patients prefer less inconvenience and therefore prefer the use of the NOACs compared to VKAs (Wilke et al., 2017).

1.11 Treatment

As already stated, guidance documents (NICE, 2014; Kirchhof et al., 2016) initially focus on stroke risk assessment and reduction. The ESC guidelines recommend prioritising the management of the symptoms of AF to improve the HRQoL of patients with this condition. Although available guidelines outline a structured approach to assessing and managing the symptoms of AF (Kirchhof et al., 2016;

Calkins et al., 2017), this guidance also outlines the importance of ensuring that clinical care is focused on the individual patient to ensure that comorbid conditions and other medications and potential drug interactions are considered within the clinical assessment. For example, doses of antiarrhythmic medications may need to be altered in patients with reduced renal function (NICE, 2014).

1.12 Medication Management

Available clinical guidance (e.g. NICE, 2014) outline the recommended medical management of AF which focuses on controlling the ventricular rate or restoring the ventricular rhythm to normal sinus rhythm. Such guidance documents are firmly based on evidence from worldwide clinical trials. The results of clinical trials supply healthcare providers with the necessary data to form relevant and evidence-based guidelines. Clinical trials such as RACE (Rate Control vs. Electrical Cardioversion for Persistent Atrial Fibrillation) and AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) (Mickel et al., 2002) have informed clinicians regarding the appropriateness of each strategy, recommending that they take account of various factors such as patients' previous AF treatments and AF symptoms (NICE, 2014).

1.12.1 Rate Control

Rate control aims to slow down the heart rate, reducing the stress that a high pulse has on the heart. This rate control is carried out by taking medications such as beta blockers (e.g. Bisoprolol), calcium channel blockers (e.g. diltiazem) or a cardiac glycoside (e.g. digoxin). These all work slightly differently but they predominately control the rate of the ventricles by reducing the conduction rate of the AV node and cause the heart to pump more efficiently. Although rate control medications pose slightly less risk than rhythm control medications, they nevertheless can be accompanied by severe side effects; for example, the use of cardiac glycosides requires close monitoring as toxicity can occur. Other side effects of rate control medications include lethargy, dizziness and shortness of breath.

1.12.2 Rhythm Control

The aim of using a rhythm control strategy is to cause the heart to return to sinus rhythm. This can either be done by electrical means or by chemical means. The method of electrical cardioversion involves the patient receiving a direct current cardioversion under sedation in an effort to cause the heart to return to sinus rhythm. The use of chemical cardioversion aims to cause the heart to return to

sinus rhythm through the administration of an antiarrhythmic drug. This drug can be administered in various forms including a tablet, which can be taken as a pill in the pocket approach, whereby an antiarrhythmic drug is only taken when needed, or can involve the antiarrhythmic drugs being administered for a longer period of time (i.e. daily). Alternatively, this drug can be administered by an intravenous route which is given in a hospital setting.

Side effects of medications used in rhythm control such as amiodarone can be more common and potentially more severe. These can include pro-arrhythmia effects, thyroid problems, lung damage and liver damage (Camm, 2005). Another rhythm control drug called flecainide also comes with serious side effects such as depression, shortness of breath and raised potassium levels (NICE, 2014). Due to the high risks associated with these medications, the ESC recommend that they are used for short periods of time and in conjunction with life modifications which may reduce AF symptom burden (such as weight loss, exercise and blood pressure control). This management approach is not recommended in those who are asymptomatic or who have permanent AF (Kirchhof et al., 2016).

1.12.3 Rate or Rhythm Control

At present, treatment decisions regarding control of ventricular rate or rhythm are dependent on several factors including age, comorbidities, the symptomatic burden of AF and patient preference. Several landmark studies have informed clinical guidance such as NICE (2014). Most Randomised Controlled Trails (RCTs) have focused on measuring outcomes such as AF reoccurrence, mortality rates or hospitalisation rates. A recent systematic review and meta-analysis favour a rate control strategy, mainly due to the lower hospitalisation rates associated with a rate control method (Chatterjee et al., 2013).

Some RCTs have considered the impact on HRQoL, including the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) (Mickel et al., 2002; Jenkins et al., 2005); the Rate Control Versus Electrical Cardioversion (RACE) (Hagens et al., 2004); Pharmacological Intervention in Atrial Fibrillation (PIAF) (Hohnloser et al., 2000), Strategies of Treatment of Atrial Fibrillation (STAF) (Carlsson et al., 2003) and others (e.g. Grönefeld et al., 2003). However, lack of consistency reporting HRQoL has led some researchers to express difficulty reporting such meta-analysis results (Sullivan et al., 2013).

1.13 Catheter Ablation

A catheter ablation for AF is an invasive procedure which involves admission to hospital either as a day procedure or as an overnight stay. Risks and the consenting procedure are discussed. Pre-procedure fasting is necessary, but patients may receive intravenous hydration if needed. Intravenous access allows the administration of sedative medications (slight sedation or general anaesthetic) and furthermore is essential in the event of a vagal reaction (Earley, 2009). Femoral vein access is essential, so a sheath is inserted in the right femoral vein. A transeptal puncture is used to gain access into the left atrium. Energy (either cryro or radiofrequency energy) is emitted to cause damage to the heart tissue around the pulmonary veins (see Figure 1.4), which makes the cardiac tissue unable to conduct the additional electrical signals that cause AF.

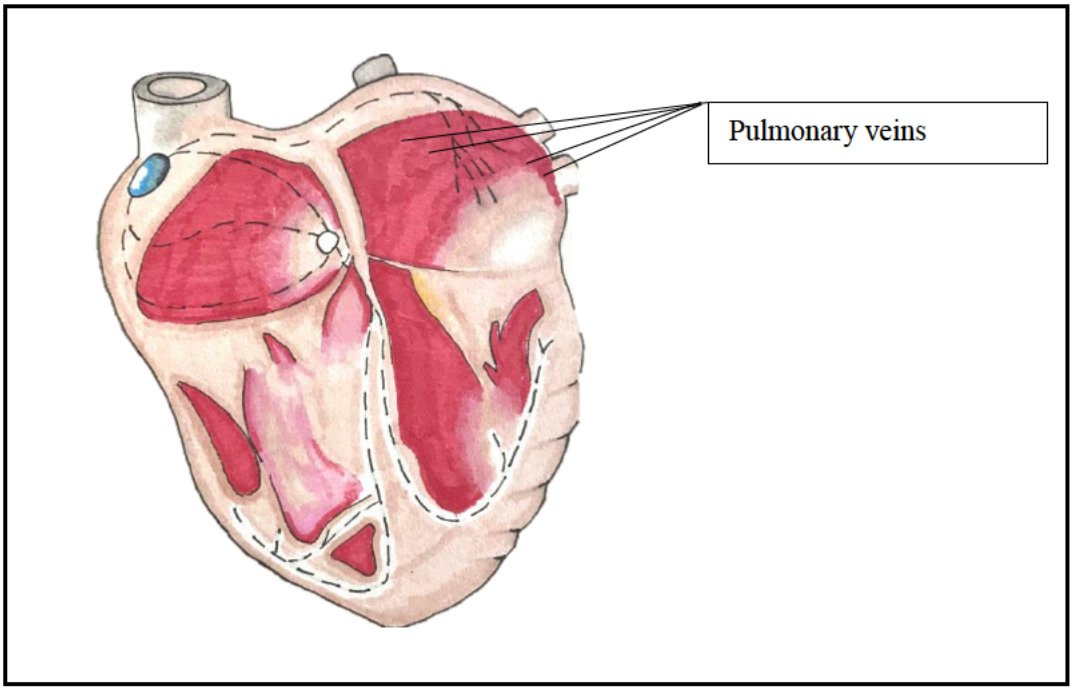


Figure 1.4: Heart Diagram: Pulmonary veins.

After the procedure, patients remain on a recovery ward and are then transferred back to the ward where they receive post-procedure care. After removal of the femoral sheaths (either in the catheter laboratory or the ward setting), the patient can slowly begin to be positioned upright over two hours and start to mobilise under observation. They continue to be monitored and clinical observations are taken regularly. Patients are reviewed by the medical team prior to discharge.

In a clinical setting, the success of the procedure may be defined by the clinician or patient as the reduction or absence of AF symptoms, however consensus guidelines by the Heart Rhythm Society,

the European Heart Rhythm Association and the European Cardiac Arrhythmia Society (Calkins et al., 2012, 2017) outline success as being the absence of more than 30 seconds of atrial arrhythmia (AF or atrial tachycardia) at twelve months post procedure. Rates of success of ablation may be dependent on several factors such as the length of time in AF, the patient's other comorbidities such as structural heart disease and the electrophysiologist performing the procedure (Haegeli and Calkins, 2014). As variations exist between techniques of ablation, it is difficult to compare the success rates and risks of different centres, leading to inconsistency with figures (Haegeli and Calkins, 2014).

Although there have been advances in technology since the ablation technique began, major risks are associated with this procedure. These include death (0.07%) (Cappato et al., 2009), cardiac tamponnade (0.5–2%), pulmonary stenosis (<1%) and stroke (0.3–1%) (Haegeli and Calkins, 2014). The risk of stroke is minimised by the administration of oral anticoagulation medication with an INR target of 2-3. The treating cardiac electrophysiologist also performs a TOE prior to the procedure to reduce this risk (Earley, 2009). As there may be a risk of tamponnade, after the procedure the patient receives a chest x-ray to identify any problems. Minor bruising or bleeding especially at the femoral vein access site is possible. Chest discomfort or increased palpitations are commonly experienced in the first three months until the myocardial and pericardial inflammation settles down (Haegeli and Calkins, 2014). Follow-up appointments are scheduled three months post procedure to assess the effectiveness of the procedure. These involve clinical review by a cardiac electrophysiologist to evaluate symptoms and medications. Depending on the success of the procedure, medications may be adjusted, reduced or stopped.

Recent ESC guidelines and AF catheter ablation consensus statements (Calkins et al., 2017) recommend that catheter ablation is initially considered in those who are symptomatic of PAF or when anti-arrhythmic drugs have been unsuccessful in managing AF symptoms. If the procedure is successful, the patient's rate or rhythm controlling medications may be discontinued, potentially allowing the patient to resume their previous lifestyle. The procedure is not always successful, however, and although the risks are explained to the patient prior to the procedure, it can be a disappointing experience if, after the hospital admission, the procedure is unsuccessful and furthermore disappointing and traumatic if they experience the risks mentioned above.

1.14 Pace and Ablate

If all treatments have been unsuccessful, a procedure of pace and ablate may be tried. This procedure cannot be reversed and is a last resort for the control of symptoms. A biventricular pacemaker is inserted around 6 weeks prior to AV node ablation (where the AV node has energy emitted to it

making it unable to allow the transmission of electrical signals). Patients will have an outpatient follow up four weeks after the insertion of the pacemaker (PPM).

The risks associated with the insertion of a PPM include haematoma, haemothorax, pain and bruising over the incision area and lead displacement. To reduce the risk of lead displacement, patients are advised to reduce the movement of the left arm until after their follow up appointment. The highest risk of this procedure is infection; if this occurs, removal of the PPM is necessary and hospital admission for an extended time is essential. Admission would involve the administration of intravenous antibiotic medications and the insertion of a temporary pacing wire. Risks involving catheter ablation are also associated with the pace and ablate procedure.

1.15 Psychological Support

The experience of AF symptoms and treatment may often affect patients psychologically. The extent and severity of these effects vary widely and influenced by such factors as symptom severity, treatment response, comorbid conditions, and premorbid adjustment. Patients who are cared for under the Barts Health NHS Trust have the option of receiving support services from an arrhythmia nurse service, where they are offered guidance regarding treatment options and further information if needed. NICE (2014) guidelines acknowledge that research has shown patients with AF can have elevated anxiety and depression and therefore recommend that patients receive psychological support if this is needed (Lip et al., 2006; Mareedu et al., 2010).Although cognitive behaviour therapy (CBT) is recommended in patients with anxiety, in clinical practice in the general population here is little evidence to support that CBT improves HRQoL specifically in patients with AF; therefore NICE (2014) suggests future research in this area.

1.16 Quality of Life

1.16.1 AF Treatment and QoL

The presenting symptom pattern and effects of the condition on the patient's function and HRQoL are major factors influencing the treatment decisions made by the clinical team. QoL has been defined as 'an individual's perception of their position in life, in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns' (The WHOQOL Group, 1994). QoL is a multidimensional concept concerning various aspects of life that are important to the individual. The meaning of QoL is dependent on its application but throughout general research its meaning often focuses on measuring satisfaction or happiness in relation to a particular aspect of a person's life such as wealth or education (Fayers and Machin, 2016). Although measuring QoL is

considered broadly throughout research, to avoid ambiguity, the term Health-Related Quality of Life (HRQoL) is used in research which considers aspects of QoL which are directly or indirectly affected by health or disease (Fayers and Machin, 2016).

It is widely documented that AF negatively affects HRQoL (Van de Berg et al., 2001; Sanoski, 2009; Spertus et al., 2011) and because available treatments are largely focussed on controlling symptoms, accurately determining the extent to which patients feel that interventions have benefitted or improved their HRQoL is a crucial issue in AF clinical studies (Reynolds et al., 2008). Although a number of AF studies have used cardiac-specific questionnaires, only a few of these were specifically designed for AF patients, and to date there has been relatively limited involvement of patients with AF in the design of AF-specific HRQoL measurement tools (Reynolds et al., 2008).

1.16.2 Health-Related Quality of Life and Generic Measurement Scales

In clinical practice, measurement of HRQoL provides a vital dimension in the assessment of the effectiveness of therapies. Although HRQoL may be measured using a range of approaches (such as using indicators of material living conditions, the natural and built environment, physical and mental health, education, recreation and leisure time, and social belonging), often HRQoL is measured using scales designed to encompass the key elements of this multi-dimensional concept. Such HRQoL tools are often a type of PROM (Patient Reported Outcomes Measure) that can provide clinicians with a better insight into the way in which conditions and their treatments affect individual patients, thereby improving the quality of clinical decisions and clinical care. As HRQoL is subjective, patients with AF are best placed to identify and elaborate on how the condition impacts their HRQoL. For this key reason, participants from the target population should be involved in the development and validation of measures of HRQoL to ensure that their perspective is appropriately captured (Thompson et al., 2016).

The Department of Health (DoH) initially published guidance on the use of PROMs in routine clinical practice, introducing their use throughout England for several orthopaedic procedures and making it a requirement to collect this information when working in these areas (DH, 2009). The DoH has since recognized the value of this information and has emphasized the significant need in other areas, highlighting it as a ‘key priority’ (DoH, 2010).

Generic HRQoL questionnaires are designed to assess broad domains of HRQoL. The change in HRQoL following treatment in patients with AF may not be captured effectively using a generic HRQoL tool (Streiner and Norman, 2008). For example, in the EQ-5D questionnaire which asks participants to select the statement which best reflects their health today, one question considers pain

and discomfort. It gives participants three options: “I have no, moderate or extreme pain or discomfort” (The EuroQoL Group, 1990). These questionnaires may be limited in their ability to measure the full impact of specific medical conditions (or treatments) on HRQoL in conditions such as AF. For example, chest pain is a potential side effect in patients with AF following treatment. If the EQ-5D is used post treatment, the patient could respond with extreme pain, but this may be due to chronic back pain and not chest pain. This supports the hypothesis that use of generic questionnaires as an objective measure of condition-specific outcomes are limited and a PROM that is condition-specific may provide a more detailed insight into the impact on HRQoL.

1.16.3 Disease-Specific Health-Related Quality of Life Measurement Tools

Assessments of HRQoL in patients with AF have so far been carried out using various scales that are either poorly standardised or non-disease-specific (Reynolds et al., 2008). A disease-specific HRQoL tool will ensure all items are relevant to the patient and there should be no items that are not applicable. Therefore, a disease-specific HRQoL assessment tool is required to provide a detailed measurement of treatment therapies (Reynolds et al., 2008; Streiner and Norman, 2008). Measuring the effectiveness of AF treatments will provide important information that health care providers need to evaluate the cost effectiveness of treatments. A specific HRQoL tool for AF is essential to establish that these treatments that can be life changing for individuals.

There have been several advances in the guidance on the construction of HRQoL scales (Bruce and Fries, 2005; Fries et al., 2005). Advances in research methods and statistical analysis have transformed the method through which these scales are produced from the development of a series of questions put together by an interested clinician to a well-established and rigorous process that can produce high-quality, sensitive instruments based on patient-generated information such as EORTC QLQ-C30 (Osoba, et al., 1994, 1997) and AFSymp (Medin et al., 2014). Clinically useful scales are generally short, easily administered and address the concerns of the patient (rather than those of the clinician). It is intended that these rigorous techniques will be used to construct and provide preliminary analysis of the psychometric properties of a PROM scale for routine clinical use in the management of AF.

1.17 Conclusion

This chapter has provided an initial overview of the medical background related to AF and its treatments. Symptoms of AF along with the associated increased risk of stroke and other medical conditions can lead to psychological concerns about the future progression of the illness, potential

complications and the adverse effects associated with treatments. This combination has been shown to have a negative impact on the HRQoL of patients with this condition (Ong et al., 2006; Aliot et al., 2014). This chapter has introduced the reader to the patient perspective on a life with AF and its impact on their HRQoL. It has also briefly considered the measurement of HRQoL using generic and disease-specific questionnaires and their limitations for this population. The importance of accurate measurement of the impact of AF on HRQoL will be discussed in greater detail in the next chapter, with emphasis on the patient perspective.

Chapter 2: Health-Related Quality of life in Patients with Atrial Fibrillation

This thesis discusses the process of development of a Patient Report Outcome Measure (PROM) for patients with atrial fibrillation (AF). Chapter One introduced the reader to the patient perspective on a life with AF and its potential negative impact on health-related quality of life (HRQoL) (Ong et al., 2006; Aliot et al., 2014). That chapter also introduced the reader to the importance of accurate measurement of HRQoL and how the use of generic and disease-specific questionnaires may be limited in an AF population. Chapter Two will further examine the concept of HRQoL and make use of the quantitative and qualitative research that has examined HRQoL in an AF population. This chapter will also consider the literature concerning the development of PROMs and highlight the importance of patient involvement throughout the development of such measures.

2.1 Introduction

Atrial fibrillation (AF) typically presents with symptoms such as breathlessness, dyspnoea, palpitations, dizziness and chest discomfort and is associated with substantially increased risks of stroke, thromboembolism and heart failure. These presenting features together with worry about future illness course and the potential for complications, and adverse effects associated with treatments, have a clear detrimental effect on patients' health-related quality of life (HRQoL) (Ong et al., 2006; Aliot et al., 2014). The purpose of this chapter is to examine the impact of AF on HRQoL. This chapter will commence with a consideration of HRQoL and its measurement in an AF population. Guidance for the development of these measures and patient involvement in development will be highlighted. This chapter will then focus on the qualitative and quantitative literature examining HRQoL.

2.2 Quality of Life

Although quality of life (QoL) has been considered by philosophers since antiquity and typically conceptualised in terms of a good life, living well, human flourishing and well-being (Schuessler and Fisher, 1985), the modern origins of QoL stemmed from social science literature in the 1920s (Schuessler and Fisher, 1985; Armstrong and Caldwell, 2004; Pennacchini et al., 2011). In both America and Europe following World War II, increases in economic growth and social changes led to the increase of objective measurement of QoL for social research (Schuessler and Fisher, 1985). Although initially social indicators such as the possession of material goods indicated a good QoL,

following the social and political upheavals of the 1960's, the understanding of QoL changed, with more emphasis placed upon aspects of QoL such as satisfaction, freedom, leisure and emotions and not solely the possession of material goods (Schuessler and Fisher, 1985). This change of view is reflected in a speech from the American President Lyndon Johnson in 1964, in which he asserted that 'the Great Society is concerned not with how much, but with how good – not with the quantity of goods, but with the quality of our lives' (Campbell et al., 1976; Campbell, 1981; Schuessler and Fisher, 1985; Ebbs et al., 1989).

The main focus of outcome in traditional medicine has been the physical impact of the disease, mainly measured by objective assessments of symptoms, and mortality or morbidity rates. The predominance of this perspective through much of the history of modern medicine is supported by a review by Mosteller et al. (1980) that noted that although many oncology clinical trials had reported survival and reoccurrence rates of cancer, QoL was never measured in these studies. This focus on objective and symptom-focused measurement has provided a limited view of the impact of disease and treatment on patients. The shift of focus to QoL as an outcome measurement provided a more comprehensive subjective understanding of the impact of disease and allowed the evaluation of the benefit-burden impact of treatments. This has become more advantageous as medical technology has advanced at the same time as financial restrictions have reduced the allocation of healthcare, research and training funds (Sprangers et al., 2000; Moons et al., 2006). The need to justify decisions about care and treatment in the clinical setting as well as in a political setting led to the promotion of evidence-based care in clinical practice (Ayers et al., 2007), wherein clinical decision-making is based on systematically gathered evidence drawn from the best available research. QoL outcomes are recognised as a key aspect of treatment effect, and there has been a growing emphasis on their measurement over past decades (Wong et al., 2008; Alakärppä and Alho, 2012).

QoL information is routinely collected in many countries as an outcome measure to indicate the effectiveness of treatments as well as an indicator of the need for support, care or intervention (Devlin and Appleby, 2010; Thompson et al., 2016). This growth of interest may be a result of the general population living longer (Office for National Statistics, 2014) therefore leading to an increase in chronic conditions (Leidy et al., 1998; Crosby et al., 2003; Moons et al., 2006; DoH, 2013). Typically, there is no cure for these conditions and frequently the overall clinical objective is to relieve symptoms and ensure a good QoL is attained (Han et al., 2005).

2.2.1 Definitions Quality of Life

There have been numerous attempts to define the concept of QoL and there is no consensus on a single definition (Lauer, 1999; Ruggeri et al., 2001; Taillefer et al., 2003; Moons et al., 2006).

However, it is generally accepted that QoL is a broad subjective multidimensional concept (The WHOQOL Group, 1995; Haas, 1999; Bowling et al., 2002; Taillefer et al., 2003; Tobita and Hyde, 2007; ISOQOL, 2014).

The International Society for Quality of Life Research (ISOQOL) (2014) define QoL as 'subjective and multidimensional, encompassing physical and occupational function, psychological state, social interaction and somatic sensation'. One of the most widely known definitions is presented by the World Health Organisation (WHO) Quality of Life Group (1995, p. 43):

> Quality of life is defined as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad-ranging concept incorporating in a complex way the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of the environment.

A major strength of the definition presented by WHO is its ability to describe the domains of HRQoL across different ages, cultures and health conditions (Bakas et al., 2012; Thompson et al., 2016). Several reviews have examined the main components of QoL (Felce et al., 1995; Ferrans et al., 1996; Hagerty et al., 2001; Ferrans et al., 2005; Thompson et al., 2016). Table 2.1 (below) outlines the components of QoL domains presented by WHO (1997), including physical health, psychological, level of independence, social relationships, environment and spiritual/religion/personal beliefs.

Table 2.1 QoL Domains (as described by WHO, 1997)	
QoL domains	**QoL subdomains**
Physical health	Energy and fatigue Pain and discomfort Sleep and rest
Psychological	Bodily image and appearance Feelings: Negative/Positive Self-esteem
Level of Independence	Mobility Activities of daily living Dependence on medicinal substances Work capacity
Social relationships	Personal relationships Social support Sexual activity
Environment	Financial resources Physical safety and security Health and social care: accessibility and quality Home environment Participation in and opportunities for recreation/ leisure
Spirituality/Religion/Personal beliefs	Religion/Spirituality/Personal beliefs
Source: WHO, 1997	

2.2.2 Health-Related Quality of Life (HRQoL)

Health-related quality of life (HRQoL) concerns those aspects of QoL that are influenced by health status and treatment (Harrison et al., 1996; Bowling, 2005). The emphasis is on the impact of disease, disability or disorder on the health of the patient and the consequent effect on QoL. It involves symptoms, treatment side effects, treatment satisfaction, physical functioning, social functioning, well-being, life satisfaction, mental health including emotional well-being and cognitive functioning. As the concept of HRQoL and health are so closely related, the concept of health will be briefly considered.

As with QoL, there is no universally accepted definition of health; however, probably the most influential definition of health was formulated by World Health Organization (WHO, 1948), which described it as 'a state of complete physical, mental, and social well-being, not merely the absence of disease'.

Although this definition is often quoted in the literature (Bergner and Rothman, 1987; Saylor, 2004; Sartorius, 2006; Huber et al., 2011), it has attracted much criticism, with some researchers suggesting that this conceptualisation reinforces the medical model and does not define well-being (Saylor, 2004; Huber et al., 2011). They also go on to critique this definition by stating that when it is applied to the general public, 'everyone lacks health' (Saylor, 2004). However, it is acknowledged that this definition was one of the first to move away from a medical definition of health by encompassing social well-being (Saylor, 2004; Huber et al., 2011). Although the classic WHO definition has not been formally amended, when WHO (1986) addressed The Ottawa Charter for Health Promotion, they stated:

> [T]o reach a state of complete physical, mental and social well-being, an individual or group must be able to identify and to realize aspirations, to satisfy needs, and to change or cope with the environment. Health is, therefore, seen as a resource for everyday life, not the objective of living. Health is a positive concept emphasizing social and personal resources, as well as physical capacities.

Revicki et al. (2000, p.888) define HRQoL 'as the subjective assessment of the impact of disease and treatment across the physical, psychological, social and somatic domains of functioning and well-being'.

Operational definitions of HRQoL include at least three domains: social, mental/psychological and physical (Leidy et al., 1999; Malkina-Pykh and Pykh, 2008; Bullinger and Quitmann, 2014). The detail of each of these domains varies and often extra domains may be identified depending on the study (Bullinger and Quitmann, 2014). The domain activity has been added to the three domains above by some researchers in QoL and in AF specific research (Lüderitz and Jung, 2000; Bowling, 2001).

2.2.3 Operational Definition HRQoL: AF PROM

Including elements of HRQoL which are important to clinicians (such as symptoms and clinical features) (medical model) and also to patients (such as emotional and social impacts of the conditions) is important (Bowling, 2001). The NICE Guidelines for the management of AF (2014) suggest that

diagnosis of AF may be indicated by an irregular pulse along with symptoms such as shortness of breath, dizziness/fainting, chest pain/discomfort and palpitations. However, as discussed (in Chapter One), not all patients are equally affected symptomatically.

For instance, a patient (1) might experience all of the above symptoms without their HRQoL being significantly affected, therefore the patient would not desire medical intervention. The opposite is also possible: the HRQoL of a patient (2) might be significantly affected because of the psychological impact of stroke risk and resulting commencement of anticoagulant drugs despite this patient being asymptomatic. If the patient in the first example (1) was reviewed by a clinician (following a traditional medical model), because the patient is symptomatic, interventions such as medication might be advised, which will carry risks and side effects. If the second patient (2) was assessed (by a clinician using a medical model), identification of the psychological impact stroke risk is having on HRQoL might be limited, leading to patient 2 not receiving adequate support. It is argued that using a combined approach is of much benefit, both for the patient and also for the efficiency of care delivery.

In line with the approach used by the WHO (1996), the main focus of consideration of HRQoL in patients with AF will be on the physical, psychological, social and relationship, and level of independence domains. However, for the purposes of this study, domains will not be restricted to these four concepts. It is accepted that additional domains such as symptoms of AF and treatments of AF may have an impact on HRQoL (Dorian et al., 2000; Thrall et al., 2006) and therefore may be appropriate for inclusion. Consideration of which HRQoL domains are most relevant and important will be based upon review of the relevant literature, including a detailed consideration of the coverage of existent AF-specific HRQoL measures. Importantly, this study will seek to identify and clarify the HRQoL domains most pertinent to AF patients by directly consulting with patients (and their carers) by means of series of focus groups, panel meetings and interviews (methods discussed in Chapter Four) (Bullinger and Quitmann, 2014).

2.2.4 Patient-Reported Outcome Measures (PROM)

A Patient Reported Outcome Measure (PROM) is a tool, usually in the form of a questionnaire, which is used to measure the status of a patient's health, including, or focusing on, symptoms, QoL or physical functioning at a particular point in time; this measurement may be taken before and after an intervention allowing a comparison and giving an indication of the effectiveness of the treatment (Black, 2013). PROM were initially developed for clinical research use to evaluate treatment benefit. Their use has expanded for the wider purpose of monitoring clinical care and evaluating the performance of care providers. For example, the NHS and American Centres for Medicare and Medicaid Services (CMS) now routinely use these tools for such quality improvement purposes

(Devlin et al., 2010; Black, 2013). The Department of Health (DH, 2009) introduced PROM use throughout England for four elective procedures. The DoH (2010) highlight this use of PROM as a 'key priority'. The use of PROM in various settings (such as primary care settings) is currently being investigated in patients with long-term conditions (Peters et al., 2014) with the aim of providing an opportunity to influence future change in the organisation and the delivery of care.

Many researchers would suggest that a PROM is no different from other HRQoL questionnaires (whether they be generic or disease-specific) or a symptom tool, proposing that any such tool could be used to measure health status as an outcome of an intervention (Devlin et al., 2010; Black, 2013; Health and Social Care Information Centre, 2014). The Department of Health (England) and Social Care Information Centre (2014) defines PROM as measures of a patient's health status or HRQoL at a single point in time.

2.2.5 Patient Input

There is a growing recognition that patients possess vital knowledge about their health and their experience of health care, and that considering and including their perspective is crucial in the development of PROM tools (Acaster et al., 2012; Staniszewska et al., 2012; Arthritis Research UK, 2013; Graham, 2013; Frew et al., 2013; Wiering et al., 2017). The patient perspective is essential to establish which outcomes are the most relevant and important and to ensure that these aspects of health status and HRQoL are communicated in a manner that is understandable and acceptable for patients (Wiering et al., 2017). There is a developing consensus that in order to capture the patient's perspective it is essential that patients are involved in PROM development (Skevington and McCrate, 2012; Wettergren et al., 2014). This involvement should be such that patients have input into identifying the particular PROM outcomes, the generation of items and assessing the comprehensibility and validity of the PROM tool (Wiering et al., 2017).

It has been noted that patients are becoming more engaged and interested in treatment options and the impact this will have on their lives, a development which is encouraged by clinical staff (Crosby et al., 2003; Asadi-Lari et al., 2004; Pomey et al., 2015; Fayer and Machin, 2016). Although measures developed by clinicians or researchers may be reliable, their relevance to the population may be compromised if they fail to capture all aspects of HRQoL affected by health conditions such as AF (Thompson et al., 2016).

The evidence from a recent systematic review of existing PROM reveals that patient involvement in the construction of these measures is often absent or limited. From studies describing the development of 193 new PROM, Wiering et al. (2017) identified that there was no patient involvement in more

than a quarter (25.9%) of studies, and that patient involvement in the crucial role of determining which outcomes to measure was evident in only one in ten of these studies (10.9%). Patients were most commonly involved in the processes of item development and checking for readability and understanding of the instrument.

Although involving patients in the development of PROM is considered necessary, the extent and type of their involvement often varies considerably between studies. Wiering et al. (2017) highlight this, noting that although 74.1% (n=193) of studies reviewed included patients in the development of a PROM, this involvement was often limited to only one stage of development (in 34% of the studies), with only 6.7% of studies including patients in all three stages of development (identification of the focus of the outcome measure, questionnaire item generation and assessment of the comprehensibility of the questionnaire).

It is important to consider that differing perspectives on the effect of illness on HRQoL held by patients, relatives and healthcare professionals are evident and documented within the literature (Wilson et al., 2000; Ring., 2017). For example, poor correlation is noted between patient and clinician scores in the psychological components of HRQoL. This leads to the conclusion that how patients feel and the 'values and opinions [they hold] cannot be assumed' (Bowling, 2001). Therefore, ensuring patients' perspectives are captured is crucial. This is highlighted throughout the literature (Bowling, 2001; Cappelleri et al., 2013). Mount and Cohen (in Haas, 1999, [p.218]) succinctly propose that 'we let the people whose QoL we are attempting to measure teach us what QoL means to them'.

It is also noteworthy that reports of QoL from relatives are often closer to patient scores than clinician scores, indicating that although relatives may not completely understand the impact of a condition, they may have a better understanding than do clinicians. This has led to some researchers advocating the inclusion of relatives in the development of QoL Measures or PROM (Ebbesen et al., 1990; Bowling, 2001; Fast et al., 2009; King and Hinds, 2011).

2.2.6 Guidelines for Development of PROM

PROM are increasingly being used in research studies involving patients with chronic conditions where the intention of the treatment is to reduce symptoms and improve QoL. The results of these research studies may be used by the pharmaceutical industry to substantiate product guidance in relation to symptom reduction or other benefits of treatment (Doward et al., 2010). Product labelling allows the communication of the benefits and side effects of treatments. Patients are becoming increasingly involved in in decision-making about their treatment (Shah et al., 2003), and product

labelling that communicates the benefits and side effects of treatments may play a part in this active selection between treatment options. The strengthening of methodological rigour in science and the increased use of validated outcome measurement in clinical research has led to the need for clearer guidance in the development and use of PROM. Standardisation of PROM improves the overall quality of these tools and also ensures consistency of terminology, which enables greater clarity for patients and clinicians making decisions regarding treatment choice.

Although clear regulatory guidance for PROM was initially welcomed, there has been much discussion and controversy surrounding the different guidance documents, especially the United States (US) Food and Drug Administration (FDA) guidance (Sloan et al., 2009). All standards must be met to permit an FDA labelling claim; however, since the release of the FDA guidance document there has not been the expected increase in labelling claims by pharmaceutical companies (DeMuro et al., 2012), which could support the argument by some researchers that this guidance is too restrictive compared to other guidance documents such as that produced by the European Medicines Agency (EMA) (EMA, 2005; Bottomley et al., 2009). The FDA guidance led to many questions being raised about the evidence needed to demonstrate good practice in research (Speight, 2010) as many developed PROM were deemed by the FDA as unfit for purpose (DeMuro et al., 2012; Gnanasakthy et al., 2012).

Although the main guidance documents (FDA and EMA) share similarities such as the requirement of evidence of reliability, validity and the ability to detect change, one clear difference between these two guidance documents is in the terminology regarding patient-based end points. The FDA (2009) grants labelling claims of PROM for symptoms, physical functioning and HRQoL. However, the EMA only provides labelling claims for PROM for HRQoL, suggesting that simple claims such as improving symptoms should be classed as a clinical end point (EMA, 2005).

Although we do not anticipate developing a PROM which will require FDA labelling approval, there is much benefit in applying some of the principles from the FDA guidance in the development of a PROM. This guidance has increased the level of required documentation and scientific rigour in the development and psychometric evaluation of these measures. Perhaps more importantly, it also has emphasised patient input in development. This focus on developing PROM with extensive patient input along with evaluation of the PROM in a population with similar characteristics is anticipated to facilitate the development of a PROM that will be a valid and reliable tool which ensures that health care providers are adequately equipped to understand the impact of AF on HRQoL.

The development of twelve minimum standards for PROM by the Patient-Centred Outcomes Research Institute (PCORI) was based on relevant PROM guidance documents (Dworkin et al., 2005,

2008; EMA, 2005; Turk et al., 2006; FDA, 2009; Devlin and Appleby, 2010; Mokkink et al., 2010; Aaronson et al., 2011; Basch et al., 2011; Acaster et al., 2012) and advocated a patient-centred approach to this research activity.

The importance of including patients in PROM development is strongly advocated by researchers, health scientists, policy makers and patient organisations (Acaster et al, 2012; Cappelleri et al, 2013; Streiner et al, 2014). The FDA guidance requires patient involvement throughout the development and validation stages, including the stages of item development, and content validity and psychometric testing, as shown in Figure 2.1 (below) (FDA, 2009; Varma et al., 2010).

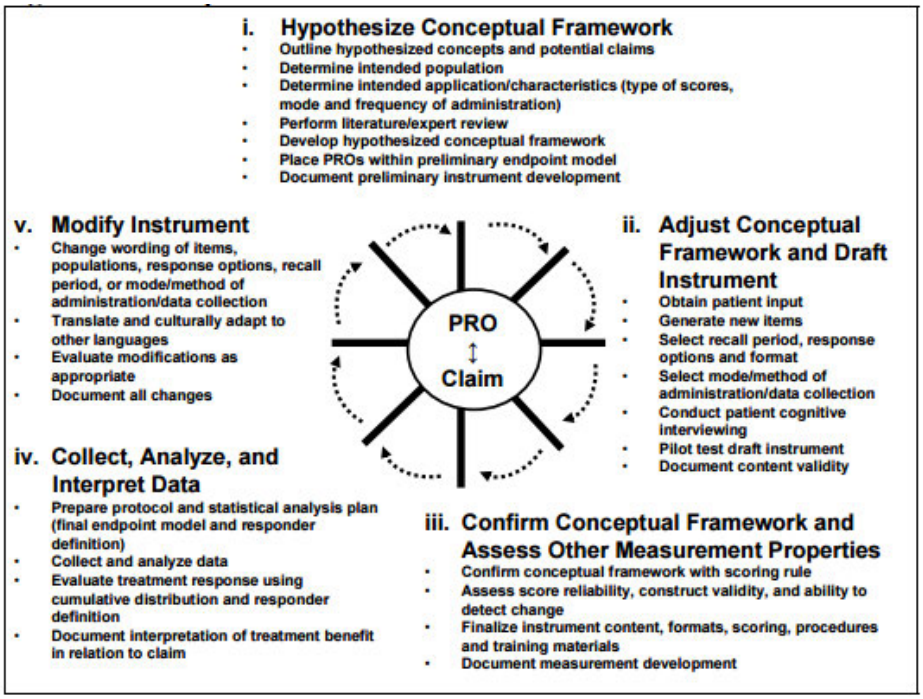


Figure 2.1 Development of a PRO Instrument according to FDA.
(FDA, 2009; used with permission)

The conceptual model of a PROM involves a description and a diagram of the relationships between concepts, domains and items (FDA, 2009). The FDA guidance places a greater focus on the development of the conceptual model and the psychometric validation of the measures compared to other guidance such as EMA (Bottomley et al., 2009). Within FDA guidance (2009), the initial conceptual model can be developed solely from literature reviews and expert input, and this approach is noted in other sources (Streiner et al., 2014). However, including patients in the generation of concepts and domains is increasingly acknowledged to be a necessity (Trujols et al., 2013), as this enables the views about which outcomes are most important to patients to be captured (Wiering et al., 2017). The inclusion of patients in this initial stage has led to the production of valid and reliable

measures such as the FACT&GOGNtx (Ward et al., 1999), EORTC QLQ-C30 (Osoba et al., 1994, 1997), AFSymp (Medin et al., 2014). Nevertheless, Wiering et al. (2017) identified that a lower number of studies (only 10.9%) (n=21 of a total n=189) were including patients in this early stage of development when compared to later stages such as item development (n=113; 58.5%).

The explicit involvement of patients in the early stage of PROM construction – in the initial identification of the key outcomes – enables the resulting measure to be rooted in the patients' illness experiences. Patient involvement at this stage may enhance the validity of the PROM and influence the conceptual framework around which the measure is built. This may in part challenge the models upon which PROM are designed (Staniszewska et al., 2012). The outcomes focused on will be more relevant to patients, therefore preventing their alienation by irrelevant concepts, and the consequent non-compliance in later stages (Acaster et al., 2012). The Patient-Centred Outcomes Research Institute (PCORIS) (Selby et al., 2012) stresses the importance of PROM being developed based on qualitative data from patients about areas that affect them, and that patients should be included in the choosing of the appropriate outcomes for the PROM (Acaster et al., 2012).

The FDA recommend that once a draft instrument is developed, patient input should be gained to ensure content validity, and that this should be clearly documented. The same standard of clear documentation expected in the item generation phase must be maintained throughout the development and psychometric testing phases of the measure to achieve the FDA standard. This documentation allows the justification of any changes to the measure whilst also ensuring transparency throughout the process.

A potential limitation of the FDA guidance is that the extent of patient involvement is not clearly defined (Bottomley et al., 2009; FDA, 2009). However, the FDA highlight that sample size in development is not as important as the quality of data collected from patients and the involvement of patients with differing population characteristics (FDA, 2009). PCORI (Acaster et al., 2012) similarly recommend that the quality of qualitative data is of utmost importance and recommend that instead of pre-determining sample sizes in qualitative stages, data saturation should occur (where no new information is yielded) from focus groups or interviews.

Including patients in cognitive debriefing to assess the content validity allows aspects of the questionnaire to be considered, i.e. the readability and understanding of the PROM items, instructions and the appropriateness of the recall period. The EMA do not have requirements for the recall period, however the FDA advise short recall periods (24-48 hours) to reduce patient burden. The FDA suggest that feedback is acquired from patients to indicate the appropriateness of this recall period. It

is important to consider that a short recall period (i.e. 24 hours) would not be appropriate to this population of patients with PAF, who may only have one episode a week.

The FDA promote collecting a wide range of views from diverse populations in regard to severity of the condition and population characteristics such as ethnicity, age gender and education level which will be similar to the study population (FDA, 2009; Acaster et al., 2012). As the PROM developed in this study will be used in a multicultural area such as London, including patients who are representative of this diverse patient population in its development increases the content validity of the instrument.

As already noted, although FDA labelling approval is not required for this study, many of the principles of the FDA guidance (especially patient involvement) are recognised as useful in the development of PROM and will be considered and utilised in the construction of the AF PROM for this study. It is hoped that through the application of principles from FDA guidance, the scientific rigour of the development stage will be improved, enhancing the validity and reliability of the resulting measure. Having a PROM that is valid and reliable in the intended population will improve the quality of the data collected and extend understanding of how patients with AF are affected, which is valuable for clinicians, researchers and the funders and commissioners of services (Turner et al., 2007; Doward et al., 2010; Basch, 2011).

2.3 HRQoL in AF

The impact of AF on HRQoL and changes in HRQoL as a result of treatment will be considered in this section. To allow this exploration, a literature review was conducted using the Ovid database which was updated in September 2018 by SH. Search terms and databases included are presented in Appendix A.2.1. All study designs were included (randomised control trials (RCTs), cohort studies, cross-sectional and observational studies). This review included studies which examined HRQoL in other comorbidities (such as diabetes and atrial flutter), but only if examining HRQoL of AF was the main condition of focus. The results of this literature review are shown in Figure 2.2.

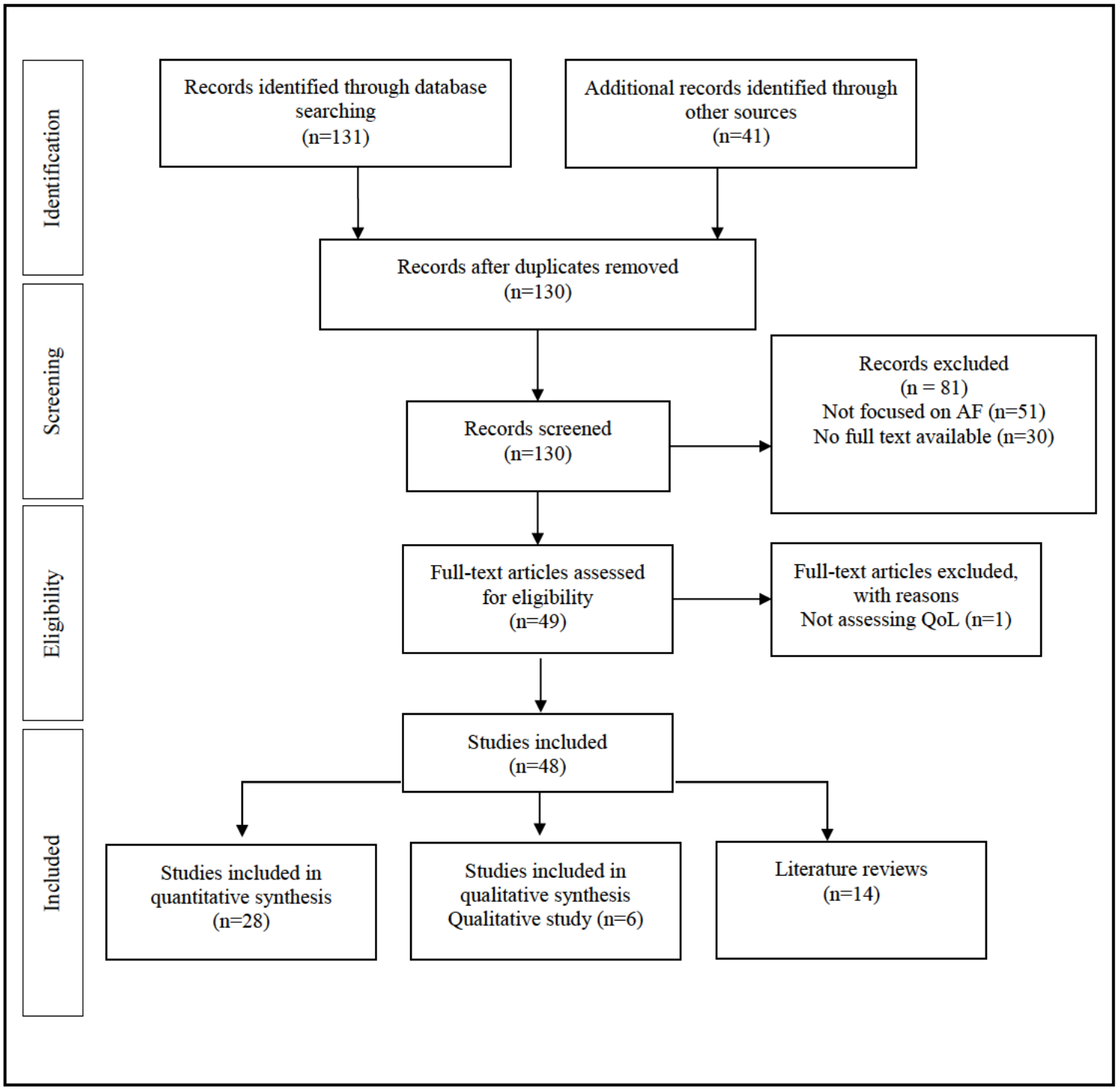


Figure 2.2: Flowchart showing the studies identified in literature search

2.3.1 Findings

This literature search identified 130 pieces of literature which considered AF and HRQoL. This was reduced to 49 articles after removing articles for which the full text was unavailable and those which were not primarily focused on AF. The findings were categorised under three headings: quantitative studies exploring HRQoL in patients with AF (n=28), qualitative research exploring HRQoL in patients with AF (n=6) and literature reviews (n=14) exploring this concept. The details are summarised in Tables 2.2- 2.4.

Table 2.2 Overview of studies identified in search

Author	Study Name/aim	Study Design	Participants (n=)	Participants: Type of AF	Study aim	Type of measure(s) used	Measures used	Results: QoL
Akintade et al., 2015	The influence of depression and anxiety symptoms on health-related quality of life in patients with atrial fibrillation and atrial flutter.	Cohort/cross-sectional study	150	PAF=26; Persistent AF=34; Permanent AF=50; Atrial Flutter=40	Evaluate the influencing factors of HRQoL in patients with AF and AFL.	Generic	SF-36; Symptom Checklist; Beck Depression Inventory II; the State Trait Anxiety Inventory	Findings indicate that further research examining psychological status and HRQoL is needed. Being female ($p<0.001$, $R2=0.391$) and having depression and anxiety ($p<0.001$, $R2=0.482$) appear to be indicators or lower HRQoL. Study included diverse population, including Afro-Americans (+).
Bakker et al., 2012	Results of clinical application of the modified maze procedure as concomitant surgery.	Control Trial	169	PAF n=60; Longstanding n=109	Modified maze procedure for atrial fibrillation.	Generic	SF-36	Quality of life not measured at baseline, so no comparison made. But QoL reported as similar to that of the general Dutch population.
Carlsson et al., 2003	The STAF study	RCT; multi-centred	200	Permanent AF	Compare rate control and rhythm control management over a 3-year period.	Generic	SF-36	Those with persistent AF had lower QoL scores than the general population. Rhythm control; scores in 2 subgroups (physical role function; mental health) improved significantly ($p<0.05$) between baseline and end of study, Rate control; scores in five subgroups (physical functioning, physical role function, bodily pain [$p<0.01$], social functioning and mental health [$p<0.01$]) improved significantly ($p<0.05$) between baseline and end of study. QoL scores improved but not to same levels of general population.

Table 2.2 Overview of studies identified in search: Continued (1)								
Cooper et al., 2004	The AFFIRM Study	RCT; multi-centred	118	PAF	Compare outcomes when using rate control of AF strategy.	Generic	SF-36; QoL Index; Symptom Checklist: Frequency and Severity	QoL only assessed in subset of population. No significant association between rate control and QoL measurement.
Dabrowski et al., 2010	Depression and HRQoL in patients with different patterns of AF	Observational	150	PAF; Persistent AF; Permanent AF	Examine depression and HRQoL in patients with different patterns of AF	Generic	Nottingham Health Profile question-naire	Depression noted to be higher in women than in men with AF. AF noted to reduce HRQoL in various aspects of HRQoL including work, household activities and sex life.
Dorian et al., 2000	Dorian et al., 2000	Observational	152	PAF	Assess impact of AF on HRQoL compared to control (healthy individuals) and those with existing heart disease	Generic and disease-specific symptom questionnaires	SF-36; Specific Activity, Symptom Checklist; Illness Intrusivenes s; University of Toronto AF Severity Scales	HRQoL reduced in (all 8 domains of SF-36) all patients with AF compared to general population. Subjective measurement of illness is important in clinical care.
Fiala et al., 2016	Functional improvement after successful catheter ablation for long-standing persistent atrial fibrillation.	Registry; single centre	171	Long-standing persistent atrial fibrillation	Considering factors which may impact successfulness of functional improvement following CA.	Generic	EQ-5D	Single centre study. At 12 months follow up significant improvement in QoL scores following ablation (0.7 ± 0.12).

Table 2.2 Overview of studies identified in search: Continued (2)								
Flaker et al., 2005	The AFFIRM study	RCT; multi-centred	481	Asymptomatic	QoL assessed in subpopulation over 3.5 years enrolled in the AFFIRM study (compares rate and rhythm strategy).	Generic	SF-36	Anticoagulation needed in those with asymptomatic AF.
Forleo et al., 2009	PVI versus Drug Therapy in Diabetics	RCT	70	PAF; Persistent AF	Comparison of AAD therapy and CA in patients with diabetes over 12-month period.	Generic	SF-36	Significant improvement in QoL scores in CA group compared to AAD ($p<0.05$, CA vs AAD group) in 5 of 8 SF-36 subscales. Difference in general health general health was 8.9; social functioning was 7.7; physical functioning was 8.4; bodily pain was 5.9; role emotional was 6.8.
Hagens et al., 2004	Rate Control versus Electrical Cardioversion (RACE) Study	RCT	352	Persistent AF	Comparing rate control and rhythm control management.	Generic	SF-36	Persistent AF = lower QoL scores than general population. Rate control group; scores in 4 subscales (general health; role physical; mental health; social functioning) improved significantly ($p<0.05$) between baseline and 12 months. Rhythm control group; scores improved in 3 subscales (general health; physical functioning; role physical) ($p<0.05$) between baseline and 12 months. No significant differences noted when compared with baseline scores between groups.

Table 2.2 Overview of studies identified in search: Continued (3)								
Jais et al., 2008	The A4 study	RCT; multi-centred	112	PAF	Comparison of AAD therapy and CA over 12-month period. Inclusion of patients with PAF with resistance to at least 1 AAD.	Generic	SF-36	No significant difference between QoL scores groups at baseline. 12-month follow-up scores significantly higher in CA group compared to AAD in both physical and mental domains using SF-36. Noted significant improvement in 6 out of 8 domains. Findings suggested CA can be done earlier in treatment pathway when one AAD has failed.
Kuck et al., 2016	FIRE and ICE trial.	RCT; Multicentred	750	PAF	Comparison of outcomes of CA: cryoballoon versus RFC catheter ablation	Generic	SF-12; EQ-5D-3L	Both groups showed improvement in mental and physical quality of life at 6 months after ablation and this was maintained at 30 months of follow-up. No significant difference between groups.
Lonnerholm et al., 2000	Effects of the maze operation on health-related quality of life in patients with atrial fibrillation	RCT	48	PAF; Persistent AF; Permanent AF	Measure the impact of MAZE procedure on HRQoL	Generic	SF-36	HRQoL scores lower in AF population compared to general population before procedure. HRQoL scores significantly ($p<0.001$) improved at 6 months and 12 months post procedure in all domains (except bodily pain [$p<0.09$]). Full HRQoL data available for 25 patients.
Mont et al., 2014	The SARA study	RCT	146	Persistent AF	Comparing CA against AAD.	Disease-specific	AF-QoL	No significant difference between groups following treatment at 12 months.

Table 2.2 Overview of studies identified in search: Continued (4)								
Cosedis Nielsen et al., 2012	MANTRA-PAF	RCT; multi-centred	294	PAF	Comparison of first line treatment in patients with PAF. Antiarrhythmic drug therapy versus catheter ablation over two-year period.	Generic	SF-36	Significant improvement in both physical and mental components of SF-36 in both groups. Greater improvement noted between baseline and two-year follow up in physical domain in Ablation group.
Ogawa et al., 2009	The J-RHYTHM study	RCT; multi-centred	823	PAF	Comparing rate control and rhythm control management.	Disease-specific	AFQLQ	Significant improvements over time in all three subsets of QoL questionnaires in both groups. Significant difference only noted between groups in AFQLQ1 (symptoms domain).
Pontoppidan et al., 2009	Pontoppidan et al., 2009	Observational	149	Asymptomatic	Measure impact of reoccurrence of AF after CA.	Generic	SF-36	No difference between HRQoL scores in symptomatic and asymptomatic population at baseline. However, at 12 months follow up, those who were asymptomatic had significantly higher HRQoL scores than baseline in three domains (role physical [$p<0.001$]; vitality [$p<0.001$] and general health [$p<0.05$]) of the SF-36.

Table 2.2 Overview of studies identified in search: Continued (5)								
Pürerfelln er et al., 2004	Restoration of QoL to normal after pulmonary vein ostial isolation	RCT	89	PAF	QoL measured in patients who had a CA for PAF, follow up 6 months post CA.	Generic and disease-specific symptom questionnair e	SF-36; SCL	Significant ($p<0.0001$) improvement in QoL scores after 6 months in all subscales.
Raine et al., 2015	Effect of catheter ablation on quality of life in patients with atrial fibrillation and its correlation with arrhythmia outcome	Control Trial	80	PAF; Persistent AF	Assess the impact of CA on AF on HRQoL	Generic and disease specific	SF-36; AFEQT	Significant improvement in patients in sinus rhythm after CA. AF specific measures able to identify disease specific changes in HRQoL.
Reynolds et al., 2006	The FRACTAL study	Registry; multi-centred	963	PAF; Persistent AF; Permanent AF	QoL assessed over various time periods over 30 months period.	Generic and disease-specific symptom questionnair es	SF-12; University of Toronto AF Severity Scale; Arrhythmia Symptom Frequency and Severity Checklist	Positive association between comorbid conditions, gender, age and QoL scores shown in newly diagnosed PAF (within 1 year).
Roalfe et al., 2012	Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) study	Cross-sectional study	1762	PAF n=70; other types of AF not specified	Comparison of HRQoL in patients with AF against the general population.	Generic	EQ-5D; SF-12	Impact of AF on QoL under examination. Generic quality-of-life scores compared with general population. Lower QoL scores associated with gender (female), increased medication use and increasing comorbidity. However, without comorbidity, AF has little impact on generic QoL in those over 75.

Table 2.2 Overview of studies identified in search: Continued (6)								
Shelton et al., 2009	The CAFE-II Study	RCT	61	Persistent AF	Comparing rate control and rhythm control management over 14-month period in patients with persistent AF and heart failure.	Generic	SF-36	Those in rhythm control group had greater improvements in QoL scores than rate control group, but these were non-significant (p=0.020) changes over 12 months.
Tsuneda et al., 2006	THE QOLAF Study	RCT	29	Permanent AF	Comparing drug therapy groups: β-blocker (BB) or calcium antagonist (CAA) with digitalis.	Generic and disease-specific	SF-36; AFQLQ	Generic measures; Significant difference between scores in one domain (role function-physical) in CA group (54.1±7.6). Disease-specific results. Score of one domain (symptoms) significantly ($p<0.05$) improved in CAA group (17.0±5.6). BB did not impact disease-specific scores in any domains.
van den Berg et al., 2001	Importance of autonomic nervous system; predicators of QoL in PAF,	Observational	73	PAF	Measure impact of AF on HRQoL	Generic	SF-36	Significant ($p<0{\cdot}001$) impairment of HRQoL in patients with PAF in four subscales of measurement (general health, vitality, physical role function and emotional role function). Predictors of HRQoL may include autonomic function and symptoms.
Walfridsson et al., 2014	The MANTRA-PAF trial.	RCT	294	PAF	Comparison of CA and AAD therapy as first line treatment.	Generic and disease specific	SF-36; EQ-5D; ASTA	Randomized study; RFA (n=146) versus AAD (n=148) as first-line treatment. At 24 months, significant improvements in SF-36 and EQ-5D. RFA group showed greater improvement in physical scales (SF-36) and the EQ-visual analogue scale.

Table 2.2 Overview of studies identified in search: Continued (7)

Wilber et al., 2010	ThermoCool AF Trial	RCT; multi-centred	167	PAF	Comparison of AAD therapy and CA over 9-month period.	Generic	SF-36	Significant difference ($p<0.001$) noted between mean scores of SF-36 of groups at 3 months. Mean score difference between groups (AAD v CA) at 3 months in the mental component was 6.9 (2.6 to 11.2); and the mean difference in the physical component was 6.6 (3.6 to 9.4). Cross-over from AAD to CA prevented meaningful analysis of QoL scores at 9 months.
Wokhlu et al., 2010	Examination of relationship between QoL and symptoms in AF patients who have had CA.	Observational	502	PAF; Persistent AF; Long-standing persistent AF	Examination of relationship between QoL and symptoms in AF patients who have had CA.	Generic and disease specific symptom measure	SF-36; MAFSI	323 of the 502 patients included in the 2-year follow up. Benefit of including disease-specific symptom measure; captures additional information not captured by generic measures. QoL not solely associated with efficacy of CA.
Yamamoto et al., 2014	J-RHYTHM II	RCT; multi-centred	233	PAF	Examining asymptomatic PAF and QoL	Disease-specific	AFQLQ	Lower QoL scores appear to be associated with asymptomatic AF episodes. This association was noted in two domains of disease-specific measures (the perception of the AF symptom severity and mental anxiety/limitations in daily activities). Suggests that reducing episodes of asymptomatic AF could improve QoL.

AF: Atrial Fibrillation; AAD: Anti-arrhythmic Drug; ASTA: Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia; AFEQT: Atrial Fibrillation Effect on QualiTy-of-Life; AFQLQ: Atrial fibrillation Quality of Life Questionnaire; CA: Catheter Ablation; EQ-5D-3L: EuroQol five-dimensional (EQ-5D) descriptive system; MAFSI: Mayo-AF Specific Symptom Inventory
; SF-36: The Medical Outcomes Study Short Form Health Survey; SF-12: The Medical Outcomes Study Short Form Health Survey-12; PAF: Paroxysmal Atrial Fibrillation;
(-) Limitation; (+) Benefit/Positive

Table 2.3 Overview of qualitative studies				
Author, Year, Location	**Design**	**Participants**	**Total (n)**	**Summary of Themes**
Altiok et al., 2015 Turkey	Interviews (semi-structured)	AF (type not specified)	32	Psychological impact Social impact Physical impact Coping with AF
Dalteg et al., 2014 Sweden	Interviews	PAF/Persistent AF and partner	24	Uncertainty and apprehension of AF Management of uncertainty of AF
Deaton et al., 2003 USA	Interviews (semi-structured)	PAF and Persistent AF, ICD-AT therapy	11	Poor clinical treatment and misdiagnosis Impact of symptoms Limitations to ADL's Negative impact from treatments Pursuit of treatment
Ekblad et al., 2013 Sweden	Interviews (semi-structured)	PAF/Persistent AF, Permanent AF	25	Physical impact Psychological impact Adapting to AF Health care
McCabe et al., 2015 USA	Interviews (open-ended)	AF patients hospitalised (type not specified)	41	Symptoms of AF and difficulties in diagnosis Acceptance of AF Good clinical treatment
McCabe et al., 2011 USA	Interviews (open-ended)	PAF and Persistent	15	Symptoms of AF Difficulties in diagnosis and poor clinical treatment Avoiding and managing episodes of AF Emotional impact Accepting AF Treatment

Table 2.3 Overview of literature reviews considering AF and HRQoL.

Author	Design	Title/Aim	Total (n)	Summary of Themes
Aliot et al., 2014	Review	Review of HRQoL and symptom measures used in AF population.	n=12 measures identified as being used in AF population (includes generic and disease-specific HRQoL measures and disease-specific symptom measures).	The development and validation of new QoL assessment tools will have a central role in the advancement of therapies and treatment guidelines for AF.
Fuster et al., 2010	Review	Global collaboration needed for AF.	Not published	Importance of measuring HRQoL in this population. Agreement needed to establish universal HRQoL measure.
Hakalahti et al., 2015	Systematic review and meta-analysis	Systematic review and meta-analysis of safety and efficacy of RFA and AAD therapy as first-line treatment.	Meta-analysis: 3 studies included (n=491 patients)	All studies used generic measures (SF-36 and EQ-5D) (-). No disease-specific measures used. (-). QoL scores improved in CA group in all studies when compared to AAD group in patients with PAF. Findings suggest first-line treatment with CA is effective in healthy young patients with PAF. Focus of review efficacy (not impact on HRQoL) (-). Only RCT included in review (-). Results not generalisable to other AF groups or patients with existing comorbidities.
Khan et al., 2014	Systematic review	Meta-analysis comparison of safety and efficacy of CA against AAD.	11 Studies (including 1481 patients)	4 studies used SF-36 (11,15,18,19), 1 study used EQ-5D and 1 study used AF-QoL. QoL scores improved when using SF-36 (both components) in patients undergoing CA. CA appears to improve QoL scores.
Kim et al., 2016	Systematic review and meta-analysis	Identify impact of CA of AF on HRQoL using SF-36.	13 studies included in review and meta-analysis	Systematic review and meta-analysis of SF-36 measure use in CA. Used random effects model. Meta-analysis investigating whether there is association between successful CA of AF and improved QoL scores using SF-36. Results: Significantly improved scores in both components of SF-36 (PCS and MCS) in successful CA of AF when compared to those who had AF return.
Kotecha et al., 2016	Systematic review	A review of PROM used in AF.	8 articles reviewed which included PROM used in AF population	Review of HRQoL measures available for use in AF. COSMIN criteria used to critique available tools.
Lane et al., 2009	Review	Quality of life in older people with AF.	Not published	15 measures of HRQoL (generic and disease-specific identified) from a systematic review published in 2006.
Patel et al., 2013	Systematic review	Systematic review considering anxiety and depression in AF.	18 studies included (n=12 focused on depression and anxiety; n=2; focused on anxiety; n=4 focused on depression)	Complex interaction between QoL, depression, anxiety and AF. Unclear about the relationship and whether new AF is caused by depression/anxiety. Complex interaction with drug treatments (anxiety and depression) and AF management (such as anticoagulation). Further research needed.

Table 2.3 Overview of literature reviews considering AF and HRQoL. Continued (1)				
Pepine et al., 2013	Systematic review	Systematic review on impact of pharmacotherapy on HRQoL in patient with AF >65 years.	15 studies included: observational studies (n=5); RCT examining rate versus rhythm (n=5); RCT examining pharmacologic (n=3); studies focusing on anxiety and depression (n=2).	Varying study duration (6 months to 4.5 years) (-). HRQoL considered in sub-population of the studies (-). Mostly generic HRQoL measures used (-). No studies consider elderly population (-). Importance of measuring HRQoL in AF population highlighted. Further studies needed to evaluate AFEQT measure. Worldwide registry data needed for real-world impact of HRQoL.
Reynolds et al., 2008	Review	Review of HRQoL in AF population and questionnaires used in this population.	Not a systematic review. Details of search strategy or number of articles reviewed not provided.	Identify the need of standardised tools for measuring HRQoL in AF population. Recommend disease-specific HRQoL tool for patients with AF.
Siontis et al., 2016	Systematic review	Comparison CA against AAD in patients with PAF or persistent AF.	12 RCT included in review (which included n=1,707 patients).	CA appears to improve QoL scores more than AAD; however, this effect does not appear to last over time. Generic HRQoL measures mostly used. Differences in information presented for individual patients (such as if repeat CA are needed) may limit comparison between studies (-). Cross over behind study arms may have impacted QoL results of studies considered (-).
Thrall et al., 2006	Systematic review	Impact of AF on HRQoL in the general population and comparison of interventions.	49 studies included	QoL noted to be lower in patients with AF when compared to the general population and patients with other cardiac disease. Mostly generic measures used (SF-36) especially in studies comparing rate and rhythm control. No AF-specific HRQoL measures considered in review (-) due to time period carried out (>10 years ago). Significantly improved QoL scores in both rate and rhythm management when assessing with generic measures.
Xiong et al., 2015	Systematic review	A systematic review of differences in age, gender and cardiovascular outcomes in asymptomatic and symptomatic atrial fibrillation.	6 studies included in meta-analysis (RCT n=2; observational studies n=4)	QoL not main focus (-); briefly mentioned but no main findings discussed.
Zhang et al., 2015	Systematic review	Literature review on impact of pharmacotherapy on HRQoL in patients with AF >65 years.	15 studies included in review (observational, n=3; descriptive, n=5; RCT, n=7).	Patients with AF >65 years old had significantly reduced HRQoL. Some aspects of HRQoL improved with treatment but no treatment was identified as being best.

2.3.2 HRQoL in AF: Summary of Findings

Literature reports significantly lower HRQoL scores in AF patients compared to the general population (Thrall et al., 2006). Various aspects of HRQoL are shown to be significantly negatively affected in both qualitative and quantitative studies (Thrall et al., 2006; Altiok et al., 2015). This is supported by the findings of this review. The findings of this review are summarised in Tables 2.2 and 2.3 (above).

This review considers areas of HRQoL affected by AF. Until recently, AF HRQoL literature has focused on the quantitative comparison of interventions (such as medication and catheter ablation) (Thrall et al., 2006). Aspects of HRQoL such as anxiety, depression and physical symptoms of AF have also been examined in quantitative studies. The measurement of HRQoL in quantitative studies may involve the use of instruments that examine general health status, referred to as generic HRQoL measures, and those designed for specific groups or patient populations, referred to as disease-specific HRQoL measures. Whether a generic, disease-specific or a combination of both types of measure was used in each study is identified in Table 2.2. This review will also present the literature considering HRQoL changes as the result of interventions.

Qualitative research has examined HRQoL in further depth and identified those aspects of HRQoL affected by AF, which can include physical symptoms, activities of daily living, psychological and social and relationships. However, there are very few studies measuring the HRQoL impact on patients qualitatively (Kang and Bahler, 2004; McCabe et al., 2011). Only six qualitative explorations have been identified in this review (Deaton et al., 2003; McCabe et al., 2011; Ekblad et al., 2013; Dalteg et al., 2014; Altiok et al., 2015; McCabe et al., 2015) whose methods included focus groups and interviews with patients with AF. The overall findings are summarised in Table 2.3.

2.4 Findings: Qualitative Research – Exploring QoL in AF

Research has investigated the impact of AF on HRQoL in both qualitative and quantitative studies. Qualitative studies report that AF affects multiple domains of HRQoL simultaneously. For the purposes of this thesis, results were collated under the QoL domains identified by WHOQOL-BREF (WHO, 1996): Physical, Psychological, Social and Relationships. In addition, level of independence and healthcare were also identified as being affected or influencing HRQoL. It is understood that the HRQoL domains Physical, Psychological, Social and Relationships are more likely to be affected in earlier stages of AF. However, it is important to consider that additional domains such as level of independence and healthcare may be affected or have an effect on HRQoL in later stages of AF.

2.4.1 Physical Symptoms

Both participants and clinicians were reported to commonly misdiagnose AF, attributing symptoms of AF to stress, anxiety, other comorbidities (respiratory problems), reduced fitness or ageing (Deaton et al., 2003; McCabe et al., 2011; McCabe et al., 2015). For example, one participant attributed dyspnoea (breathing difficulty) to a preceding respiratory problem: "I said to her [the healthcare provider], 'I think I have bronchitis because I can't get my breath and I can't lay down and sleep – I can't breathe'" (McCabe et al., 2015).

Misdiagnosis of AF was reported to delay treatment (McCabe et al., 2015), which can negatively impact patients psychologically and also negatively impact physical function within the broader literature (Benjamin et al., 2009; Camm et al., 2010; January et al., 2014), such as increasing the risk of chronic heart failure, sudden death and thromboembolic episodes (Wolf et al., 1991; Benjamin et al., 1998; Wattigney et al., 2003; Fang et al., 2007).

Qualitative studies reported that symptoms of AF which either changed in frequency or severity or did not self-terminate were associated with a feeling of concern, creating a need for urgent medical attention which negatively impacted HRQoL (McCabe et al., 2015).

2.4.2 Activities of Daily Living

Difficulty or an inability to carry out activities of daily living because of symptoms such as shortness of breath, palpitations and fatigue were reported by over half of participants (n=24 out of n=32) by Altiok et al. (2015). Participants often identified that activities such as exercise, housework, social activity and sexual activity were associated with triggering or increasing symptoms (Altiok et al.,

2015). As a result, participants used tactics such as limiting or avoiding activities to reduce symptoms (Lane et al., 2009; Altiok et al., 2015). Avoidance or reduction of activities interfered with participants' normal daily lives and had a negative psychological impact (Altiok et al., 2015). It is suggested that a reduction in activities could cause decreased self-esteem and increased dependence on others, potentially leading to the breakdown of relationships (Altiok et al., 2015).

2.4.3 Psychological Impact

Deaton et al. (2003), McCabe et al. (2011) and Ekblad et al. (2013) reported that emotional distress was related to the symptoms of AF. McCabe et al. (2011) and Altiok et al. (2015) noted that symptoms left participants feeling exhausted and burnt-out and led to a feeling of worthlessness and failure. This contributed to anxiety, depression and the feeling of loss of control (McCabe et al., 2011).

2.4.3.1 Anxiety

Much of the experience of anxiety by AF patients appears to result from the unpredictability of AF symptoms (McCabe et al., 2011; Ekblad et al., 2013; Dalteg et al., 2014; Altiok et al., 2015). Increased stroke risk was also shown to impact patients psychologically (McCabe et al., 2011). The potential consequences of stroke or other thromboembolic episodes were a major concern (McCabe et al., 2011). Some patients revealed less fear of death than of the consequences of a catastrophic stroke causing paralysis (Altiok et al., 2015).

2.4.3.2 Level of independence

Participants also reported a reduced level of independence, with almost half of participants (n=15 out of n=32) reporting an inability to attend hospital appointments alone. Altiok et al. (2015) further reported this caused an increase in dependence on relatives, negatively impacting relationships.

2.4.4 Social and Relationships

The qualitative literature also identifies that AF can affect work, family and sexual relationships and can have a negative impact on an individual's social life (Deaton et al., 2003; Ekblad et al., 2013). The unpredictability of AF symptoms in particular was noted to cause restriction and avoidance of social activities. This reaction was reported by half of participants interviewed with AF (n=16 out of n=32) by Altiok et al. (2015). McCabe et al. (2011) also reported participants felt the need to alter work and travel practices in addition to social events because of AF symptoms. Altiok et al. (2015)

reported a third of participants interviewed (n=11 out of n=32) avoided sexual activity for fear of triggering symptoms of AF. Participants reported relatives and friends were often unable to understand the unpredictability of AF and the impact of symptoms. This resulted in participants feeling unsupported or unable to complete tasks usually expected of them (McCabe et al., 2011) leading to feelings of unworthiness. Dalteg et al. (2014) noted that AF also had an impact on the partner as well as the patient and presented strategies used by both to alleviate the uncertainty of AF, although this uncertainty was not fully eliminated. Altiok et al. (2015) suggested that AF symptoms can affect relationships and cause increased burden or breakdown of relationships as a consequence.

2.4.5 Healthcare

Qualitative studies have highlighted that the quality of healthcare had an impact on how participants coped with AF. McCabe et al. (2011) and further work by McCabe et al. (2015) noted that some participants had difficulties receiving the initial diagnosis. Participants described feeling initial relief but acknowledged a 'roller coaster of emotions' post diagnosis, including anxiety and depression (McCabe et al., 2011). According to Deaton et al. (2003), participants reported that health care providers did not acknowledge the seriousness of AF and its effect on their HRQoL. This led to a feeling of being unsupported to cope with the emotional burden of AF.

Patients who were very symptomatic and had limited treatment options remaining were noted to be keen to pursue any treatment in the hope of improving HRQoL. Deaton et al. (2003) quotes a participant's interview transcript to highlight this:

> Yeah. I had chest pain constantly for two years. I couldn't breathe. I couldn't go anywhere. My quality of life was about as close as it can get before you want to think about taking things into your own hands. I couldn't do anything. Just no quality to my life. I was a hardship to my family. I felt like if there was a chance that I could get back into the mainstream of civilization, I surely wanted to do it. I was willing to take substantial risks to do that. p. 296

As described in Chapter One, some food and drink restrictions may be imposed because of anticoagulation medication (Altiok et al., 2015). Poor clinical management of anticoagulation was reported to impact patients. For example, many patients followed the imposed dietary restriction but due to poor communication, patients were oblivious to the rationale. This caused reduced compliance and embarrassment when relaying the information to relatives and friends.

2.5 Findings: Quantitative Research – Exploring HRQoL in AF

This review identified that most studies reviewed focused on symptomatic AF and only three (Flaker et al., 2005; Pontoppidan et al., 2009; Yamamoto et al., 2014) included patients who were asymptomatic of AF at the time of enrolment. Most of the studies identified (n=19 out of n=28) were randomised control trials or trials which compared or examined the impact of interventions such as antiarrhythmic drugs, catheter ablation or surgical procedures. Half (n=7 out of n=14) of the literature reviews focused on the impact of AF interventions on HRQoL. The time for follow-up in studies after an intervention ranged from six months to four and a half years. Some of the studies identified in this review were of an observational design (n=9). Four literature reviews focused on the general impact of AF on HRQoL in an older population (n=1), in those who were asymptomatic or symptomatic (n=1), in those with depression or anxiety (n=1) or in the general population (n=1). Three literature reviews focused on the tools measuring the impact of AF symptoms or impact of AF on HRQoL.

Disease-specific and generic HRQoL measurement tools have been used to measure HRQoL in the AF population, both independently and together (Thrall et al., 2006; Zhang et al., 2015). The overall results of a literature review revealed significantly lower HRQoL scores in patients with AF when compared to the general population and also to age-matched controls (Thrall et al., 2006), independent of the severity of AF (Dorian et al., 2000).

2.5.1 Generic Questionnaires

Used in 20 out of the 28 studies identified, the SF-36 was the most commonly used questionnaire in this review. This is supported by existing literature (Thrall et al., 2006; Zhang et al., 2015). When measuring HRQoL using the SF-36, some studies found all domains of HRQoL to be negatively affected by AF (Dorian et al., 2000). Several literature reviews identified aspects of HRQoL that were negatively affected, including physical role functioning, general health perceptions, vitality, emotional role functioning, social functioning, mental health and physical functioning (van den Berg et al., 2001; Zhang et al., 2015). Pain scores were noted to be either lower (indicating less pain) in AF patients than in the general population or were the only area of HRQoL not affected (Lonnerholm et al., 2000; Zhang et al., 2015). Some domains such as anxiety and depression in the psychological domains found to be negatively affected by AF have also been further explored by quantitative studies. Only one not AF-specific measure identified domains of HRQoL such as sexual life, home activity and professional activity were reduced or limited because of AF (Dabroski et al., 2010).

2.5.1.1 Anxiety

Patients with AF were noted to have higher levels of anxiety when compared to the general population, which can result in poorer HRQoL (Thrall et al., 2006). Thrall et al. (2007) identified that 28% and 38% (of n=101) of patients with AF possessed state and trait anxiety following completion of the State-Trait and Trait Anxiety Inventory (STAI). A systematic review (Patel et al., 2013) described the complex interaction of AF, anxiety and depression. AF can cause anxiety and depression; conversely, some research suggests the pathology of anxiety and depression may build an environment favourable for the initiation and continuation of AF episodes (Patel et al., 2013). However, Patel et al. (2013) concluded that literature investigating whether depression and anxiety are triggers of AF is limited.

Perception of AF, personality traits and the style of clinical management have been shown to negatively impact the psychological well-being of patients with AF (Patel et al., 2013). It was noted that patients who were recipients of better clinical treatment such as sufficient information upon diagnosis or those who self-researched AF, had reduced anxiety levels (Lane et al., 2009). It is suggested by both qualitative and quantitative studies that thorough clinical assessment of patients' understanding and perception of AF (McCabe et al., 2011; McCabe et al., 2015) and additionally addressing concerns of AF and its management would reduce anxiety and depression (Lane et al., 2009).

2.5.1.2 Depression

In addition to anxiety, the unpredictability of AF is also thought to increase the risk of depression (Van den Berg et al., 2001). Dabrowski et al. (2010) reported that patients with AF had significantly higher rates of depression compared to the general population. The results of Thrall et al.'s (2007) study revealed 38% (of n=101) of AF participants met criteria for clinically significant depression symptoms according to the Beck Depression Inventory (BDI). Similarly, Lane et al. (2009) reported depression to be significantly higher in patients with AF, especially within the first year of diagnosis (Lane et al., 2009). Although depression was noted to reduce after the first year of AF, it remained more prevalent in this patient group than in the general population (Lane et al., 2009).

2.5.2 Disease-Specific HRQoL Questionnaires

Seven studies in this review used an AF-specific symptom measure, five studies used a disease-specific HRQoL measure and nine studies used a combination of both generic and disease-specific measures. The use of disease-specific questionnaires in addition to a generic measure also suggests HRQoL in AF patients is lower than in age-matched individuals (Dorian et al., 2000; Zhang et al., 2015). Using a disease-specific questionnaire instead of a generic measure ensures that more relevant

information for clinicians and patients is captured, therefore providing a more detailed account of the patients HRQoL**,** which is advantageous. For example, a disease-specific HRQoL measure may ask questions not included in generic HRQoL measures e.g. questions relating to symptoms such as palpitations which are experienced by patients with AF but not by the general population (Wokhlu et al., 2010; Spertus et al., 2011; Raine et al., 2015).

2.5.2.1 Physical: Symptoms

Only seven studies used an AF-specific symptom measure. This was used alongside a generic HRQoL measure. The recurrence of AF may negatively impact HRQoL scores in quantitative studies (Pürerfellner et al., 2004; Wokhlu et al., 2010). Some investigators found that symptom severity is the greatest determinant of HRQoL, especially in physical domains (Zhang et al., 2015), therefore accurate assessment of symptoms is essential.

2.6 Changes in HRQoL as a Result of Treatment

There are two broad questions in the literature regarding the change of HRQL as a result of treatment. Firstly, does AF treatment improve HRQoL, and secondly, if so, which treatment is best?

2.6.1 Does Treatment Improve HRQoL?

Both generic HRQoL measures and disease-specific HRQoL measures have shown improved HRQoL following treatment.

2.6.1.1 HRQoL changes observed by generic HRQoL measures

The meta-analysis by Siontis et al. (2016) compared the mean changes in SF-36 scores in seven out of nine trials which compared catheter ablation to anti-arrhythmic drugs for the treatment of AF at baseline, three, six and nine months. Initial comparison of treatments results from baseline to three months indicated significantly higher scores compared to baseline for catheter ablation in physical functioning, vitality and mental component, therefore indicating improvements in the mentioned domains of HRQoL. However, changes in scores from the physical component summary between treatments were not significant. Siontis et al. (2016) noted that the scores in the role emotional domain were no longer statistically different at six months' follow up. Similarly, differences in scores for physical functioning and mental component were no longer significant after nine months.

A systematic review and meta-analysis (Kim et al., 2016) examining HRQoL scores using the SF-36 in patients with AF undergoing a catheter ablation identified 13 relevant studies which compared HRQoL scores before and after ablation. Following ablation, there was a significant ($p<0.001$) increase in the weight mean scores of SF-36 in both components of the measure, the mental component summary score (MCS; 7.80) and the physical component summary score (PCS; 6.33), in all studies. This review also considered ablation success and its impact of HRQoL, reporting greater improvement in the weighted mean SF-36 scores of those who had successful procedures than in those whose symptoms of AF returned'. The difference in the weighted mean scores of these groups was noted to be 7.59 (for the MCS) and 7.46 (for the PCS) when using the SF-36.

In a systematic review and meta-analysis, Khan et al. (2014) identified four studies reporting improved HRQoL scores in the physical and mental component domains of the SF-36, indicating improved HRQoL. The mean scores of only two out of the four studies considered by Khan et al. (2014) were available. These improvements in HRQoL were reported to be statistically significant in both the physical and mental components of the SF-36 in both studies (Jais et al., 2008; Cosedis Nielsen, et al., 2012). Although Wilber et al. (2010) did not report the mean scores of the SF-36, the mean score changes were reported from baseline to three months in patients undergoing catheter ablation (CA) (n=90) and those on antiarrhythmic drug therapy (AAD) (n=39); in the mental (8.5 [CA group] vs. 1.6 [AAD group]) and physical component domains (6.9 [CA group] vs. 0.4 [AAD group]). The mean scores increased, which indicates improved HRQoL. The mean change between treatments was significant in both the physical (6.9 mean change $p<0.001$) and mental component domains (6.6 mean change $p<0.001$) of the SF-36. Similarly, Forleo et al. (2008) did not report mean results but rather improved HRQoL life in both treatment groups (CA vs. AAD) and statistically significantly higher HRQoL scores ($p<0.005$) following AF treatment with catheter ablation.

Khan et al. (2014) further reported improvement in HRQoL in participants who had treatment with ablation, reporting the pooled mean difference for physical component domain (5.0) and the mental component domain (4.2). This suggests that ablation improved HRQoL in patients with AF. The pooled mean scores of participants in drug therapy groups were not provided; Khan et al. (2014) acknowledged difficulties in comparing results as methods assessing HRQoL varied between studies.

2.6.1.2 HRQoL changes observed by disease-specific measures

A small number of disease-specific HRQoL measures have been developed and used in research. This review identified three studies which reported using an AF-specific HRQoL measure.

One of these is the AFQLQ, which has been used in Japan in the J-RHYTHM I, J-RHYTHM II study and QOLAF study (Tsuneda et al., 2006; Ogawa et al., 2009; Yamamoto et al., 2014). Yamamoto et al. (2014) investigated the association between HRQoL and asymptomatic episodes of AF, concluding that the reduction of AF episodes, even asymptomatic episodes, would benefit patients psychologically.

The AF-QoL was used in a randomised controlled trial (SARA) which compared catheter ablation and drug therapy in patients with persistent AF in Spain (Mont et al., 2014). It is noted that both treatments had significant improvement in HRQoL scores (indicating improved HRQoL), but there is no significant difference between treatment groups. However, lack of significance may be due to small sample size and insufficient statistical power and further studies are recommended (Mont et al., 2014).

The AFEQT was used in a trial examining the impact of ablation on patients with AF undergoing catheter ablation (Raine et al., 2015). This study reported significantly greater change (improvement) in HRQoL scores after ablation when using the AFEQT measure compared to the SF-36. However, significant improvement in scores was only reported in those who had a successful procedure. Specific changes in HRQoL as a result of treatment have been noted when using disease-specific measures in areas of symptoms, limitations of daily life, sexual domains and psychological effects of AF. These would not have been captured if solely using a generic HRQoL measure such the SF-36. The results of the subdomains of the disease-specific measures are not published, which limits ability to provide further comment on more specific changes in these areas.

2.6.2 Which Treatment Provides Best HRQoL Improvement?

The impact of various interventions on QoL in the AF population has been examined. Clinical trials of invasive clinical procedures such as catheter ablation, pacing procedures, maze procedure and cardioversion are most frequently investigated (Pepine, 2013). It is noted that pharmacologic therapy is less often investigated, even though the majority of patients will receive pharmacologic therapy (Pepine, 2013). Hakalahti et al. (2015) acknowledged that most clinical trials which involve invasive procedures such as catheter ablation include patients who have failed to respond to pharmacologic therapy. The majority of clinical trials, including RACE (Hagens et al., 2004), AFFIRM (Cooper et al., 2004), STAF (Carlsson et al., 2003), J-RHYTHM (Ogawa et al., 2009) and CAFE-II (Shelton et al., 2009) are focused on the comparison of rate or rhythm control to establish which is best treatment.

A review by Zhang et al. (2015) considered fifteen studies investigating HRQoL in patients over 65 years. All studies showed improvement of HRQoL scores (in both generic and disease-specific

HRQoL measures), indicating higher HRQoL following treatment. Similarly, following a review of pharmacologic therapy in observational, non-randomised and randomised controlled trials in an older (above 65 years) AF population, Pepine (2013) also concluded that any treatments may improve HRQoL scores. Both Thrall et al. (2006) and Pepin (2013) concluded that no best treatment option currently exists but all treatments may increase QoL.

Even though much research has been carried out, there is currently no clear answer to the question of which AF treatment provides best improvement in HRQoL. Clinicians and more importantly patients require this information to allow informed decisions to be made about their care. To answer this question, a valid, reliable, AF-specific measure is needed to capture aspects of HRQoL important to patients.

2.7 Discussion

2.7.1 Qualitative Research

It is understood that over time, AF symptoms can have a differing impact. As already discussed (in Chapter One), AF can progress to become more symptomatic following the remodelling of the atria due to natural progression of AF (Naccarelli and Allessie, 2006). Invasive treatments of AF can also alter the atria, causing patients to potentially experience differing symptoms (Wokhlu et al., 2010). Whilst studies which investigated patients' experiences over a long range of time (i.e. years since diagnosis) provide a deeper overall insight into individual experiences of AF and allow patients to reflect and elaborate with hindsight, recall over such a time period may influence accuracy (Deaton et al., 2003; McCabe et al., 2011; Ekblad et al., 2013). The patient's subjective view of the impact on HRQoL from their chronic condition may change over time. Patients may compare their previous experiences to their current experience as a strategy to cope better, a phenomenon which is known as the response shift (McDowell, 2006). For example, when asked about their current HRQoL, a patient who has had AF for 10 years and has had numerous hospital admissions during this time may indicate they have a very high HRQoL (mainly because they are not currently admitted to hospital) even though they cannot leave their house due to the impact of AF. When examining the impact of symptoms of AF on HRQoL, studies with time limitations such as a few months since diagnosis (e.g. McCabe et al., 2015**)** may provide a more accurate understanding of the initial impact.

Although no qualitative data reflects the impact of AF on HRQoL in asymptomatic patients, according to NICE guidelines (2014) patients with AF are at a higher risk of stroke than the general population and therefore may require anticoagulation therapy. Therefore, healthcare and treatments can negatively impact HRQoL in the asymptomatic population as well as the symptomatic population. Further research exploring the impact of AF on the asymptomatic patient is needed.

A complex interaction exists between HRQoL and external factors. Whilst all the qualitative literature indicated that AF negatively impacted HRQoL, one qualitative study (Deaton et al., 2003) included patients who were treated with an implantable cardioverter-defibrillator (ICD) which have been shown qualitatively to have an impact on QoL (Duru et al., 2001; Schron et al., 2002). This treatment is not common practice; therefore, this study (Deaton et al., 2003) may not be a true reflection of the current AF population.

One study (Altiok et al., 2015) considered took place in Turkey which has a different healthcare system from that of the UK and which does not currently provide additional support services such as arrhythmia nurse specialists (Altiok et al., 2015). Conversely, poor clinical management and poor communication by clinicians are also shown to impact patients' HRQoL in other studies (McCabe et al., 2011). Implications of regular hospital anticoagulation appointments, such as long waiting times, have been shown to affect working life, leading to some financial implications (Altiok et al., 2015). However, since publication of this research, recent advances in anticoagulant options have taken place in the UK which reduce the number of appointments and blood tests for some patients.

2.7.2 Quantitative Literature

Quantitative literature indicated significant improvement following treatment, there may be several reasons for this. Thrall et al. (2006) acknowledges that this could be a result of the reduction in AF symptoms or severity following invasive procedures. Some literature suggests this symptom reduction may cause an initial placebo effect following the achievement of sinus rhythm; i.e., as the patient has had an invasive procedure, they expect they should feel better and any reduction of symptoms due to being in normal sinus rhythm will result in feeling better than previously (Smith et al., 2010). It is also suggested that simply by receiving treatment patient satisfaction could improve, causing a Hawthorne effect (Thrall et al., 2006). Literature comparing invasive ablation treatments and HRQoL impact may be methodologically weakened because of variation in ablation techniques which may potentially affect the outcome of treatment (Siontis et al., 2016). Changes between medical treatment and invasive interventions required by patients may impact the outcome of treatments (Siontis et al., 2016). Thrall et al. (2006) suggested that anxiety associated with invasive procedures may have a negative impact on baseline scores. For example, HRQoL may not be lower because of AF, but because there is additional anxiety about the risks of treatments and having a hospital admission which may further reduce HRQoL. Depending on treatment, patients may be advised to stop some medications. This may increase symptoms, further negatively impacting HRQoL scores; conversely stopping drug side effects may potentially positively impact HRQoL scores (Thrall et al., 2006).

The literature reviewed has highlighted that highly symptomatic AF patients are the main recipients of intervention and their HRQoL is reflected in the literature. Literature focusing on HRQoL in less severe or asymptomatic AF patients is limited (Aliot et al., 2014). Current literature therefore reflects a skewed population (Reynold et al., 2008; Lane et al., 2009) which may be a source of bias and imprecision in considerations and estimates of the effect of this condition (Thrall et al., 2006; Lane et al., 2009; Pepine, 2013).

The use of a generic HRQoL questionnaire has many advantages, one of which is to allow comparison against control groups and general population. Some researchers suggest the SF-36 is less sensitive to change when compared to disease-specific HRQoL measures in the AF population, especially in older patients with numerous comorbidities (Aliot et al., 2014). It is also suggested that demographics and comorbidities strongly influence the SF-36 scores in the AF population, which is a limitation (Reynolds et al., 2008; Aliot et al., 2014). Therefore, it is suggested that disease-specific questionnaires may provide a more detailed account of the HRQoL of patients with AF.

2.7.3 Generic Measurement Scales

Many generic HRQoL measures provide a wealth of information in a range of diseases and also in healthy populations (Patrick and Deyo, 1989; Brazier et al., 1999; Fayers and Machin, 2016). Generic and disease-specific measures differ slightly in their approaches to HRQoL. This means that generic measures have some limitations when used in patients with AF.

2.7.4 Limitations

There is great benefit in using validated generic measures in the AF population. One example is the WHOQOL-BREF, which is considered by some researchers to be one of the leading QoL questionnaires due to its conceptual structure and its being a cross-cultural international measure which incorporated languages and concepts of users (Skevington et al., 2004). It is considered to be fairly quick to complete, which increases response rate (WHO, 1997), containing a total of 26 items; 24 of these are scored in one of the four domains: physical health, psychological, social relationships and environment. It considers both positive and negative aspects of QoL (WHO QOL Group, 1997; Skevington et al., 2004). The final score is on a 0-100 scale, with a higher score indicating a higher QoL (WHO, 1997). Generic measures such as the WHOQOL-BREF enable key aspects of health and functional status to be measured whilst also allowing comparison to other populations and assessment of the economic value of an intervention (Brazier et al., 1999). However, the complexity of AF and the influence of other comorbid conditions on QoL scores have raised questions about their ability to

fully capture HRQoL changes in the AF population in relation to treatment (Reynolds et al., 2008; Pontoppidan, 2012; Aliot et al., 2014).

2.7.4.1 Responsiveness

It has been suggested that generic measures are not as sensitive to changes in HRQoL as disease-specific measures. This is supported by several studies, in which investigators were unable to distinguish between scores of patients whose treatment was effective (no longer in AF), and those who had treatment which was ineffective (Pontoppidan, 2012; Aliot et al., 2014).

Wokhlu et al. (2010) investigated the long-term HRQoL follow up of patients (n=323) treated for AF. The results revealed significant improvement in HRQoL following treatment for AF when measured using the SF-36 and an AF-specific symptom questionnaire (MAFSI). The Medical Outcomes Study Short Form Health Survey (SF-36) contains eight domains: vitality, physical functioning, bodily pain, general health perceptions, physical, emotional role functioning, social role functioning and mental health (Ware and Sherbourne, 1992). Each section is directly transformed into a 0-100 scale (0 being the lowest QoL score and 100 being the highest/best QoL score), with a high score (over the past four weeks) indicating a more favourable health state (Ware and Sherbourne, 1992). When using the SF-36, Wokhlu et al. (2010) found no significant difference between HRQoL scores in those patients whose treatment was effective (now in sinus rhythm) and those whose treatment was ineffective (still in AF). However, scores from the disease-specific symptom questionnaire (MAFSI) indicated a stronger correlation between reduced symptoms and effectiveness of ablation. Although the SF-36 remains the “gold standard” HRQoL measurement, the items and concepts were primarily proposed by health researchers and clinicians, not by potential users themselves; this may result in items that are important to the patient not being asked or accounted for. The completion varies from 10 to 23 minutes (Pickard et al., 1999; Parker et al., 2006), therefore it is not uncommon for patients to leave the questionnaire incomplete, leading to difficulty performing analysis.

Pontoppidan et al. (2009) reported improvement in the physical component score of the SF-36 following treatment in patients with persistent AF. In a review, Pontoppidan et al. (2009, 2012) reflected on past work and suggested that as AF is a complex condition, the SF-36 fails to capture the full burden of AF on HRQoL and suggests a disease-specific measure is essential to capture changes effectively. This conclusion was also reached by the FRACTAL (Fibrillation Registry Assessing Costs, Therapies, Adverse Events, and Lifestyle) investigators (Reynolds et al., 2006; Aliot et al., 2014).

2.7.4.2 Items

HRQoL, health care use, symptoms and functional status (such as cardiac function and exercise duration) are used as outcomes to indicate the effectiveness of treatment (Schron and Jenkins, 2005). Although HRQoL in patients with AF has been of growing interest for the last two decades (Lane et al., 2009), some reports consider HRQoL as an additional secondary outcome of interest rather than the primary outcome of treatment (Pepine, 2013). However, the literature indicates that HRQoL is the most important outcome to patients (Fuster et al., 2010; Pepine, 2013).

Comparison of HRQoL results in quantitative studies can be difficult as participant selection, time assessment points, treatments and the presentation of results vary between studies.
As already highlighted, most research includes patients with symptomatic AF, indicating that symptomatic AF can cause significant impairment of HRQoL. However, HRQoL in asymptomatic patients has also been shown to be negatively affected (Pontoppidan et al., 2009; Yamamoto et al., 2014), with some research finding 12-40% of participants to be entirely asymptomatic at baseline (Kerr et al., 1998; Flaker et al., 2005; Reynolds et al., 2006; Boriani et al., 2015). This suggests that patients HRQoL can be negatively affected regardless of the type of AF. Even if there was a difference in HRQoL between types of AF, results of the AFFIRM study indicated no difference in mortality risk in patients with AF who are symptomatic or asymptomatic (Xiong et al., 2015). Therefore, there are implications such as regular anticoagulation assessment and the potential lifelong need of preventative medication for all groups.
Although using a combination of both generic and disease-specific measures provides a more complete view of HRQoL, some research has only used generic questionnaires (Thrall et al., 2006). As generic measures are developed to be used in a variety of conditions and not just AF, they do not include questions that are specific to the condition. For instance, a generic questionnaire may ask "How often do you experience pain?", to which the patient may respond "daily" as they experience back pain. However, when asked in an AF-specific questionnaire, "How often do you experience chest pain?", the answer may be "never". This may have a significant effect on final HRQoL scores. Difficulty can also arise when attempting to identify which condition is influencing the HRQoL changes. For example, if HRQoL is being assessed in a patient after a heart operation using a generic questionnaire, it may be difficult to distinguish whether pain is due to the surgical procedure or the result of a different long-term condition (e.g. back pain) (Abbot, 2000). The impact of side effects of drug therapy (such as bleeding from anticoagulation therapy) or catheter ablation (such as an increase in heart palpitations) are unlikely to be captured using a generic questionnaire.

Items that evaluate the individual's symptoms of AF and HRQoL are therefore essential to provide a more detailed understanding about how AF affects individuals and how treatment impacts HRQoL.

This firstly allows clinicians and patients to make informed decisions regarding treatment options; secondly, it provides quantitative information regarding treatment effectiveness and economic value which can be presented to healthcare policy providers who influence future policy.

2.7.4.3 Subtypes of AF

The complexity of AF may limit the ability of generic measures to adequately identify and delineate the effects of AF on function and well-being. Disease-specific measures may better address the particular effects of this condition and its treatment. Subtle differences between the subtypes of AF can result in differing impacts on HRQoL. It would be understandable to accept the hypothesis that if a patient is continually symptomatic with AF, they would have a lower HRQoL score than a patient who has AF symptoms less often (e.g. paroxysmal AF). However, current literature suggests otherwise. When measuring HRQoL using a disease-specific HRQoL questionnaire, differences between the subtypes of AF are noted. For example, Peinado et al. (2010) noted that patients who have permanent AF had higher scores (indicating better HRQoL) in the psychological domain of a HRQoL measure than patients who had paroxysmal or persistent AF.

Although NICE (2014) endorses use of the European HRQoL assessment (EQ-5D), it acknowledges its use may be inappropriate in some patient groups and validity may be difficult to prove when a gold standard measure is absent (Brazier and Longworth, 2011). This generic questionnaire (EQ-5D) may have difficulty recording changes in HRQoL in patients who have asymptomatic or paroxysmal AF mainly because of the limited time frame and unpredictability of symptoms (Rabin and de Charro, 2001). The EQ-5D is a two-part questionnaire; the first section contains five domains reviewing mobility, self-care, pain/discomfort, usual activities and anxiety/depression. These are scored on a three-point scale as “no problems”, “some problems” and “extreme problems" (Hurst et al., 1997). The second section is a visual analogue scale (VAS) which contains a vertical 20cm scale with the end points labelled: “best imaginable health state” is at the top of the scale (numeric value = 100) and “worst imaginable health state” at the bottom of the scale (numeric value = 0) (EuroQol Group, 1990). The EQ-5D asks patients to indicate their health on the day of completion. It is important to consider that changes in patients with paroxysms of AF may not be reflected, unless patients are having an episode whilst completing the scale. Therefore, the validity of this questionnaire in this population is questionable and the responsiveness of the EQ-5D in this population is uncertain. For example, it could be expected that patients with PAF who are not experiencing an AF episode at the time of completion would have a low score in the first section (e.g. responding that they have no or some problems with certain activities), indicating a better HRQoL, and a low VAS score, indicating a lower HRQoL in the second section (e.g. perhaps responding with a score of 40 as they had an episode of AF the previous day). This scale would make it problematic to measure the true impact on HRQoL in

patients with paroxysmal AF. Patients who are asymptomatic of AF may have a high overall score from the EQ-5D, indicating a high HRQoL. However, this may not be a true reflection of the impact of AF on their HRQoL. For example, the psychological impact from side effects such as increased bleeding from essential anticoagulants will not be captured.

2.7.5 Disease-Specific Health-Related Quality of Life Tools

In a review carried out by Lüderitz and Jung (2000), seven out of thirteen HRQoL questionnaires were found to have not been validated prior to use. Similarly, Thrall et al. (2006) identified four studies that used a non-validated HRQoL questionnaire. Schron and Jenkins (2005) highlighted the need for researchers to ensure validated questionnaires are used in research. Although limited in number, there are newer HRQoL AF specific measures which have been developed since these reviews.

A systematic review demonstrated that a combination of generic and disease-specific questionnaires (Thrall et al., 2006; Zhang et al., 2015) allows a more comprehensive view of HRQoL (Reynold et al., 2008). All of the disease-specific questionnaires which will be later considered include questions regarding symptoms of AF, which is an important aspect of HRQoL to both clinicians and patients; this is not captured by the generic HRQoL questionnaires.

Assessments of HRQoL in patients with AF to date have been obtained using various scales that have either been developed before available guidance from governing bodies or are non-disease-specific (Reynolds et al., 2008). A disease-specific HRQoL tool will ensure that all items are relevant for the patient and there should be no items that are not applicable. Therefore, a disease-specific HRQoL assessment tool is required to provide a deeper understanding of the impact of disease and of available treatments (Reynolds et al., 2008; Streiner and Norman, 2008). Measuring the benefits of AF treatments will provide the information health care providers need to evaluate effectiveness and cost-effectiveness. A disease-specific QoL tool for AF is essential in order to reflect that these treatments that can be life-changing for individuals.

To conclude this section, generic measures and disease-specific measures involve different approaches to assessing HRQoL and both provide valuable information pertaining to HRQoL in AF patients. However, disease-specific questionnaires are more effective at capturing additional specific HRQoL changes in patients with AF. This highlights the need for disease-specific measures to capture HRQoL changes in patients with AF. Several disease-specific HRQoL measures have been developed for patients with AF (Badia et al., 2007; Braganca et al., 2010). These will be examined in Chapter Three.

The need for a disease-specific questionnaire was highlighted by a recent literature review (Pepine, 2013) which suggests this need may have been met by the AFQET but stresses that further research is required. Interestingly, Pepine (2013) explained that assessment of HRQoL (which includes physical health, psychological health, patient satisfaction and interference with activities of daily living) is needed to improve HRQoL in this population, alongside the clinical assessment of stroke and cardiovascular prevention, including the assessment of heart failure. The disease-specific measure AFEQT questionnaire does not encompass all these domains, and additionally had limited patient involvement in its construction.

2.8 Conclusion

To conclude, quantitative studies of the effects of AF treatments on HRQoL have provided results that enable some comparison between these therapeutic approaches, though the inconsistency of definitions of QoL or HRQoL and the use of different QoL measures limit this. The qualitative studies have provided a deeper understanding of the experiences of patients with AF. As a whole, the current literature provides an incomplete understanding of the changes in HRQoL that may result from treatment. This is because many of the disease-specific questionnaires were not validated prior to use and the available validated questionnaires failed to capture all areas of HRQoL impacted, as defined by patients in qualitative studies. The finding that the available disease-specific measures omit to examine some of the areas of HRQoL affected by AF identified by qualitative research reveals an important limitation in current measurement tools for this patient population. This further highlights the need for appropriate patient input in all the stages of development of disease-specific measures, to ensure a valid tool is constructed that encompasses the perspective of patients as well as clinicians.

Chapter Three: Literature Review of Health-Related Quality of Life Measurement Tools for Patients with Atrial Fibrillation

AF is a common cardiac arrhythmia affecting 33.5 million people globally (Chugh et al., 2014). Patients may be asymptomatic or suffer from differing symptoms of AF such as palpitations, dizziness and chest pain (NICE, 2014). Patients with both symptomatic and asymptomatic AF have substantially increased risk of stroke and been shown to have reduced HRQoL (Pontoppidan et al., 2009; Yamamoto et al., 2013). The management of AF is predominately aimed at the reduction of the associated risk of stroke and the symptomatic control of AF, with the intention to improve HRQoL. Treatment options include invasive costly procedures such as catheter ablation, or likely lifelong medications which carry many potential side effects such as tiredness, risk of abnormal bleeding and skin rashes (NICE, 2014). The final treatment decision should be based on detailed discussions between the clinician and patient to assess how AF affects their HRQoL and the potential benefits or side effects of treatments.

3.1 Introduction

Quantitative and qualitative research which identified domains of HRQoL affected by AF and its treatment were considered in Chapter Two. Quantitative research reported domains such as physical symptoms and psychological domains being negatively affected (Thrall et al., 2006). However, the qualitative research provided greater depth and further detail of the effects of AF, identifying several additional domains of HRQoL which were (predominately negatively) impacted by AF, and which were not measured and reported in the quantitative studies. Domains included physical symptoms, activities of daily living, psychological aspects, social and relationships (Ekblad et al., 2013; McCabe et al., 2015). Changes in HRQoL due to AF treatments were examined, and it appeared that the currently available treatment options were all associated with improved HRQoL (Thrall et al., 2006). The instruments (generic and disease-specific) used to measure HRQoL were considered and it was concluded that although generic measures may have the benefit of enabling comparison between other population groups including the general population, they are often limited by the constituent items' inability to measure aspects specific to the disease (for instance, symptoms of AF such as palpitations). This limits the ability of such measures to detect whether HRQoL improvement is due to AF treatment (Reynolds et al., 2008; Pontoppidan, 2012; Aliot et al., 2014). Disease-specific measures allow a deeper understanding of the impact of AF (Aliot et al., 2014) and of the effects of treatments. Therefore, it is important to identify available disease-specific questionnaires suitable for the AF population.

3.1.1 Aim

The aim of this chapter is to identify disease-specific HRQoL measures appropriate for patients with AF and to examine the reliability, validity and feasibility of their use in an AF population.

3.1.2 Objectives

This aim will be achieved by performing a literature review to determine: (i) what AF-specific HRQoL measures already exist, (ii) the extent of patient involvement in the development process for these measures and (iii) the evidence of validity for these measures. The critical appraisal of available tools will be based upon the approaches developed by Fitzpatrick (1998, 2006), Smith et al. (2005) and ISQoOL (International Society for Quality of Life Research, 2014) wherein the measures' reliability**,** validity**,** responsiveness**,** interpretability of scores and burden are examined.

3.2 Methodology

A literature review was carried out to search for HRQoL disease-specific measures suitable for use in patients with AF. The literature review used the Ovid platform to access all available online databases except books. Duplicates were removed, and the search was limited to original articles. The list of databases used are noted in Appendix B (3.1).

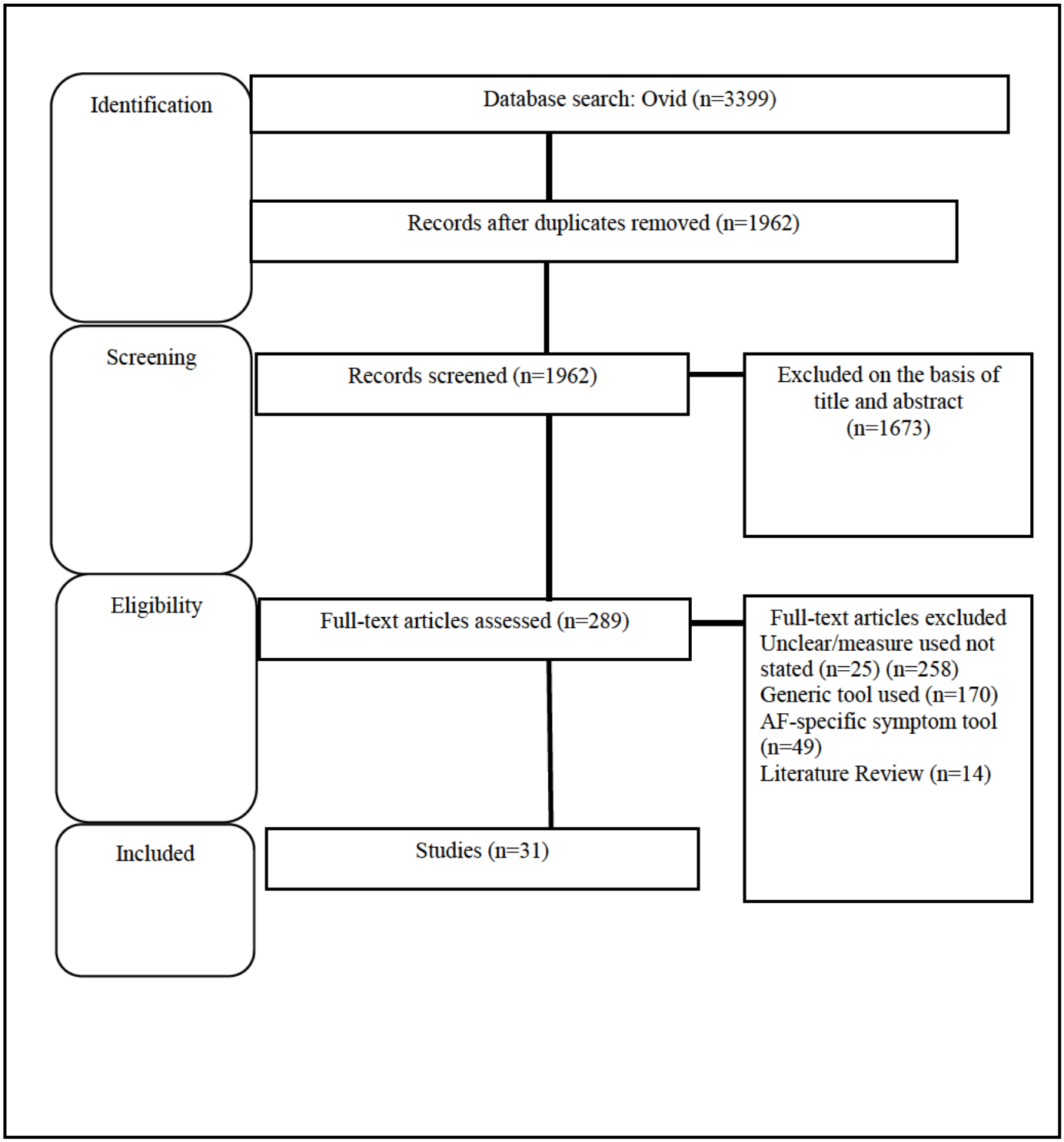
3.3 Search Terms

The search terms used on the databases were:

- AF
- atrial
- atrial fibrillation
- fibrillation
- health
- health-related quality of life
- hrqol
- life
- measure
- outcomes
- patient
- patient-reported outcomes measure
- proms
- qol
- quality
- quality of life
- questionnaire
- related
- reported

The above terms were combined as shown below:

Atrial Fibrillation **OR** AF **AND** Quality of Life **OR** QoL **OR** Health-Related Quality of Life **OR** HRQoL **AND** Patient-Reported Outcomes Measure **OR** PROMS **OR** Questionnaire.


Identification
Database search: Ovid (n=3399)
Records after duplicates removed (n=1962)
Screening
Records screened (n=1962)
Excluded on the basis of title and abstract (n=1673)
Eligibility
Full-text articles assessed (n=289)
Full-text articles excluded
Unclear/measure used not stated (n=25) (n=258)
Generic tool used (n=170)
AF-specific symptom tool (n=49)
Literature Review (n=14)
Included
Studies (n=31)

3.4 Results

The results of the literature search (shown in Figure 3.1 above) identified four AF-specific HRQoL assessment tools:

- Atrial Fibrillation Effect on Quality of Life (AFEQT).
- Health-related quality of life (HRQoL) in patients with Atrial Fibrillation (AFQoL).
- Atrial Fibrillation Quality of Life Questionnaire (AFQLQ).
- Quality of life in AF patients (QLAF).

An overview of identified measures is presented in Table 3.1. Aspects of the measures identified will be discussed in Sections 3.5 and 3.6. The psychometric properties of each measure will be assessed using appraisal criteria in Section 3.7. The extent of patient input will be considered and discussed in Section 3.13.

Table 3.1 Descriptive Table Comparing AF-specific HRQoL Measures								
Questionnaire Name Country	**Development**	**Domains Items (n) Scale**	**Adequate Sample size**	**Reliability**	**Validity**	**Responsiveness**	**Time to complete**	**Language level**
AFEQT Atrial Fibrillation Effect on Quality of Life America and Canada Spertus et al., 2011; Dorian et al., 2013 USA	√ Literature review √ Expert Input √ Patient rate items Validation (n=214)	**Domains**: 4 Symptoms; Daily Activities; Treatment Concern; Treatment Satisfaction **Items:** 20 **Numerical 0-100** 0 = ↓HRQoL 100 = ↑HRQoL	Yes	√ **Internal Reliability** Cronbach coefficient Alpha √ **Test-Retest Reliability** Intraclass correlation coefficient (ICC)	√ **Construct Validity** SF-36; EuroQol (EQ-5D); Atrial Fibrillation Severity Scale (AFSS); Symptom Checklist (SCL); Generalized Anxiety Disorder Scale (GAD-7); AF Patient and Physician Global Change Forms √ **Convergent Validity** √ **Discriminant Validity** √ **Known Group Validity** Clinician Assessment	√	42-item AFEQT: 9.3 minutes to complete 20-item AFEQT: not stated	Not published in this study; however: Estimated Lexile level 1770; Dale-Chall readability scale = grade 11-12 (American grading system) (Aronis et al., 2017)

Table 3.1 Descriptive Table Comparing AF-specific HRQoL Measures continued (2)								
AFQoL Health-related quality of life (HRQoL) in patients with Atrial Fibrillation Spain Badia et al., 2007; Arribas et al., 2010	√Literature review √ Expert Input √ Patients interviewed with questionnaire in pilot (n=17) Validation (n=112)	**Domains: 3** Psychological Physical Sexual activity **Items:** 18 **Numerical 0-100** 0 = ↓HRQoL 100 = ↑HRQoL	Yes	√ **Internal Reliability** Cronbach coefficient Alpha √ **Test-Retest** Reliability Intraclass correlation coefficient (ICC)	√**Discriminant validity** SF-36	√	10 mins	Not published in this study; however: Estimate Lexile level 1750; Dale-Chall readability scale = grade 9-10 (American grading system) (Aronis et al., 2017)
AFQLQ Atrial Fibrillation Quality of Life Questionnaire Japan Yamashita et al., 2003, 2005	NK	**Domains:** 3 Frequency and severity of symptoms Limitations of daily and specific activities Anxiety **Items: 26** **Numerical 0-100** 0 = ↓HRQoL 100 = ↑HRQoL	NK	NK	NK	NK	NK	NK

Table 3.1 Descriptive Table Comparing AF-specific HRQoL Measures continued (3)								
QLAF Quality of life in AF patients Brazil Braganca et al., 2010	√ Expert input √ Pilot patient tested Initial validation (n=63) Validation (n=231)	**Domains:** 7 Palpitations; Breathlessness; Chest pain; Dizziness; Drug; Direct Current Cardioversion; Ablation **Items: 22** **Numerical 0-100** 0 = ↑HRQoL 100 = ↓HRQoL	Yes	√ **Test-Retest**	√ **Content validity** √ **Construct validity; Convergent validity** (3, 6, 9 and 12 months) SF-36 QLAF	√	3 mins	NK
NK = Not Known (not published in English)								

3.5 Item and Scale Development

Streiner et al. (2014) consider the various ways to develop HRQoL measures. Methods of item and scale development can include patient interviews, focus groups, canvassing of expert opinion, use of item banks or the conduct of literature reviews. There are many benefits and disadvantages of using these different methods and item and scale development is unlikely to use one method alone (Streiner et al., 2014). The approaches used in the development of the four identified tools were considered and are presented in summary form in Table 3.1.

As outlined in Table 3.1, a literature review was the initial stage in the development of the AFEQT. Specialists created initial items and patients with AF indicated relative importance by rating these initial items (Spertus et al., 2011). The AFQoL was also developed following a literature review. Domains and items apparent from the review were considered with the input of three cardiologists; participants (n=17), were interviewed concerning the items' relevance (Badia et al., 2007). The QLAF was created by eight specialists; it was then administered to a small pilot group and questions and comments arising from this group formed additional questionnaire items. A total of 63 patients (initially 87 but 24 patients excluded) then completed the questionnaire verbally via a one-to-one interview. Publications relating to the AFQLQ development and validation are not currently available in English, which is a limitation of this review.

All three tools considered had significant input from healthcare professionals involved in providing care for patients with AF. It is acknowledged that expert opinion may allow the application of years of knowledge and experience to the construction of the measure. Some researchers not yet persuaded of the benefit of patient input in PROM may argue that the expert clinician is the only person able to objectively measure changes in symptoms and their effects on HRQoL (El-Matary, 2014), and so would likely favour clinicians having predominant input in development. However, limitations may arise from use of this method, such as a skewed view of AF and its effect on HRQoL based on a specific viewpoint and the consideration of specific or memorable clinical encounters. It is also important to consider if there are various viewpoints, disagreements between experts on which aspects of HRQoL are important and may be highlighted (Streiner et al., 2014).

Literature reviews may appear to ascertain the different aspects of HRQoL that can be affected by AF and are more likely to identify the range of HRQoL domains. However, the quality of a literature review depends on the appropriateness and rigour of the methods used, together with the quality of the existing literature. As far as the author is aware, none of the above studies have published the literature reviews conducted as part of their measure development, so it is unclear how appropriate

their methods were, or whether and topic coverage was focused on existing measures or a wider consideration of the impact of AF on HRQoL. As already noted, many researchers have highlighted that quantitative studies do not measure the full impact of AF on HRQoL adequately (Pepin, 2013), suggesting that qualitative studies would improve the quality of this data.

Recently, item banks have been constructed using item response theory (IRT). These items cover domains commonly affected by medical conditions such as pain, fatigue, emotional distress, physical functioning, general health perception and social role participation (Rose et al., 2008; Cella et al., 2012; Rose et al., 2014). Further research is being carried out by the National Institute for Health Research (NIHR) to measure the validity of generic items in various clinical populations (Cella et al., 2012). Although there is much benefit in having access to and using items that have been shown to be valid and reliable (Rose et al., 2014), when considering the AF population, it is uncertain whether there is any additional benefit in using these items compared to an existing generic measure such as the SF-36. As already discussed, generic measures have much benefit when used in clinical practice but have been unable to discriminate changes in HRQoL in different treatment groups of patients with AF (Devlin and Appleby, 2010; Devlin et al., 2010). It therefore would be considered inappropriate to solely use this method of item development for a specific disease such as AF until disease-specific items are available and shown to be reliable and valid.

Another method of item generation is eliciting the views and experiences of participants who have the condition (AF) by means of either individual interviews or focus groups. Patients are becoming more engaged and interested in treatment options and the impact particular treatments will have on their lives; this is also being encouraged by health professionals (Crosby et al., 2003; Asadi-Lari et al., 2004; Pomey et al., 2015; Fayer and Machin, 2016). Streiner et al. (2014) and Reeve et al. (2013) acknowledge that involving patient participants is an excellent way of collecting the data needed to develop items. Crucially, it ensures that those aspects of HRQoL which are important to patients are captured, thus increasing face and content validity at different stages. The identification of additional domains and items not considered by healthcare professionals is a major advantage of this method (de Wit et al., 2013). The data from these interviews and focus groups could be considered initial research in the area and could be added to the existing literature regarding AF and HRQoL alongside creating initial items. It is noted that the input from patients with AF varied, although most authors reported that patients were asked to complete the questionnaire and provide feedback after completion in the initial stages.

3.5.1 Demographic Information

The AFEQT questionnaire was developed and validated with patients recruited from six different sites, five in the USA and one in Canada. Participants (n=125) were asked to rate initial items in the item generation stage. Following this, participants (n=24) were interviewed as part of the item reduction and content validity stage. Then participants (n=214) were asked to complete the questionnaire alongside other questionnaires for the validation stage. Most of the study participants were male (n=123) and most were white Caucasian (n=207); however, this appears consistent with studies of the AF population which indicate that AF is more common in Caucasian males (Borzecki et al., 2008).

There is an absence of demographic information concerning the participants involved in the development of the AFQOL for the pilot stage. However, Badia et al. (2007) state that once the items were developed, the questionnaire was administered to 112 people with AF. Demographics for this group of participants showed that 72 were male, 40 were female and the mean age (SD) was 60.5 ± 13.4 years.

The AFQLQ was developed in Japan, and the two publications detailing its construction and validation are published in Japanese. While there is little published in English regarding the development of AFQLQ and the input from patients with AF, this measure appears to have been developed with input from Japanese patients with AF. A recent review by Kotecha et al. (2016), who translated the article into English as part of their review, reported that 40 participants were involved in the initial study (Yamashita et al., 2003), and 172 patients were involved in the internal consistency and reproducibility validation stages (Yamashita et al., 2005 cited in Kotecha et al 2016). The age (SD) of these participants is reported as 64 ± 10 years.

The QLAF questionnaire was developed in Brazil by eight cardiac specialists. The pilot questionnaire they constructed was administered to a small group of patients with AF for feedback. No demographic information is published about the patients involved in the pilot phase. However demographic information relating to the 63 patients involved in the initial validation phase is presented. Fifty-seven percent (n=36) of the participants were male, the remaining were female (43%, n=27) and their mean age (SD) was 62.8 ± 12.2 years (Braganca et al., 2010).

3.5.2 Type of Atrial Fibrillation in Initial Stages of Development

The AFQET included patients with paroxysmal (n=141), persistent (n=51), longstanding persistent (n=11), permanent (n=11) and asymptomatic AF (n=18). The AFEQT was the only questionnaire to report the inclusion of patients with asymptomatic AF. The pilot stages of the AFQoL involved participants with paroxysmal (n=59) and permanent AF (n=53). The initial validation stages of the QLAF involved participants with paroxysmal (n=24), permanent (n=19) and persistent AF (n=20). It is not documented if any asymptomatic patients were included in this stage. As identified in a recent review by Kotecha et al. (2016), most participants involved had persistent AF and a smaller number had paroxysmal AF. However, as the type of AF is presented in percentages, it is presumed that these percentages reflect the total number in each study (n=40; n=172).

3.5.3 Other Comorbidities in Participants in Initial Stages of Development

The journal articles detailing the development of both the AFEQT and the AFQoL provide information about the participants' type of AF, durations and treatments, but neither provide information about comorbidities that the participants experienced. The researchers developing the QLAF questionnaire note previous cardiac conditions, but no details of other medical conditions are provided. The information recorded showed 60% (n=38 out of 63) had hypertension and 16% (n=10 of 63) of participants have no other underlying cardiac conditions (Braganca et al., 2010). Due to the limited amount of information available in English about the AFQLQ, details of any comorbidities of patients involved in its development are not known.

3.5.4 Domains

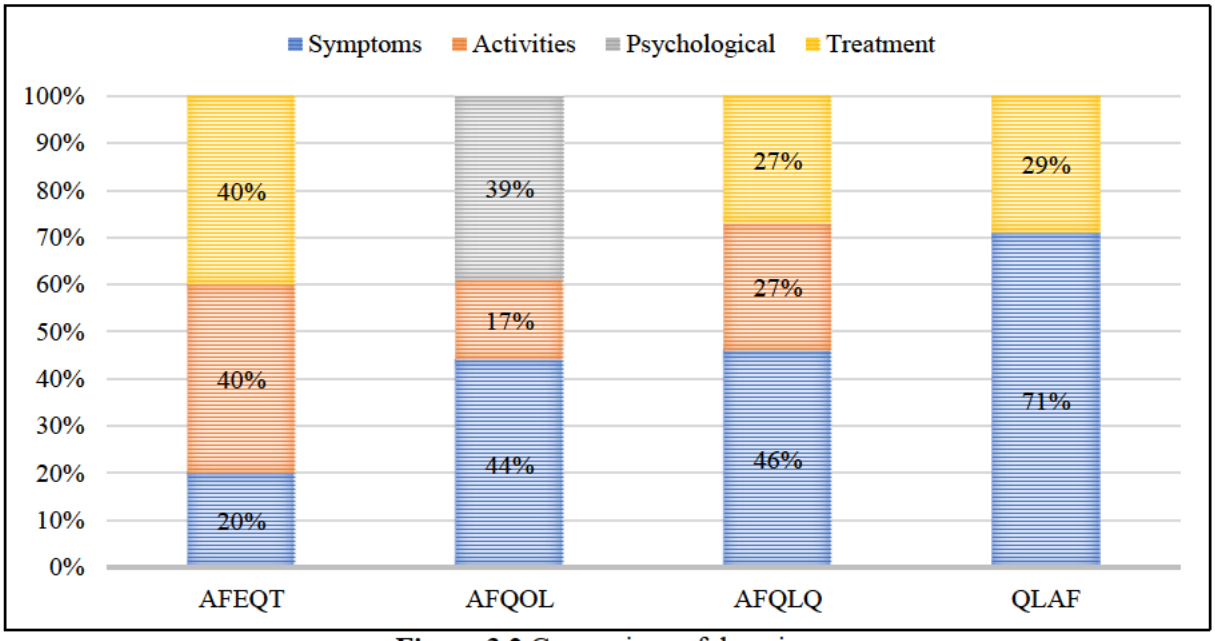


Figure 3.2 Comparison of domains.

Each questionnaire covers a variety of domains. In the AFEQT, for example, the domains are symptoms, daily activities, treatment concerns and treatment satisfaction (Spertus et al., 2011). For comparative purposes, the names of the different sections are merged in Figure 3.2 (above). As that figure demonstrates, 40% of the items relate to treatment, 40% relate to activities and 20% concern symptoms associated with AF.

Figure 3.2 shows that 44% of the questions in AFQoL concern the symptoms associated with AF, 39% of the questions relate to the psychological aspects associated with AF and 17% of the questions are about activities that are affected by AF. The domains of the AFQoL are: psychological, physical and sexual activity.

In the AFQLQ questionnaire, 46% of the items concern symptoms, 27% concern activities affected by AF and 27% are about the psychological effects of AF. The names of the domains in the AFQLQ questionnaire are: frequency and severity of symptoms, limitations of daily and specific activities, and anxiety (Aliot et al., 2014).

Most items in the QLAF questionnaire focus on symptoms (71%) (such as palpitations, breathlessness, chest pain, dizziness), with the remaining 29% relating to treatment for AF (such as drug, direct current cardioversion and ablation). The QLAF questionnaire has recently been updated and the newer version called the AFQLQ v2 is now available. This will be discussed later in this

chapter. The therapy domain has been removed from the new version, and domains concerning fatigue, wellbeing and illness perception have been added (Moreira et al., 2016).

3.5.5 Items

As noted, a key benefit of these disease-specific measures compared to generic measures is the inclusion of domains concerning the specific symptoms and treatments associated with AF. Despite all being developed for AF patients, it can be seen that there are considerable differences between these measures in the domains covered. This perhaps is influenced or characterised by the population it was intended for or by the process of development.

The identified AF-specific HRQoL measures comprise a similar number of items. The AFEQT has 20 items, the AFQoL has 18 items, the AFQLQ has 26 items and the QLAF questionnaire has 22 items. The number of items in the updated version of the QLAF questionnaire (referred to as AFQLQ v2) has increased from 22 to 30 (Moreira et al., 2016). The number of items provides an indication of the length of time required to complete and the patient burden associated with measure completion.

3.5.6 Expert and Patient Input

Patient involvement in the initial development of PROM for chronic conditions appears highly variable (Branski et al., 2010; Frew et al., 2013; Weiring et al., 2016), with the type of involvement being often poorly reported by researchers (Haywood et al., 2012; Staniszewska et al., 2012). When reviewing these four measures, the extent and type of patient input was specifically considered, and this is summarised in Table 3.2.

Table 3.2 Patient Input in the Development and Validation of Disease-Specific Questionnaires

	Questionnaire	AFEQT	AFQOL	AFQLQ	QLAF
Development	**Authors**	Spertus et al; 2011	Badia et al, 2007; Arribas et al, 2010	Yamashita et al, 2003; 2005	Braganca et al 2010
	Stage 1 of Development	**Item Generation:** Literature review	**Item Generation:** Literature review and expert opinion formed interview script	**Item Generation:** NP	**Item Generation:** Expert opinion
	Patient role in development	**Item Generation:** Patients rated items **Item Reduction:** Patients interviewed **Content Validity:** Patients interviewed	**Item Generation:** Patients interviewed	NP	None
	Patients in development (n)	**Item Generation:** 125 **Item Reduction:** 12 **Content Validity**: 12	**Item Generation**: 17	NP	None
	Patient role in pilot stage	No pilot stage noted	Patients asked to complete AFQoL (n=112)	NP	Small pilot group administered QLAF (method of feedback NP)
Validation	**Patient role in validation**	Questionnaires at baseline, 1 and 3 months: AFEQT EQ5D SF-36 (Short Form 36 Survey) AFSS (Toronto Atrial Fibrillation Severity Scale) Symptom checklist GAD-7 (Generalised Anxiety Disorder Scale)	Questionnaires: (intervention group completed at baseline and 3 months l: stable AF group completed at baseline and 1 month) AFQoL SF-36	NP	Patients asked to complete the following questionnaires at baseline, 3, 6, 9 and 12 months: QLAF SF-36
	Patient role in validation (n)	n=214	Validation Total: n=417 Patients with AF: n=341 Control Group: n=76	Reported by Kotecha et al. (2016) n=40 (Yamashita et al., 2003) n=172 (Yamashita et al., 2005)	n=63

NP = Not published

The items of the AFEQT were constructed from the results of a review of literature. Patients (n=125) rated items, feedback was gained from interviews with patients (n=12) and a further twelve participants were interviewed for content validity (Spertus et al., 2011). Items of the AFQOL were generated following a literature review and expert opinion which formed an interview script for a focus group with participants (n=17). A pilot group of patients (n=112) was asked to complete the questionnaire (Badia et al., 2007; Arribas et al., 2010). Items of the QLAF were generated from expert opinion. This was tested on a pilot group; however, details of patient role or feedback in this process are not documented (Braganca et al., 2010). As described, the AFQLQ development and validation stage is not published in English; limited access to development information is also highlighted by a recent review by Kotecha et al. (2016) which reports that a total of 212 participants over two studies were involved in validation studies reported in Japanese (Yamashita et al., 2003; Yamashita et al., 2005).

3.6 AF-Specific Questionnaires: Format and Content

Aspects of the content and format of the four questionnaires are considered below. The full content of each of the measures can be reviewed in Appendix B (3.2-3.5).

3.6.1 AFEQT

Although the AFEQT appears to have good domain and content coverage (i.e. impact of AF on daily activities, treatment concerns and satisfaction and symptoms) and its development involved appropriately sized samples of patients (n=125 patients rated the items, n=24 patients took part in interviews for item reduction and content validity and n=214 participated in the validation stage), aspects of AFEQT have highlighted important considerations in questionnaire development.

The AFEQT has two sections. Section One measures the occurrence of AF, requesting participants to identify if they are in AF. However, it is important to consider that some patients find difficulty in recognising when they are in AF, for example if a patient is permanently in AF but mostly asymptomatic. This limitation may have been overcome by providing another response option of "unsure or unknown" for the first question.

There remains uncertainty concerning the benefits of adopting 5-point, 7-point or other numbers of potential responses in Likert scales (Krosnick et al., 2010). Unlike the other AF-specific HRQoL measures, the AFEQT employs a 7-point response scale. Section Two is split into six stem questions which ask participants to rate the effects of AF or report the amount the participant has been 'bothered by' the listed symptoms, feelings and treatments during the past four weeks, using a 7-point response

scale. Although some studies suggest that a 5-point Likert scale response does not provide enough options for participants to indicate the impact or effect (Russell and Bobko, 1992), further suggesting that additional options increase the sensitivity of the measure (Cummins and Gullone, 2000; Finstad, 2010), it may be that for AF patients and HRQoL indicators, seven points provide so fine a distinction as to make the measure frustrating and difficult to complete. This may be supported by a recent abstract (Singh et al., 2013) which described investigating the validity of modifying the AFEQT to reduce the number of Likert scale responses from seven to five, which may support its practical limitations.

The second stem question of Section Two asks participants to rate how much their AF limited them in activities during the past four weeks. This is considered an appropriate time scale for participants. However, the word measuring the effect (i.e. *limited* in Question 5 and *difficulty* in Question 7) perhaps could be highlighted to aid reading. To the author's knowledge, the required reading ability is not reported in the development and validation paper. However, Aronis et al. (2017) has highlighted that the AFEQT requires a high reading level compared to some AF-specific measures and generic HRQoL measures. The estimated Lexile measurement a universal scoring system through which readability is assessed, with a lower score indicating the content is easier to read. The score of AFEQT was 1770 (out of a total of 2000), which is higher than that of the AFQoL (score=1750) and higher than that of the SF-36 (score=1250) (Aronis et al., 2017). This study also reports the estimated results using the Dale-Chall readability formula which indicates a required reading ability as a function of school grade (American schooling system), estimating that the AFEQT would require an 11^{th} to 12^{th} grade reading level. However, Aronis et al. (2017) suggest that documents intended for patients should be written for a 6^{th} grade level reader (in the American schooling system), this is further outlined by the appraisal criteria by ISOQOL (Reeve et al., 2013). Aronis et al. (2017) further report that requiring a higher reading level may mean some populations are not being assessed accurately (for example, in populations whose first language is not English).

The AFEQT is available in English. The availability of measures in other languages clearly extends their potential use to wider populations and may enable pooling of results. However, there are some concerns about the pooling of data from different languages and cultures (FDA, 2009; Cella et al., 2012) as poorly translated or culturally adapted questionnaires could lead to an inaccurate view of the effect on HRQoL and changes or differences between groups may be undetected (Wild et al., 2005; Wild et al., 2009; Cella et al., 2012).

Cross-cultural adaptation of existing questionnaires involves ensuring the conceptual and linguistic terms are equivalent in both questionnaires. It is important to consider that this can be a time-consuming process with many significant cost implications resulting from translation and licence fees

(Guillemin, 1995; Mathai et al., 2016). There is agreement in the literature that the adaptation of questionnaires not only involves the translation from different languages but also the adaptation to the culture of the intended population. Ideally this should be done by someone who has a good understanding of both cultures and also medical knowledge. Following this, a thorough testing of the measure following translation is also required to ensure content validity (Guillemin, 1995; Beaton et al., 2000; Lima et al., 2016).

Although the AFEQT may not require language translation, we would suggest there is a need for it to be culturally adapted prior to use in the UK population. The UK population is a diverse multicultural population and vastly different from that of the USA and Canada. Differences in cultural practices, religious and educational backgrounds may impact participants' perception and understanding of HRQoL. It is also important to consider that the validity of the data attained from the questionnaires is reliant on a mutual understanding of the question and also the response options (Mallinson, 2002). Therefore, it is of utmost importance that the questions and response options are equivalent in concept but also make linguistic sense in both languages and cultures. This is also relevant for the category responses. Szabo et al. (1997) describes equivalence between category responses in different cultures; for example, "quite often" in England is comparable to "often" in India.

The final AFEQT questionnaire does not ask any questions relating to the impact of healthcare appointments or the effects of the condition on sexual activity, which were identified as important in qualitative studies. It is also noted that items concerning symptoms fail to consider commonly reported symptoms such as fatigue, shortness of breath (on rest) and also chest pain. Chest pain or discomfort is a likely side effect in the first three months following catheter ablation and therefore at face value appears essential in a PROM for patients with AF.

The final score of the questionnaire is calculated (see Figure 3.3) without the use of a computer, which reduces the cost of this process. Although the time to complete these calculations has not been reported, it is hypothesised that this may take a few minutes and potentially may not be feasible for health professionals working in a busy outpatient department. The scoring for the four subscales requires several calculation steps which may involve error risks.

Example of calculation of one domain score

$$100 - \left[\frac{\text{(sum of severity for items 1,2,3 and 4 answered – number of items answered) X100}}{\text{(total number items answered multiplied by 6)}}\right]$$

Figure 3.3: AFEQT domain score calculation example (source: Spertus et al., 2011).

3.6.2 AFQOL

It is unclear if translation back to the original language (Portuguese or Spanish) was carried out in the AFQoL and QLAF questionnaires. The questionnaires may have been just crudely translated for the purposes of publication in English and not for clinical use. The authors of the AFQoL were contacted on two occasions to request more information regarding this questionnaire but did not respond. The translated English questions are published (Arribas et al., 2010) (Appendix B 3.3) but without the overall format of the questionnaire a full evaluation of the measure cannot be made. As the stem questions are not presented, it is unclear how patients would be expected to respond. It is also unclear how scores would be calculated or how taxing this would be for the clinician, which limits the ability to critically assess this aspect of feasibility.

There are some obvious literal translation errors, limiting use in clinical practice in the UK. One example is: 'What affects more is the impotence that I feel when I have tachycardia' (Braganca et al., 2010); it is difficult to understand what this question is asking (Appendix B 3.5).

It should be acknowledged that this is the only questionnaire that covers the domain of sexual activity. Yet other important aspects of HRQoL are not covered in this questionnaire. Domains regarding treatments or the impact of anticoagulants or healthcare are not covered. Perhaps most notably, the domain symptom is not comprehensive; for example, symptoms such as shortness of breath, dizziness/light-headedness and chest pressure are not included. This would limit this questionnaire's ability to measure HRQoL in patients following treatment.

3.6.3 AFQLQ

The AFQLQ questionnaire was developed in Japanese and is not available in any other language. To examine the content of the questionnaire for the purposes of this thesis, translation of the AFQLQ questionnaire into a crude English version was arranged with permission of the author. As resources were limited, arrangements to translate it back to Japanese to check the consistency and to further culturally adapt the measure for a UK population could not be made. The Japanese version and

translated English version can be seen in Appendix B 3.4. The AFQLQ questionnaire asks items relating to the symptoms and severity of AF, the treatment of AF and the inconvenience of increased hospitalisation due to treatment. Other questionnaires do not include items about hospitalisation due to treatment. The AFQLQ does not include any questions regarding the impact of AF on sexual activity, which was identified as important in the qualitative literature. However, lack of consideration of this may relate to cultural norms: the corresponding author highlighted in correspondence that the questionnaire was suited to a Japanese population. This can be seen clearly in Questions 3-11, which ask about 'dietary restrictions (for example, do not eat natto)'. Information regarding how the AFQLQ questionnaires scores are calculated is not available in English, and so the ease and acceptability of this aspect of the measure cannot be reviewed.

3.6.4 QLAF version 1

As has been noted, the first version of the QLAF was published in 2010. A newer version has subsequently been published (Moreira et al., 2016). However, no new development methods are presented in this more recent publication. For the purposes of this thesis, the first version and then the second version will be considered.

Authors of the QLAF were contacted on two occasions to request more information regarding this questionnaire but did not respond. A copy of the questionnaire is published in Bragnaca et al. (2010). This questionnaire has eight stem questions. The first five cover the five main symptoms of AF. The translation from Portuguese to English has limited face validity, with problems apparent in the phrasing. For example, item 5 asks, 'Does the palpitation bother your daily activity?' (Bragnaca et al., 2010) The response options are 'very much, medium, little or not at all' (Bragnaca et al., 2010). It could be suggested that the options "medium" and "little" should be rephrased.

It is also important to consider the response options for symptom length of time (items 3 and 4). It is also important to consider the response options for symptom length of time. We suggest the symbols "<" and ">" in items 3 and 4 be replaced with the words "less than" or "more than" as appropriate. This would increase the readability of the questionnaire.

The first five stem questions cover the main symptoms of AF. While this questionnaire appears to be the most thorough of all the questionnaires in regard to the symptoms of AF and would give clinicians a clear understanding of the impact of the symptoms, the impact on HRQoL may not be fully captured. As this is a brief questionnaire, its use in clinical practice would be more feasible.

The final three stem questions relate to treatments of AF**,** namely drugs, direct current cardioversion and ablation. Although this measure generally asks about drugs, it fails to ask about drugs which are commonly used in patients with AF such as anticoagulants. It also fails to ask questions regarding other treatments, such as the insertion of a pacemaker. This treatment is a final option for the symptomatic control of AF in the UK. It is unknown if the clinical guidance in Brazil is similar. This questionnaire also fails to capture domains such as the impact on relationships and social interactions, sexual activity, impact of healthcare appointments and general health. It is unclear how participants are asked to rate the questions or the final score calculations as there are no published instructions available.

3.6.5 QLAF, now referred to as AFQLQ Version 2

Similar to the AFEQT, version two of the AFQLQ begins with demographic information. However, as shown Appendix B 3.5, most of this is only available in Portuguese. Version 2 of the questionnaire has an updated format which is a noticeable improvement. However, it has increased substantially in length. This would have the benefit of providing a more thorough assessment of HRQoL. However, use of this questionnaire may be better suited in a research study where participants and clinicians have more allocated time. The length of the questionnaire would limit its feasibility in clinical practice such as outpatients or on a ward setting.

Some weaknesses in the translation from Portuguese to English are apparent in both versions of the questionnaires. For example, a question in Domain 2: Dyspnoea asks, “Do you have shortness or breathlessness?” to which the response options are ‘Shortness of breath occurs on effort, minimum, medium or large’. This would lead to difficulties in understanding the questions and is likely to produce poor data or low response rates (Bowling, 2005).

Some of the items are difficult to understand and would likely need further explanation to the patient and perhaps even the clinician. For example, in Domain 4, Question 13 asks, “How is your dizziness?” to which the response options are ‘transient sensation of unbalance, rotational movement: you or the environment, fainting sensation or fainting’. These response terms are not likely to be used in some clinical settings and therefore even less likely to be used and understood by the general public.

Another limitation of this item is the response ‘fainting’. It is acknowledged that the sensation of fainting is most appropriately asked in this domain compared to other domains (e.g. shortness of breath). However, fainting is a separate symptom and should be considered as such. The faint should be investigated independently and thoroughly as this symptom could indicate other serious cardiac

arrhythmias. Moreira et al. (2016) acknowledge that the domain concerning therapy received substantial critique (in Version 1), resulting in the removal of this domain from Version 2. The second version added domains concerning fatigue, wellbeing and illness perception (Moreira et al., 2016).

This questionnaire provides information about the value of each of the responses (i.e. A=1, B=2 etc.). No information is available to describe the calculations needed to work out the final score. It is assumed that the calculation would not require a computer system. If correct, this would reduce cost. However, this method could increase the chances of calculation errors.

3.7 Appraisal Criteria

There is substantial literature describing the attributes of high-quality HRQoL measures. These include guidelines for developing such questionnaires developed by the U.S. Food and Drug Administration (FDA), COSMIN (COnsensus-based Standards for the selection of health Measurement INstruments) and the European Organization for Research and Treatment of Cancer (EORTC), and the NIH PROMIS network guidance. A review of guidance and appraisal documents for PROM carried out by ISOQOL resulted in the development of minimum standards by ISOQOL (Reeve et al., 2013).

After careful consideration of the available appraisal criteria, it was concluded that criteria adapted from Smith et al. (2005), Fitzpatrick et al. (1998, 2006) and ISOQOL were the most appropriate and authoritative for this review. ISOQOL have on the basis of literature reviews and member surveys developed guidance on aspects that are essential to HRQoL measures (Reeve et al., 2013). The appraisal criteria provided by Smith and Fitzpatrick encompass all the desired attributes and provide clear guidance on psychometric evaluation (Fitzpatrick et al., 1998, 2006; Smith et al., 2005; Reeve et al., 2013), and this is used by experts in measure development to present to NHS governing bodies such as NICE (Lohr, 2002; Davis, 2009; Haywood et al., 2012; Gibbons et al., 2013). Although some other appraisal criteria (such as COSMIN, Terwee et al., 2012) capture key psychometric evaluations, some do not attempt to assess the level of patient involvement throughout development, which is a limitation of such criteria.

Aspects of these appraisal criteria will also be applied to the new measure (AF PROM) in future research, enabling clear comparison with existing measures. An outline of the attributes for consideration is provided in Table 3.3. A descriptive comparison of each of the measures is shown in Table 3.1, and the application of the applied adapted appraisal criteria from Fitzpatrick et al. (1998, 2006) and Smith et al. (2005) to the four measures considered is shown in Tables 3.4 and 3.6. This is discussed in Sections 3.6-3.14.

Table 3.3 Attributes and Criteria for Consideration			
	Attributes	**Definitions**	**Criteria**
	Conceptual and measurement model	Description and framework for constructs to be measured.	Description of how items relate to concepts measured and relationships between concepts.
Validity	**Content**	Measuring whether a scale represents the conceptual domains intended: the degree to which the instrument includes appropriate items to adequately represent the construct being measured.	Pre-testing involving quantification of experts' ratings of item relevance; development clearly based on appropriate literature review; qualitative evidence from key respondents.
	Construct	Evidence the scale is correlated to other measures in a hypothesised direction. Level of consistency between scores of the measure and hypothesis. Consideration can be in relation to the internal relationship (within the measure) and its external relationship (its relationship with other measures or noted differences between known groups).	**Internal:** Factor analysis can be used to indicate the consistency of factor structure. <0.4 = not significant. Intraclass correlation coefficient (ICC) values of <0.40 = poor; 0.40-0.75 = average; and >0.75 = strong. **External:** Convergent and discriminant validity: convergence (correlation) between the new measure and other measures of related constructs. **Criteria:** 0.0-0.19 = very weak correlation; 0.2-0.39 = weak; 0.40-0.59 = moderate; 0.60-0.79 = strong; >0.8 = very strong. **Known group:** Able to distinguish between known group scores, e.g. control group scores differ significantly (p=<0.05) from participant group.
Reliability	**Test-retest**	Test-retest reliability measures the stability of the measure. It does this by assessing the correlation between scores of separate completions of the same measure by the same participants on two different occasions. For example, the measure is completed by one participant on day zero and again 14 days later. The correlation between the scores is then assessed to indicate the test-retest reliability.	Intraclass coefficient (ICC) (95% CI). Good = ≥ 0.70 Moderate = 0.5-0.7 Poor = < 0.5
	Internal consistency reliability	The internal consistency assesses the ability of each item to measure the construct under consideration. For example, if an item is measuring palpitations, it would be expected that this would correlate highly to the construct or domain of symptoms of atrial fibrillation within a symptom measure.	Measured with Cronbach α. Score ranges from 0-1. Scores closer to 1 indicate that item is exploring a similar concept/subscale; scores closer to 0 indicate the item is not exploring a similar concept/subscale. <0.6 = Poor ≥0.70 = Acceptable

Table 3.3 Attributes and Criteria for Consideration (1)			
Responsiveness	**Responsiveness**	The instrument's ability to detect change. Typically associated with a criterion-based determination of the clinical significance of identified changes.	Measured by: standard deviation and standard error of measurement; minimum detectable change; minimum important change. Assessed over period of time. Comparison scores before and after intervention. Significant changes between scores between time points (and/or between intervention). **Cohen's d effect size:** Small = 0.2; Medium = 0.5; Large = 0.8; Very large = 1.3 **Standardised response means (SRM):** assesses the stability of the response. This is calculated by dividing the mean change between two time points by the standard deviation (SD).
Interpretability	**Interpretability of scores**	The quantitative scores of a measure should indicate a qualitative meaning. For example, a high score could indicate that the individual has a higher level of symptoms than those who have a low score, which would indicate fewer symptoms and vice versa.	The PROM should document what high and low scores represent for the concept.
Practical properties	**Acceptability**	**Response rates:** This will reflect the compliance rates. Rates of completion will also impact the quality of data reported. **Missing data:** Participants may fail to respond to all items of the measure, which can make calculating the total score difficult. The reporting on reasons why or how this data is dealt with may be reported by the researchers. **Floor and ceiling effects**: Ability to measure, to determine central tendency and to identify changes.	**Response rates:** 80% or more of the data should be completed by participants. **Missing data:** The reasons for missing data and how this is dealt with should be reported. **Floor and ceiling effects**: >15% of respondents gain the best or worst score, this may indicate the measure is unable to distinguish between respondents at either end of the scale. Summary score should be < 15% for total score (either domain or complete measure).
	Feasibility	Impact on resources: time, financial, personnel or energy	For consideration: Translations available? Licence cost? Patient burden? Required reading level? Average completion time? Method of administration? Training?
	Translation of PROM measure	PROM translated to one or more language	Documentation of methods of translation
Criteria adapted from Fitzpatrick et al. (1998; 2006), Smith et al. (2005) and the minimum standards for PROM developed by ISQOL (Reeve et al., 2013).			

3.8 Psychometric Properties

An overview of the psychometric testing of these tools is presented in Table 3.4 Following this, aspects of reliability and validity will be considered. Patient input throughout development will be specifically considered in Section 3.12.

Table 3.4 Appraisal Criteria Applied to AF-specific HRQoL Measures								
		Validity		**Reliability**		**Responsiveness**	**Practical Properties**	
PROM	Conceptual and measurement model	Content	Construct	Test-retest reliability	Internal consistency	Responsiveness	Acceptability	Feasibility Translation Patient Burden
AFEQT: Spertus et al. (2011) Dorian et al. (2013)	++	+++	+++	++	+++	+++	++	++
AFQOL: Badia et al. (2007) Arribas et al. (2010)	++	+++	++	++	++	+	++	+
AFQLQ: Yamashita et al. (2003, 2005)	++	0	0	*0*	0	0	0	0
QLAF: Braganca et al. (2010)	++	+	++	++	++	+	0	+
0 = No Evidence/Not reported/Not available in English; + limited evidence; ++ some evidence but some aspects not reported; +++ Acceptable								

Table 3.5 Appraisal Criteria Applied: Evidence to Support								
		Validity		**Reliability**		**Responsiveness**	**Practical Properties**	
PROM	**Conceptual and measurement model**	**Content**	**Construct**	**Test-retest reliability**	**Internal consistency**	**Responsiveness**	**Acceptability**	**Feasibility Translation Patient Burden**
AFEQT: Spertus et al. (2011); Dorian et al. (2013)	Item linked to the following domains: Symptoms; Physical function; Emotional function; Treatment concern	√ Literature review √ Expert input √ Patient rate items	**Convergent and Discriminant validity** (baseline correlation coefficient r) SF-36; PCS: 0.57; MCS: 0.47; physical functioning: 0.6; role physical: 0.62; bodily pain: 0.49; general health: 0.36; vitality: 0.55; social functioning: 0.57*;* role emotional: 0.48 mental health: 0.48; EuroQol (EQ-5D): 0.54; Atrial Fibrillation Severity Scale (AFSS) Total symptoms score: -0.79; Total AF burden: -0.42; Symptom Checklist (SCL): Severity score: -0.67; Frequency score: -0.70; Generalized Anxiety Disorder: -0.54: *NB Only comparisons against global score reported for this thesis* **Known group:** comparison of mean scores (p<0.001)	Overall 0.8 (+) Daily Activities 0.8 (+) Treatment Concerns 0.7 (+) Treatment Satisfaction 0.7 (+) Symptoms 0 5 (-)	Overall 0.8 (+) Daily Activities 0.9 (+) Treatment Concerns 0.94 (+) Treatment Satisfaction 0.9 (+) Symptoms 0.88 (+)	**Group 1: No Treatment** Overall 0.2 (**s**); Daily Activities 0.2 (**s**); Treatment Concerns 0.3 (**s**); Treatment Satisfaction NR (**?**); Symptoms 0.1 (**s**); **Group 2: Medication change** Overall 0.5 (**m**); Daily Activities 0.4 (**s-m**); Treatment Concerns 0.3 (**s**) Treatment Satisfaction 0.3 (**s**); Symptoms 0.5 (**m**) **Group 3: Ablation** Overall 1.2 (**l**); Daily Activities 0.9 (**l**); Treatment Concerns 1.1(**l**); Treatment Satisfaction 1.1(**l**); Symptoms 1 (**l**)	**Floor/ceiling effects:** Not reported. **Interpretability of scores:** Higher score indicates Higher QoL Baseline: 42 items ranging from 94% to 100% 3 months: 42 items ranging 92% to 100% Questions about sexual relationships: 15% missing response rate in the 42-item questionnaire. This is not included in the 20-item questionnaire.	42 item AFEQT = 9.3 minutes to complete. 20 item AFEQT = not reported Copyrighted; License fee: Clinical practice/Non-profit research: $500.00 For profit research: $2,500.00

Table 3.5 Appraisal Criteria Applied: Evidence to Support continued (1)

AFQOL: Badia et al. (2007); Arribas et al. (2010)	Item linked to the following domains: Physical Psychological	√ Literature review √ Expert input √ Patient interviewed with questionnaire in pilot (n=17)	**Discriminant validity** (baseline correlation coefficient) SF-36 physical functioning: 0.69; role physical: 0.60; bodily pain: 0.32; general health: 0.64; vitality: 0.65; social functioning: 0.59; role emotional: 0.52; mental health: 0.57 *NB Only comparisons against global score reported for this thesis.* **Known group:** comparison of mean scores ($p<0.01$) **Effect Size** **'Feel worse' Group:** - 0.12 (n=11) (**s**); Psychological domain: 0.24 (n=13) (**s**); Physical domain: - 0 39 (n=12) (**s-m**); Sexual activity domain: 0.11 (n=13) (**s**); **'Feel the same' Group:** Total: 0 25 (n=138) (**s**); Psychological domain: 0.29 (n=153) (**s**); Physical domain: 0.21 (n=145) (**s**); Sexual activity domain: 0.1 (n=145) (**s**); **'Feel better' Group:** Total: 1.06 (n=47) (**l**) Psychological domain: 1.02 (n=54) (**l**); Physical domain: 1 (n=52) (**l**); Sexual activity domain: 0.26 (n=51) (**s**)	Arribas et al. (2010): Overall 0.86 (+) Subdomains not reported	α 0.95 (+) (Badia et al., 2007) α 0.92 (+) Arribas et al., 2010 Overall: 0.92 (+) Subdomains not reported	Minimal clinical important difference (to indicate improvement in HRQoL) noted as 12.10. The change in score was reported as 17.4 (19.5), indicating MCID was reached. Effect size noted as 1.06 (l) in those who felt better after intervention at 12-month follow up. Effect size noted as 0.24 (s) in those who reported no change after intervention at 12-month follow up. NB: Arribas et al. (2010): groups compared against self-perceived health status	**Ceiling effect:** Occurred in two participants (0.5%) **Floor effect:** Occurred in two participants (0.5%) **(+)** 89.4% completion rate Questions about sexual relationships: **no response rate** between 5% and 6%.	Median time to complete: 10 mins. **Copyright:** Unknown. Not published.

Table 3.5 Appraisal Criteria Applied: Evidence to Support continued (2)

AFQLQ Yamashita et al. (2003, 2005)	NK	NK	NK	NK	NK	NK	NK	NK
QLAF / AFQLQ v.1; Braganca et al. (2010)	No description of conceptual and measurement model provided. Item linked to the following domains: Clinical Manifestation Usual Treatments	√ Expert Input √ Pilot patient tested	**Convergent validity (+)** **Mean (SD) SF-36 scores and the total QLAF** Baseline: physical functioning: 59±39*;* role physical: 66±28*;* bodily pain: 61±28*;* general health: 62±26; vitality: 59±24*;* social functioning: 73±30*;* role emotional: 72±38*;* mental health: 66±26; Total QLAF: 24±18 12 months: physical functioning: 65±43; role physical: 73±29*; bodily pain: 76±30*; general health: 78±19*; vitality: 64±21; social functioning: 85±27*; role emotional: 79±38; mental health: 70±26; Total **QLAF:** 13±11*; *p<0.05 *NB* B*aseline and 12 month scores reported.* **Baseline mean scores** Palpitation: 7.5±0.9; Breathlessness: 4.7±0.8; Chest pain: 1.5±0.5; Dizziness: 5.2±0.8; Drugs: 2.7±0.2; DCC: 1.3±0 2; Ablation: 0.4±0.1; Total: 23.6±2.3 **12-month mean scores:** Palpitations: 3.7±0 9*; Breathlessness: 2.3±0.7*; Chest pain: 0.5±0 3; Dizziness: 3.2±0.7**; Drugs: 1.9±0 1*; DCC: 1.3±0.2; Ablation: 0.4±0 1; Total: 13.3±1.8* *NB* *p<0.05 and **p=<0.06; DCC = direct-current cardioversion.	Bartko's ICC Palpitation: 0.53 (+) Breathlessness: 0.94 (+) Chest pain: 0.81 (+) Dizziness: 0.78 (+) Drugs: 0.41 (+) DCC: 0.98 (+) Ablation: NA (?) Total: 0.91 (+)	Overall Cronbach's alpha= 0 98 (+)	Significant changes between scores at baseline and 12 months indicated responsiveness. Improvements (reduction) in QLAF total scores (from 24±18 at baseline to 13± 11 at 12 months) noted. Improved (increase in) general health scores (from 62±26 at baseline to 78± 19 at 12 months); using the SF-36 supports the responsiveness of this measure over time. Mean (SD) baseline and 12-month scores reported: see Braganca et al. (2010).	NR	3 minutes **Copyright:** Unknown. Not published

NK = Not Known (not published in English)

All four measures were developed and intended for use in an AF-specific population, which is outlined in the appraisal criteria in Section 3.7. Although the conceptual frameworks may have been developed based on literature reviews or some patient input, none of the measures (except the AFEQT) present how the conceptual framework was developed or related to the items. However, all measures appear to describe the items included in each domain. This is most clearly presented in the supplementary material for the AFEQT in which the factor loadings are presented for each of the items included in the four domains.

The item reduction stage reduced the AFEQT from 117 to 47 items by using exploratory factor analysis. This was further reduced to 39 items after psychometric testing. Psychometric testing included assessing the internal reliability (using Cronbach coefficient alpha) and test-retest reliability. The validity of the questionnaire was estimated using Pearson correlation coefficients. Some well-used and validated questionnaires (SF-36, EuroQol (EQ-5D), Atrial Fibrillation Severity Scale (AFSS), Symptom Checklist (SCL), Generalized Anxiety Disorder-7, AF Patient and Physician Global Change Forms) were administrated and tested at the same time (Spertus et al., 2011).

The AFQoL was developed following a literature review which, along with a focus group of clinicians, helped form the basis of the interview questions which were put to 17 participants. The interviews were transcribed, and relevant phrases were allocated into domains (Badia et al., 2007). These were then qualitatively analysed by experts who rated the phrases/domains by frequency, importance and clarity, then analysed using Cronbach's alpha. The methodology used for item reduction and selection for this scale is good; a pilot questionnaire was administered to participants (n=112). The responses were analysed using Classical Test Theory (CTT) and Item Response Theory (IRT), then the questionnaire was reduced in size after using Rasch analysis (Badia et al., 2007). After this process the 18-item AFQoL was created.

As limited published material is available in English regarding the AFQLQ, the item reduction and validation process cannot be discussed.

The QLAF questionnaire was created after the researchers met with eight specialists (Braganca et al., 2010). Validation of the QLAF questionnaire involved completion alongside the generic SF-36 questionnaire in an interview setting. Researchers examined reliability, validity and responsiveness. When analysing reliability, researchers tested inter- and intra-observer agreement using test-retest. The internal consistency was tested using Cronbach’s alpha coefficient. The content validity was assessed by comparing the literature and also involving expert opinion. Convergent validity was assessed and compared to the generic SF-36 questionnaire. When measuring the responsiveness of the QLAF, researchers compared and then analysed the difference after the follow-up clinics at 3, 6, 9 and

12 months (Braganca et al., 2010). The literature suggests an acceptable size (n=40) was used for the test-retest analysis; however, the authors suggest further validation is needed for this questionnaire in different AF subgroups and also in different treatment groups (Braganca et al., 2010).

3.9 Reliability

3.9.1 Test-Retest Reliability

As seen in Table 3.4, the test-retest reliability is documented as having some evidence but not all aspects of this domain are reported for three out of four domains. The test-retest reliability coefficients of all the questionnaires were adequate, with similar results between three measures. The authors of the AFEQT report the test-retest reliability for overall domains as being α 0.8 which meets the criteria specified in Section 3.7. The overall test-retest result of the AFQOL was reported to be good at α 0.86 and meets the criteria in Section 3.7; however, subdomains were not reported (Arribas et al., 2010). The Bartko's ICC for the QLAF questionnaire was reported as being 0.91 (Braganca et al., 2010). Appraisal in this thesis of the AFQLQ could not occur due to lack of information available in the English language, which led to the critique score of '0' in Table 3.4.

3.9.2 Internal Consistency

The internal consistency was analysed using Cronbach's alpha coefficient for all questionnaires and ranged from providing some evidence of being acceptable (≥ 0.7) using the criteria outlined in Section 3.7. The overall internal consistency of the AFEQT was α 0.8 (Spertus et al., 2011), α 0.95 and α 0.92 for the AFQOL (Badia et al., 2007; Arribas et al., 2010) and α 0.98 for QLAF (Braganca et al., 2010). The AFEQT provided details of the internal consistency of the items as well as the overall score, therefore leading to an acceptable condition when appraised in Table 3.4. The internal consistency was not provided for the items in either the AFQOL or the QLAF. This resulted in a score of two (++), which indicates some evidence was provided of internal consistency, but some aspects not reported. The AFQLQ was not available in English so no evidence is reported for this psychometric testing, which is indicated in Table 3.4.

3.10 Validity

3.10.1 Content Validity

Most questionnaires (three out of four) report the content validity was assessed. As previously noted, the AFQLQ development and validation process is not available in English. The content validity of

the AFEQT was assessed by interviewing participants (n=12) who had AF (Spertus et al., 2011). The content validity of the AFQOL was assessed by patients (n=17) who were interviewed following completion of the pilot stage (Arribas et al., 2010). These measures are therefore considered acceptable in this criterion. Braganca et al. (2010) state that the content validity of the QLAF was assessed by expert opinion and supported by literature in this area. They acknowledge a limitation of the study is that patient input was lacking (Braganca et al., 2010) and would have been beneficial in assessing the content validity. For this reason, it has been identified in Table 3.4 as providing limited information.

3.10.2 Construct Validity

In the validation stage of the AFEQT, participants (n=214) were asked to complete the questionnaire alongside five other questionnaires (EQ-5D, SF-36, AFSS, Symptom checklist and GAD-7) to compare the construct against other questionnaires. This was rated in Table 3.4 as being acceptable.

In the validation stage of the AFQOL, questionnaire participants (n=417) were asked to complete the AFQOL alongside the SF-36 questionnaire. The results of the correlation coefficients are presented in Table 3.5. Arribas et al. (2010) state that there is a significant correlation between the patient's self-perceived health status and the AFQOL score, with those who stated a lower HRQoL using the SF-36 also having a low score on the SF-36. Subdomains showed moderate to strong correlation to most subdomains in the SF-36, apart from the bodily pain domain, which had a low correlation. However, the authors did not indicate the hypothesised correlation. For this reason, Table 3.4 records that some evidence was provided but some aspects were not reported (++).

The same result (i.e. some evidence provided, some aspects not reported) is recorded in Table 3.4 for QLAF. The authors of QLAF report that the SF-36 was used for comparative purposes, however the construct validity results are presented as the mean domain scores and standard deviation rather than correlation results. The authors found a correlation between higher mean scores using the SF-36 and lower QLAF scores, however the strength of this inverse relationship is not provided. Furthermore, a hypothesis of the correlation between the QLAF and the SF-36 was not outlined prior to results.

As previously stated, evidence for the AFQLQ psychometric properties was not available in English, as is indicated in Table 3.4.

Comparisons of the results of the construct validity can only be performed for the AFQoL and AFEQT as they both used the SF-36. The AFEQT and AFQOL had similar coefficient results for

domains in the SF-36. However, the AFEQT questionnaire had a slightly lower coefficient in the domains of general health (AFEQT 0.36 v. 0.64 AFQOL) and vitality (AFEQT 0.55 v. 0.65 AFQOL).

3.10.3 Responsiveness

One of the four measures is reported in Table 3.4 as meeting the responsiveness criteria. From the data presented, it appears the AFEQT was able to detect change either over time or between groups of participants. Spertus et al. (2011) describe assessment of the responsiveness of the AFEQT in each of three treatment groups (Group 1: no change to treatment; Group 2: pharmacological change; Group 3: catheter ablation) using Cohen effect size comparing five questionnaires (EQ5D, SF-36, AFSS, Symptom checklist and GAD-7). They report that the degree of responsiveness in the AFEQT was similar to other disease-specific measures (AFSS and Symptom checklist); they also describe that the AFEQT had lesser effect size compared to the generic questionnaires (EQ5D and SF-36). The responsiveness of the AFEQT was tested by effect size which was compared over a 3-month period (using *t* -tests). Small effect sizes were seen in the no treatment and medication change groups. As expected by the authors, large effect sizes were seen in the ablation group. However, effect sizes may be influenced by the patient's anxiety regarding this invasive procedure. It would also be interesting to compare effect sizes after a longer period of time.

Arribas et al. (2010) describe responsiveness of the AFQoL against their self-perceived status; a large effect size (1.06) was noted in those who felt better following an intervention. The MCID was assessed as the change reported in a domain of the measure (12.10) for this study. The mean change in the domain of those who felt better was reported as being 17.4 (19.5), which reaches the minimal clinical important difference (MCID) for this study, supporting responsiveness. Those who experienced no improvement over the 12-month period had a small effect size (0.24), as Table 3.3 shows.

The validation process of the AFQLQ has not been published in English, limiting the ability to review its psychometric properties.

The researchers assessed the responsiveness of the QLAF questionnaire was assessed by researchers by comparing the differences in domain score over the time period (Braganca et al., 2010). The QLAF was completed alongside the SF-36 in a smaller pilot validation stage involving 63 participants and then in a larger group involving 231 participants. The results are presented in Table 3.5. The mean and standard deviation of the SF-36 are presented by Braganca et al. (2010). Significant changes ($p<0.05$) between baseline and 12 months are noted in role physical (66±28 at baseline v 73± 29 at 12 months); bodily pain (61±28 at baseline v 76± 30 at 12 months); general health (62±26 at baseline v

78± 19 at 12 months); social functioning (73±30 at baseline v 85± 27 at 12 months); and total QLAF (24±18 at baseline v 13± 11 at 12 months). Improvements (reduction) in QLAF total scores alongside the improved (increase in) general health scores using the SF-36 support the responsiveness of this measure over time.

3.11 Practical Properties

3.11.1 Feasibility

As seen in Table 3.4, response rates of the AFEQT were reported. The sexual relationship domain is not included in the final 20-item version; this may have been because of the poor rate of response (15%) to the 42-item version (Spertus et al., 2011). Although the shorter questionnaire results in a briefer completion time, enabling easier use in a clinical setting (9.3 min for the 42-item version), the required formulae to calculate scores may be considered complicated, increasing the burden on clinicians and reducing overall feasibility. It is also important to note that the AFEQT is copyrighted and that its use in clinical practice or not-for-profit research requires a licence which costs 500 U.S. dollars. The price of a licence rises to $2500 for for-profit research studies. The completion rate for the AFQOL questionnaire was 89% of the patients, which is above the 80% in this appraisal criteria. The items relating to sexual activity produced the highest rate (between 5% and 6%) of no responses (Arribas et al., 2010). At 10 minutes, the time for completion is similar to that of the AFEQT. Short completion times reduce patient and clinician burden, increasing the feasibility of use in clinical practice. There do not appear to be any license fees or copyright restrictions in English. As already stated, information relating to response rates, completion times, copyright and license fees about the AFQLQ questionnaire is not available. The QLAF has the shortest completion time (within three minutes) of all the questionnaires (Braganca et al., 2010). The time required to complete version 2 of the QLAF (AFQLQ v2.) is not discussed (Moreira et al., 2016). The QLAF does not appear to have copyright restrictions or associated licence fees for its use.

3.12 Use of Measures

Although the main purpose of this review is to examine the development and assess the validity and reliability of these AF-specific measures, it is also worthwhile to consider their subsequent use in research to consider their acceptability throughout research or clinical practice. Following a PubMed search with the title of each measure updated in October 2017 and September 2018, research studies which have used the considered questionnaires were identified and are summarised in Appendix B 3.6.

Eighteen articles using the AFEQT measure were identified. An overview of the studies is presented in Appendix B 3.6. This questionnaire has been used mostly in the USA or Canada (n=9), China (n=3), Japan (n=1), Denmark (n=1) and Spain (n=1). One study was multicentre but did not report individual sites. This measure has been reported as being used in two research studies in the UK. One was a small study involving participants (n=80) with either paroxysmal or persistent AF, which compared differing techniques of catheter ablation. The other UK study describes the use of the AFEQT as part of the modification of a symptom questionnaire (Wynn et al., 2014). Further validation is reported as essential (Spertus et al., 2011; Kotecha et al., 2016).

Ten studies identified focused on comparing or examining interventions such as catheter ablation, drugs, cognitive behavioural therapy and the implementations of mobile health technologies. Only half of these (n=5) used both a generic measure (such as the SF-36 or EQ-5D) and the AFEQT measure. Only three used the AFEQT measure in their study. Two used the AFEQT and another measure (such as an AF symptom measure or a questionnaire measuring medication adherence).

The results of these studies varied and showed significant increased HRQoL scores when measuring with both disease-specific (AFEQT) and generic HRQoL (such as EQ-5D and SF-36). Some research studies showed significant improvement in only some domains in the AF-specific measure. Magnani et al. (2017), for example, showed significant improvement in only two domains (global scores and daily activities), although the results of this study may be limited by it not being randomised or by the small sample size. Another study (Raine et al., 2015) indicated that disease-specific measures have higher sensitivity compared to generic HRQoL measures when measuring the impact of ablation technologies. This study showed greater correlation and greater significant improvements when measuring changes in HRQoL with disease-specific measures compared to a generic HRQoL measure. However, this study was limited by the short follow-up period.

One study examining the impact of Cognitive Behavioural Therapy (CBT) in one small population of patients with AF identified that the scores of the mental component summary of the SF-36 significantly improved following treatment; however, the effect sizes of this domain were not significant (Särnholm et al., 2017). When assessing HRQoL using the AFEQT, the global score showed significant improvement at the 6-month follow up. Item 13 of the AFEQT, considering worry, showed significant improvements from baseline to post treatment and also had significantly large effect sizes at follow up (6 months) after CBT treatment. However, not all subdomains are presented in this article, meaning the impact on other domains cannot be compared.

Eight articles presented the results of observational studies which included real-life registries (focusing on assessing drug adherence) or questionnaire modification or observed the implementation

of differing care pathways within normal care. Half (n=4) of these observational studies included both a generic HRQoL measure (such as the EQ-5D) and the AFEQT. Only three studies used the AFEQT. One study included the AFEQT and other measures which did not measure HRQoL, such as the GAD-7.

The ORBIT-AF is the largest observational study identified in this review, with 10,135 participants completing the AFEQT. However, the participants enrolled included those with AF and heart failure (HF) and compared the outcomes of both groups. The authors report that the median overall score was significantly higher in those with AF than those with AF and HF; this was also similar to the subdomain considering activities of daily life. However, other domains showed no significant difference between these groups in other domains (symptoms, treatment and treatment concerns). Another study which examined the impact of another comorbidity was the multicentre observational study by Jackson et al. (2016), which identified that those with sinus node dysfunction had lower HRQoL using the AFEQT than those without this comorbidity at the 12-month follow up.

The observational study by Freeman et al. (2015) included the AFEQT and also used the EHRA symptom class, identifying an inverse correlation between the AFEQT score and the EHRA symptom class, indicating that those with a higher EHRA class (higher symptoms) would have a lower HRQoL score. This study was completed in the USA, the country in which the questionnaire was developed and validated. Although this measure was not used in its validation, the results of this study may not be generalisable.

The AFQLQ was identified as being used in five published studies, all of which were conducted in Japan and most of which (n=4) were observational studies. Three used generic HRQoL measures (such as the SF-36) alongside the AFQLQ and two used only the AFQLQ. This questionnaire is the only HRQoL measure which describes the impact of AF in the asymptomatic population. This study showed reduced HRQoL scores in using this measure especially in domains, surrounding activities and mental anxiety (Yamamoto et al., 2014). Another study that examined HRQoL in those who were asymptomatic after ablation identified that scores in all domains of the AFQLQ improved significantly after treatment. However, when HRQoL was assessed using the SF-36, scores were significant in only five out of the eight domains of this measure. Although this study supports the concept that AF-specific measures capture more changes in the AF population, this study is limited by its small study size and short follow-up period.

Moreira et al. (2016) describe the adaptation of the QLAF questionnaire. These authors refers to this questionnaire as AFQLQ v2 yet makes references to the authors who developed the QLAF. It is clear the questionnaire developed in Brazil (QLAF) is the same questionnaire as the AFQLQ v2. No other

literature was identified which used this measure. This may be because of publications in Portuguese which are not accessible in English. One systematic review (Kotecha et al., 2016) identified all four measures which are reported in this literature review. However, the AFQOL questionnaire was not identified by any other literature in this brief search.

3.13 Discussion

A literature review was conducted to determine (i) what AF-specific HRQoL measures already exist, (ii) the extent of patient involvement in the development process for these measures and (iii) the evidence of validity and reliability for these measures. Four validated tools were identified in a literature review. All measures have been shown to be valid for use in their intended population. However, as the development of these questionnaires occurred in America and Canada (AFEQT), Spain (AFQoL), Japan (AFQLQ) and Brazil (QLAF), the generalisability and feasibility of these questionnaires in the UK is questionable (Aliot et al., 2014). It is suggested further research is needed to increase the generalisability across age, ethnic and other socioeconomic groups for these questionnaires. The inconsistency of the domains between the questionnaires and the inability of any of the questionnaires to fully capture all aspects of HRQoL affected by AF identified in the qualitative literature highlight the need for a new disease-specific measure suitable for a diverse multicultural city such as London. When considering the development of these measures, patient input has been found to be limited in all measures, which could account for their inability to assess all areas of HRQoL identified by the qualitative literature.

In a recent review by Wiering et al. (2017), the degree of patient involvement in the development of PROM was investigated. Wiering et al. (2017) highlighted how the reporting of patient involvement is often inconsistent in the literature, which results in ambiguity and further leads to difficulty comparing the degree of patient input in the development of PROM. However, to allow comparison between various measures, Wiering et al. (2017) proposed reporting the involvement of patients into three main areas: (1) whether patients had been involved in the process of deciding which outcome or aspects of outcomes should be measured, (2) whether patients were involved in developing the items of the measure and (3) whether patients were involved testing in the measure.

When using this approach (as outlined by Wiering et al., 2017), it is assumed that AFQoL was the only measure which included patients' input in all three stages. However, it is unclear if the purpose of patient involvement at initial stages was to determine the outcome to be measured (criterion 1), was used solely to form the items of the measure (criterion 2) or was used to achieve both objectives. If the purpose of patient involvement was only to achieve one criterion, then this would reduce patient

involvement to only two stages outlined by Wiering et al. (2017). A major strength of the AFEQT is the description of patient involvement throughout; however, based upon the data presented in the article, patient involvement was restricted to two aspects of this criteria (item development and testing the comprehensibility of the items). However, it does not appear that patients were involved in determining the outcomes which should be measured at initial stages as outlined by Weiring et al. (2017). Similarly, the QLAF appears to involve patients in only two stages outlined by Weiring et al. (2017). As already reported, the involvement of patients in the development of the AFQLQ is not available in English. The variability of patient input is consistent with that presented in the literature. As outlined by Wiering et al. (2017) the development of PROM mostly only involves patients in one (34.7%) or two phases (32.6%), and input in all three stages is limited (being reported in only 6.7% of studies).

Although patient involvement is promoted and considered essential (by bodies such as FDA guidance and COSMIN criteria) and guidance regarding the reporting of patient involvement exists, such guidance is not implemented, which leads to inconsistency in the reporting of patient involvement (Wiering et al., 2017). As already mentioned, there is inconsistency in the reporting of patient involvement in these four measures, which limits comparison. Furthermore, there is a lack of consensus among the guidelines regarding the amount of patient input which is required. This is highlighted by assessment criteria which require patient involvement but do not outline the degree of required participation apart from referencing the need to assess whether the PROM is suitable for the patient population and ensuring it has been tested in such a population. Weiring et al. (2017) acknowledge that although specifying the degree of input may lead to logistics and financial consequences, the lack of consensus may affect the validity of PROM.

Although the inclusion of patients may benefit individual participants, empowering patients, the question may be raised “Will patient involvement or participation have a marked impact on the final measure?” There is only limited evidence demonstrating the effectiveness of patient involvement in improving the quality a questionnaire (Nilsen et al., 2006). However, there appears to be a growing consensus that the involvement of patients at all stages of the development of PROM improves their validity and quality (Lohr and Zebrack, 2009; Acaster et al., 2012). For the purposes of this thesis, the impact of patient involvement in the content of PROM will be considered.

Although referring to involvement of patients in the development of research studies, guidance published by INVOLVE (2012) makes a clearer distinction between the terminology of participation and involvement in research studies. This guidance considers involvement to be a more active contribution to research study, for example developing the protocol or moderating or co-moderating interviews. Participation is considered when the participants are being enrolled into the study such as

completing the questionnaires. Therefore, if this terminology is adopted, it appears that none of the reviewed measures would be classed as involving patients in their development process but rather as having patients participate (INVOLVE, 2012).

INVOLVE (2012) emphasises patient participation, consultation and involvement from an early stage. This is echoed by Weiring et al. (2017), who note that early involvement such as considering the outcome to measure is uncommon (reported in only 10.9% of studies) and such involvement or participation is mostly left to later stages of development such as item generation (58.5%) and assessing the questionnaire (50.8%). However, ensuring patient involvement throughout all stages of development provides a more thorough understanding of the key aspects of HRQoL important to patients. This also ensures aspects of HRQoL seen as priorities to patients will be embedded in the questionnaire, thus making it more relevant for the intended population and consequently enhancing the quality of the questionnaire (McLaughlin et al., 2009). This is similar to the results of a systematic review by Nilsen et al. (2006), which indicated that patient involvement in developing healthcare policy and research, as well as clinical practice guidelines and patient information material, improved the relevance and the readability of resulting materials. Although it could be argued that patient involvement may not necessarily result in additional domains or items in the final questionnaire, the literature indicates that involvement of patients at various stages does increase the likelihood of the most relevant questions being included (Lloyd et al., 1996; Hanley et al., 2001; Minkler et al., 2002; Griffiths et al., 2004; Hewlett et al., 2006; Rowe, 2006; Shah et al., 2007; Cashman et al., 2008). Weiring et al. (2017) suggested using high-quality questionnaires with significant patient input as models such as the Breast Q, which included patients from the early stages of development throughout (Pusic et al., 2009).

Much literature acknowledges discrepancies between patients and clinician's perspectives on HRQoL (Hewlett et al., 2003; Staniszewska et al., 2012). Healthcare professionals are often more interested in specific aspects of the disease, for example, symptoms of the condition. Although clinicians can attempt to see from the patient's perspective, this is limited by lack of first-hand knowledge of the condition. This limitation is highlighted by the results of OMERACT, which involved patients with rheumatoid arthritis over a period of ten years. The evolving collaboration of healthcare professionals and patients produced great benefits, including identifying five additional domains (fatigue, sleep quality, flares and work productivity) which were not included in existing PROM (de Wit et al., 2013). Patient involvement in the later stages of development should improve the quality of the final questionnaire (Nilsen et al., 2006). This is achieved by assessment of the face validity, interpretability and the feasibility of the questionnaire, thereby ensuring that it is readable and understandable (van Oort et al., 2011).

Qualitative research surrounding AF and HRQoL being limited, it would be beneficial to carry out initial research with patients with AF to lead to the foundation of a new disease-specific measure.

3.14 Conclusion

HRQoL and the impact of AF on HRQoL were considered in the previous chapter. This chapter has identified and examined four available tools to measure HRQoL in patients with AF. These specific tools were critically examined using clear criteria derived from authoritative sources to establish their psychometric characteristics together with the degree to which their development reflected emerging consensus about the importance of patient involvement in the construction of PROM (Wiering et al., 2017). The four measures were mostly developed from literature reviews and input from healthcare professionals. The extent of patient input was found to be a key limitation in the development in all of the questionnaires. It appears from review of these four AF-specific measures, that patient involvement in their construction and validation was limited, both in terms of active participation in particular development stages (such as determining key health outcomes, generating items and assessing comprehensibility and content validity) and in the extent of contribution. This input was noted to be particularly lacking in the initial stage of determining which concepts should be measured in all considered questionnaires. However, it is noted patients were involved in the later stages of development such as the selection of items (only in the AFEQT and AFQoL). Patient feedback was gained to assess the content validity in the AFEQT and AFQoL. Although a small number of patients were administered the QLAF questionnaire, the method of feedback was not published.

This review indicates the need for an AF-specific PROM developed with significant patient input (particularly in initial stages). Such a tool will provide clinicians with a better understanding of the impact of AF on HRQoL and aid decisions regarding treatments in clinical practice. It would further ensure that research in AF regarding HRQoL treatment is measured accurately, providing an indication of the effectiveness of these treatments for commissioners and service providers. An AF-specific PROM recognised by the NHS could be used in a similar way to other disease-specific PROM nationwide to compare outcomes of treatments.

Chapter Four: Study Methods

Chapter One provided an introduction to Atrial Fibrillation (AF) and its effect on 33.5 million people globally (Chugh et al., 2014), and explored the impact of symptomatic or asymptomatic AF on Health-Related Quality of Life (HRQoL) (Pontoppidan et al., 2009; Yamamoto et al., 2014). Although the management of AF focuses on the reduction of risk of stroke and symptomatic control to improve HRQoL, other aspects of HRQoL impacted by AF (such as psychological impact and the need for psychological support) have been highlighted by recent guidance (NICE, 2014). Decisions regarding symptomatic control should ideally involve patients and clinicians assessing the current impact of AF on HRQoL and weighing up potential benefits and adverse effects of treatments. Treatment options for the symptomatic control of AF include costly invasive procedures such as catheter ablation or typically lifelong medications which carry many potential side effects.

Chapter Two examined the impact of the treatments of AF on HRQoL in patients. Quantitative and qualitative research explored the domains of HRQoL affected by AF and its treatment was examined. Quantitative research predominately reported physical symptoms and psychological domains being negatively affected (Thrall et al., 2006). Although limited, qualitative research provided greater depth concerning the effects of AF and identified additional domains of HRQoL which were not measured or reported in quantitative studies. These additional domains included physical symptoms, activities of daily living, psychological aspects, social activities and relationships, which were predominately negatively impacted by AF (Ekblad et al., 2013; McCabe et al., 2015). Change in HRQoL related to AF symptomatic control was examined, and it was noted that all treatment options were associated with improved HRQoL (Thrall et al., 2006). Instruments (generic and disease-specific) which attempted to measure HRQoL were examined. This section concluded that although generic measures enabled comparison with other population groups including the general population, they are often limited by the inability to measure aspects specific to the disease (for instance, symptoms of AF such as palpitations). This limitation also restricts the ability of such measures to detect whether or to what degree HRQoL improvement is due to AF treatment (Reynolds et al., 2008; Pontoppidan, 2012; Aliot et al., 2014). Disease-specific measures allow a deeper understanding of the impact of AF (Aliot et al., 2014). However, current measures do not capture all the domains identified by the qualitative research conducted in this patient group. This limitation in coverage may be due to the development of AF-specific measures being based largely on clinicians' perspectives and lacking sufficient patient input.

Chapter Three examined four available tools used to measure HRQoL in patients with AF. These tools were evaluated using criteria which focused on their psychometric characteristics and the degree of patient involvement throughout development (Wiering et al., 2017). Although it is noted patients

were involved in the later stages of instrument development such as the selection of items (in the AFEQT and AFQoL), this input was lacking, particularly in the initial stage of determining important concepts. The four measures were mostly developed from literature reviews and input from healthcare professionals, and the extent of patient input was found to be a key limitation. This review indicated the need for an AF-specific PROM developed with significant patient input, particularly in initial stages. A tool developed with appropriate patient input will provide clinicians with a better understanding of the impact of AF on HRQoL and aid decisions regarding treatments in clinical practice. The development of such a tool would ensure that research in AF accurately measures HRQoL and treatment effectiveness can be evaluated in relation to this. Greater accuracy and clarity about this central outcome will be of benefit to service commissioners and providers.

Chapter Four will lay out the proposed method for the development of a PROM for patients with AF. This will emphasise patient involvement throughout the development process to ensure that those aspects of HRQoL that are important to patients are adequately captured.

4.1 Study Aims

The overall aim of this study was to develop a Health-Related Quality of Life (HRQoL) measure for patients with AF. The process of scale development requires several interrelated steps. This thesis will initially focus on understanding which domains of HRQoL are impacted by AF and associated treatments. Once these domains are identified, items relating to them will be developed. Involvement of patients with AF and relevant persons (such as AF patient charity lead, relatives or carers of patients with AF, healthcare professionals and academic professionals) at various stages throughout will improve the face and content validity of this measure. Once an initial measure has been developed, the initial psychometrics of this measure will be assessed.

4.1.1 Design Overview

Development of the scale involved the following steps (shown in Figure 4.1):

Study One: Item generation: 8 focus groups involving patients with asymptomatic (2 groups), paroxysmal (2 groups) and persistent AF (2 groups), healthcare professionals (1 group) and relatives (1 group) who care for patients with AF. This stage is important in identifying important domains of HRQoL affected by AF. Affected domains were generated based on thematic analysis of the transcripts of the focus groups.

Study Two: Validity Testing: To assess face and content validity of the initial domains, an expert panel (n=6) comprised of one cardiac consultant, one cardiac arrhythmia research manager, one cardiac arrhythmia research nurse, one patient charity representative and two academic lecturers reviewed the emergent themes from the focus groups. Potential questionnaire items were developed from these themes.

Study Three: Item selection: Based on the data from Study One and Study Two, researchers identified initial items for an AF-specific HRQoL measure. A further independent review (n=8) comprised of different participants (four cardiac consultants, two cardiac arrhythmia research nurses, three patients with AF involved in Study One and two senior nurse lecturers) were approached to review an initial version of the PROM to assess items for relevance and clarity, allowing the number of items in the AF PROM to be reduced.

Study Four: Content Validation: Patients with paroxysmal (n=2), persistent (n=2) and asymptomatic (n=2) AF (total n=6) were individually interviewed following their completion of the questionnaire to assess the perceived relevance and readability of the draft questionnaire.

Study Five: Content Validation continued: Patients with paroxysmal (n=3), persistent (n=3) and asymptomatic AF (n=3) and relatives of those with AF (n=3) (total n=12) were individually interviewed following their completion of the questionnaire to assess the perceived relevance and readability of the draft questionnaire.

Study 6: Preliminary Validation: Principle Component Analysis: Participants (n=104) (PAF: n=46; asymptomatic AF: n=9; persistent AF: n=22; healthy control group: n=27) were recruited from Barts Health NHS Trust and from the Atrial Fibrillation Association (AFA) website. Participants completed the AF PROM. Principle Component Analysis allowed the identification of underlying domains of the questionnaire, allowing the reduction of number of items.

Study 7: Preliminary Validation: Convergent and Discriminant Validity: The same participants included in Study Six additionally completed WHOQOL-BREF and an AF Symptom measure to allow assessment of the convergent and discriminant validity.

An overview of this process is shown in Figure 4.1.

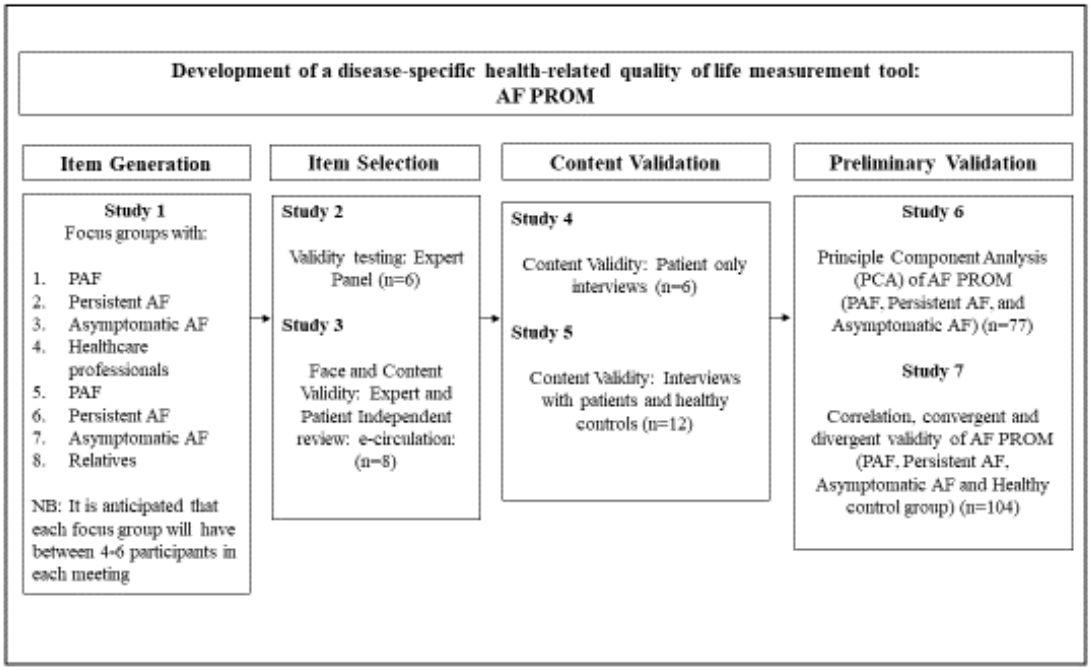


Figure. 4.1: Overview of PhD project.

4.1.2 Ethical Approval

Ethical Approval was received for this study by the NRES Committee North East – Newcastle and North Tyneside 1. REC reference 12/NE/0041. Approval was also received from Research & Development (R&D) at Barts Health NHS Trust. All participants enrolled provided written informed consent. An amendment to ethics allowed those who participated in Study Six and Seven to give implied consent by completing the questionnaires. This modification was requested to improve recruitment numbers in the validation stage.

4.2 Study One

A central part of this study involves focusing on the lived experience of patients with AF to ascertain the ways in which this condition affects HRQoL. For this reason, a series of focus groups were used to explore the experiences of people with AF. Eight focus groups involving patients with asymptomatic, paroxysmal and persistent AF were conducted with a target of 4-6 participants per group. Participants with different types of AF were allocated to separate groups as it was anticipated that alongside common issues, different themes could develop in each group.

Two additional focus groups were conducted with participants from different populations. One group was comprised of carers or relatives of patients with AF. A further group was comprised of healthcare professionals who were involved in the care of patients with AF. It was anticipated that the inclusion of input from a range of healthcare professionals and carers who have a good understanding of AF would broaden the range of perspectives and help generate a more complete understanding of AF and its effect on HRQoL.

4.2.1 Study One: Recruitment

Convenience sampling was used to identify patients diagnosed with asymptomatic, paroxysmal and persistent AF. Advertisements in the form of posters (Appendix C.4.1) and patient information leaflets with the research department contact numbers were placed in outpatient departments and cardiac wards in Barts Health NHS Trust and on an arrhythmia charity website. Cardiac consultants and arrhythmia nurses were approached by the research nurse to identify suitable participants. Participants who had AF were screened according to the inclusion and exclusion criteria summarised in Figure 4.2 below.

Inclusion Criteria:

Age: >18

Clinical criteria: application of diagnostic criteria for AF (according to NICE guidelines)

(i) asymptomatic AF

(ii) paroxysmal AF

(iii) persistent AF

Exclusion Criteria:

(i) Patients who have undergone operative treatment (i.e. catheter ablation) for their AF.

(ii) Patients assessed with cognitive impairment using clinical judgement.

(iii) Patients who voiced that participation will likely cause distress or those identified by their treating consultant as being impacted by another condition which would lead to them being too ill or too distressed to participate.

(iv) Patients who have a severe comorbid medical condition which results in significant impairments or effects on function such as severe shortness of breath (COPD) – for example, where a patient may be unable to distinguish which condition (e.g. AF or COPD) is having a negative impact on their quality of life.

v) Patients with an ICD

Figure 4.2: Study One: Item generation: Inclusion and exclusion criteria.

Eligible participants recruited from clinical settings were approached at their appointment by the researcher (SH) who explained the study and details of involvement in the focus group. If interest was shown, further information was provided (including a consent form, a map of the hospital site and a patient information sheet). Eligible participants who contacted the research department were sent the same above information. Patients were then re-contacted approximately four weeks before the focus group to confirm their interest and intention to take part in the study. This contact also allowed patients to ask any questions they had regarding participation in the research project.

4.2.2 Study One: Item Generation: Focus Groups: Method

The aim of the item generation stage was to identify key aspects of HRQoL that are important areas to patients with AF. A focus group is an interview technique which involves around four to eight participants convened to answer predefined questions relating to a topic or shared experience and which typically lasts 1-2 hours. The moderator adheres to a topic guide of open-ended questions which allows flexibility to explore issues relating to the specific topic (Robinson, 1999; Barbour, 2007). The topic guide will be discussed later in this chapter.

Both single interviews and focus groups have been used to generate PROM and HRQoL measures (Thorborg et al., 2001; Brown et al., 2010; Spiegel et al., 2010; Govender et al., 2012; Dean et al., 2014; Matteson et al., 2015). Focus groups were the preferred method, as they can incorporate an important dynamic of interaction, discussion of views and experiences that can stimulate ideas and enable elaboration of themes, which is considered important to achieve the aim of generating a large number of items. The use of focus groups involves the generation of ideas and discussion between participants, which can provide a rich and varied source of data. This group interaction allows consensus to be achieved, and also allows differing views and opinions to be further investigated. Different experiences and opinions between participants can be further explored, and the reasoning behind views and perspectives can allow others to gain a better understanding (Goodman and Evans, 2010). This method was used to identify key themes of HRQoL which enabled the development of domains for a disease-specific questionnaire.

The focus groups were arranged to be convenient for the majority of participants. Arrangements were made to allow the focus group session to coincide with other appointments at the hospital such as an ECG or holter monitor fitting or pre-assessment clinic. The focus groups were held on St Bartholomew's Hospital Site, London. It was anticipated that most participants would be familiar with the hospital site due to attendance at clinic appointments. St Bartholomew's Hospital is in the centre of London and has several easily accessible transport methods such as nearby tube stations, buses and rail stations, indicated on the map provided to participants (Appendix C.4.2). The researcher (SH)

took on the role of focus group moderator and was supported by one of the academic supervisors (MH). Upon arrival, participants were reminded that for the purposes of documentation, the focus group would be recorded. Verbal and written consent were gained prior to the commencement of each focus group.

4.2.3 Study One: Topic Guide

Two moderators facilitated each of the focus groups using a topic guide which was created to capture aspects of HRQoL that are affected by AF, allowing a consistent approach to be taken with each focus group. After a welcome and informal introductions, participants were asked to adhere to several ground rules, outlined in Figure 4.3.

i) All information which is given by participants to the focus group will remain confidential and we would appreciate if you would show the same respect to the other participants and keep it confidential.
ii) One person speaking at a time.
iii) Please respect and listen to the views of other participants (even in circumstances where you may not agree with them).
iv) Please speak clearly.
v) To ensure a clear audio recording of the focus groups, it would be appreciated to keep the talk with the whole group and not break off in smaller groups.
vi) Please allow all participants the opportunity to speak.

Figure 4.3 Study One: Ground rules for focus group participants.

The literature review presented in Chapter Three reported that although the qualitative literature was limited, it reported a greater depth concerning the effects of AF and identified additional domains of HRQoL which were not measured or reported in quantitative studies. These additional domains included aspects such as physical symptoms (e.g. chest pain), activities of daily living (e.g. work), psychological aspects, social activities and relationships, which were predominately negatively impacted by AF (Ekblad et al., 2013; McCabe et al., 2015). The topic guide was designed by researchers SH and MH and was based on findings from the literature review. This noted the main areas of HRQoL that were commonly captured by other HRQoL measurement tools available. Each topic guide had three areas:

- Introductory questions
- Main content questions

- Closing questions

All questions were neutral, open-ended questions allowing each member of the focus group the opportunity to speak and building rapport between participants and with moderators (Hennink, 2014). This provided participants the opportunity to identify with one another through shared symptoms and or past experiences with the aim of generating discussion. This process of sharing symptoms or experiences is considered to create a positive environment that stimulates discussion. The introductory questions also helped put participants at ease before responding to questions that may be more sensitive areas for participants (Morrison-Beedy et al., 2001)**.** Introductory questions are shown in Figure 4.4 below.

How did you first notice your AF? *Further Question if relevant:* What was the main thing that made you see your GP about it?

Figure 4.4 Study One: Focus Groups: Introductory questions.

The main content questions covered key topic areas relating to AF and its impact on HRQoL (Hennink, 2014) identified in the literature review (Chapter Three). These included open-ended questions to acknowledge a wide scope of answers and to allow further discussions. These main questions led to more sensitive questions being asked nearer the end of the focus group session to help participants to feel at ease, as described previously (Section 4.4.3). These questions are listed below in Figure 4.5 (and in Appendix C.4.3).

C1: What are the main ways that you find atrial fibrillation affects your quality of life?

Prompt/clarify:

- activities of daily living;
- independence;
- psychological well-being;
- physical/symptom-related effects;
- social/relationship-related activities
- burden of treatment/side effects**.**

➢ **Can I confirm these with you**? List on the board. Individual verbal ranking – most/least important.

➢ Provide opportunity to go through each point in turn and ask to expand on these areas.

C2: Are there any ways in which AF stops you doing the things you would like to be doing? Which ways in particular? (activities at home/ADL or recreational activities)

➢ **Which of these do you think is the most important for you?**

➢ **Can you expand on this?**

➢ **Do you ever not do things, for instance going out or taking part in an activity, because of your AF?**

➢ **Do you ever change your plans because of AF? How often**?

C3: Do you feel AF interferes with your social life and relationships? If so how? (Social relationships and social activities)

➢ **Are there any ways in which AF prevents you from being involved in social activities?**

➢ **Has your AF, or worry about AF, affected your personal relations?**

C4: Does AF affect your mood ... cause you worry (… affect your sleep … limit your concentration)? (Psychological well-being – anxiety, worry, acceptance, enjoyment, concentration)

➢ **Do you have any worries about the future because of your AF?**

➢ **Do you feel down or depressed because of AF?**

Figure 4.5 Study One: Focus Groups: Main content questions.

During the focus group session, themes affecting HRQoL were listed on a flip chart to allow confirmation of key discussion points and allow the exploration of these areas. The group was additionally asked to consider and rate the most important themes relating to the HRQoL of people with AF.

To close each focus group session, the researchers provided a summary of the topics discussed and closing questions were asked (shown in Figure 4.6 and in Appendix C.4.3) to ensure all considered areas of HRQoL were discussed. This recap exercise ensured participants' agreement with the main topics covered, which increases the credibility and dependability of the data and also provided closure for the focus group (Hennink and Leavy, 2014).

Is there anything else anyone would like to say? Are there any things we haven't covered that you think are relevant or important about how AF affects you?

Figure 4.6 Study One: Focus Groups: Summary questions in topic guide.

All participants were given the contact details of Barts Health NHS Patient Advice Liaison Service (PALS) prior to completing consent to allow the opportunity to voice concerns. This service provides advice and confidential support to all patients and their relatives. A short debrief between researchers SH and MH took place following each focus group to record main themes.

4.2.4 Study One: Analysis

The framework method (Gale et al., 2013) was used to condense the vast amount of transcript data generated from the focus groups. The framework method sits in a larger group of analysis often described as 'thematic analysis or qualitative content analysis' (Gale et al., 2013 p.2). This method has been used in a variety of settings, including healthcare (Gale et al., 2013), in an attempt to identify differences and similarities throughout the generated data before examining relationships throughout finally concluding with identified themes from this data (Gale et al., 2013). Although time and labour intensive, this method has been shown to be comprehensive and systematic (Gale et al., 2013; Richie and Lewis et al., 2013), allowing a level of transparency with access to original data. This method is recognised by researchers (Ritchie and Spencer, 1993) as being grounded in participants' accounts and therefore highly appropriate for the purposes of this study. Researchers SH and MH undertook training in its use prior to commencing analysis.

The framework method involves seven stages (Gale et al., 2013). Each will be discussed in terms of how they are applied in this study.

- Transcription
- Familiarisation with the interview
- Coding
- Developing a working analytical framework
- Applying the analytical framework
- Charting data into the framework matrix
- Interpreting the data

Transcription

The recorded focus groups were transcribed by a professional transcriber which allowed transcription to be completed promptly and to a high standard. As per GCP guidelines, original audio recordings and transcripts were securely stored on NHS computers and backed up on an encrypted memory stick securely stored in the research department.

Familiarisation with the interview

The accuracy of the transcript was checked by SH. This also allowed familiarisation with the content of each focus group discussion. Reading and re-reading of the data alongside audio recordings were carried out by SH.

Coding

Initial coding reduced the amount of data, allowing a manageable amount of information. The software NVivo was used by SH. Each sentence and paragraph was coded with codes created in response to the transcript data. Reoccurring phenomena from each focus group were initially listed. The content was divided into headings and subheadings. Each heading and subheading was linked to the raw data to allow comparison and ensure transparency. The original transcripts were also made available to researcher AMc, who firstly became familiar with the data and coded this data independently. Once completed, SH and AMc compared and discussed the reoccurring themes described in the following section.

Each focus group was thematically analysed to allow themes to be established. A key assumption was that different themes would predominate in different AF subgroups and the perception of patients would differ from that of relatives or healthcare professionals.

Developing a working analytical framework

Once the transcripts were coded, researchers (SH and AMc) met to discuss and check the consistency of the labels placed on reoccurring phenomena. Coding allowed the development of a preliminary working analytical framework (Gale et al., 2013).

Applying the analytical framework

Using features available on NVivo software, each transcript was analysed and the identified themes linked to the original transcript.

Charting data into the framework matrix

NVivo software includes features that allow the reduction of data by summarising the data into agreed categories and exporting them onto Windows Excel. This will allow direct quotations from original data to be easily identified.

Interpreting the data

From the analysed data, categories, concepts and themes were developed and made available for review and discussion at the panel group meetings.

4.3 Study Two: Item Selection: Expert Panel

The focus group transcripts were analysed using the framework method to identify key themes and concepts relating to HRQoL and AF. An expert panel group was convened to review the themes generated.

The expert panel was comprised of six participants: a cardiac consultant specialised in the care of patients with AF, a nurse research academic, a health psychologist research academic, a research nurse manager, a research nurse, and an AF patient charity lead representative.

The panel group met on one occasion. This meeting allowed initial introductions and familiarisation with other HRQoL assessment tools available for use in patients with AF. Aspects of these tools were considered (Chapter 3) and themes noted from the focus groups were examined and discussed. The original data was made available alongside initial analysis of the data completed by researchers SH and AMc. Following this, initial draft items were generated by SH, MC and MH.

4.4 Study Three: Item Selection

The aim of Study Three was to select and retain those items that represented the most relevant aspects of HRQoL for this patient group and covered all domains relevant to this construct. This allowed assessment of face validity and content validity whilst also ensuring that the initial PROM was readable, understandable and feasible for completion. The item selection stage enabled the formation of an initial draft scale. Other studies have identified a similar number of items ranging between 40 and 140 items for the item selection stage (Badia et al., 2007; Garratt et al., 2008; Flokstra-de Blok et al., 2009; Braganca et al., 2010). Once the initial draft items were selected, a series of draft e-questionnaires with different versions was emailed to a series of expert panels for their feedback.

4.4.1 Study Three: Review: Version One

A small panel of healthcare professionals was asked by email to review the initial measure for clarity and relevance. Participants (n=6) included one HCP involved in Study One, two members of the panel meeting, one HCP who was involved in coding 25% of the original data in Study Three and one cardiac consultant who has a research interest in AF. Participants were asked to comment on the instructions and format of the questionnaire. This information was used to ensure face validity of the PROM and support the removal of items that were considered unclear and or repetitive. This item reduction stage was conducted by the researcher (SH) together with academic supervisors. The items were reviewed to avoid duplication and overlap. This process occurred over three meetings. Feedback from participants was discussed at this time. Items considered relevant and clear with >60% agreement from participants were retained in the final draft. The discussion and review process allowed the reduction of the number of items whilst still reflecting all dominant themes identified in the focus groups.

4.4.2 Study Three: Review: Version Two

The second draft version of the AF PROM was reviewed by a series of patients who were involved in the focus groups to ensure that the content was consistent with that derived from the focus groups. This stage involved one patient with persistent AF. This patient was asked to comment on the clarity and relevance of each item. Feedback was assessed by the researchers and it was anticipated changes to the overall format of the questionnaire would occur at this stage.

4.4.3 Study Three: Review: Version Three

The third version of the AF PROM was assessed by one academic staff (academic nursing senior lecturer) and one patient with paroxysmal AF. It was expected this stage would ensure initial face validity whilst also attempting to ensure content validity and providing an opportunity to adjust and confirm the wording of the items and link to an appropriate response scale.

4.5 Study Four: Content Validation

The initial PROM was completed by six patients with AF in a cardiology outpatient setting. Following completion, each was interviewed individually by the researcher, using the questions noted in Figure 4.7 (below) as a guide to this semi-structured interview. This stage was undertaken to further assess face validity in the intended patient population, ensuring the items were relevant, clear, unambiguous and written in terms that are understood prior to administering to a larger population in the following stage. These interviews were recorded using a voice recorder and responses thematically analysed by the researcher using the framework method on the NVivo software (version 11).

Did you find any major problems with the questions?
Were there any questions which you found difficult to understand or that were unclear? Which one(s)? How so?
Did you find any question rude or off-putting? Which one(s)? How so?
Did you find any question particularly important or relevant to you? Which one(s)?
Did you feel that a question about how AF affects your quality of life was missing?
Were there any areas that you feel were left out?
Did you find the format clear?
Do you have any other comments about the questionnaire?

Figure 4.7

Study Four and Study Five: Individual interview questions

4.6 Study Five, Study Six and Study Seven: Recruitment

Although Studies Five, Six and Seven included some of the same participants, these stages are presented separately to improve clarity. It was anticipated that this self-administered pilot questionnaire would be completed by 300 participants. It was further anticipated that quota sampling would be used to obtain three groups of patients with asymptomatic (n=75), paroxysmal (n=75) and persistent AF (n=75). A fourth sample of participants (n=75) who did not have AF and were considered a healthy control group was planned to be age- and gender-matched and their results would be used in analysis to evaluate validity.

Participants were identified by convenience sampling. A poster advertisement was placed in relevant wards in Barts Health NHS Trust and on relevant websites (Appendix C.4.5). Participants were also referred from cardiac outpatient departments at Barts Health NHS Trust.

Eligible participants recruited from clinical settings were approached at their appointment by the researcher (SH), who explained the study and details of involvement. If interest was shown, further information (a patient information sheet and consent form) was provided. Eligible participants who contacted the research department were sent the same information. Information about each participant, including type of AF, age, gender, employment and ethnic group, was recorded. Patients were asked to complete the pilot questionnaire prior to an outpatient clinic appointment or complete it

at home and post it back to researchers. It was anticipated that the sample size for the four groups would be equal, with at least 50 participants per group.

4.7 Study Five: Content Validation

All participants recruited were asked to complete two other questionnaires alongside the AF PROM. These included a generic HRQoL questionnaire (WHOQOL-BREF) and an Atrial Fibrillation Symptoms Questionnaire (AFS). Following completion of the AF PROM, twelve participants (n=3 PAF, n=3 persistent AF, n=3 asymptomatic AF and n=3 healthy controls) were asked to take part in an individual interview which allowed the face and content validity of the measure to be further assessed. The transcript for this interview can be reviewed in Figure 4.7. All interviews were audio recorded and were professionally transcribed and thematically analysed by SH.

4.8 Study Six: Preliminary Validation: Principle Component Analysis

Administration of the AF-PROM in a pilot study allowed preliminary psychometric testing to be carried out. Principle Component Analysis (PCA) allowed the underlying factors of the measure to be identified, allowing a further reduction in the number of items. A general rule for sample size considers the number of participants and the number of items. This ranges from 3 to 20 participants per item (Williams et al., 2012). It was considered that at least 200 patients would be adequate, as this would ensure a ratio of ten participants to one item for this study (Field, 2005; Jung and Lee, 2011; Pallant et al., 2014; Tabachnick et al., 2014), and is also similar to other PROM item reduction stages (Jenkinson et al., 2012; Dean et al., 2014; Bodger et al., 2015). Some researchers would suggest 50 is the minimum number when using EFA (Sapnas et al., 2002; Dodou et al., 2009), and this number is considered the minimum acceptable sample for this initial measure validation.

A correlation matrix was performed prior to PCA to reveal the relationships between the variables. A positive correlation of greater than 0.4 indicates a reasonable correlation (Harris and Taylor, 2014). A p value of < 0.05 shows a significant result on the correlation matrix. The results of the PCA identify underlying components.

4.9 Study Seven: Preliminary Validation: Convergent and Discriminant Validity

Participants involved in Studies Five and Six were also asked to complete a generic HRQoL questionnaire (WHOQOL-BREF) and an AF symptom questionnaire, AFSS (Atrial Fibrillation Symptoms Questionnaire). Using SPSS (version 21), it was anticipated that the different types of AF and well patients would be distinguishable with their scores supporting the known group validity.

It was anticipated that the AF PROM score when initially produced would indicate the level of burden of AF and therefore a high score would indicate a lower HRQoL score. It was hypothesised that the scores of some AF PROM items would show a strong positive correlation with the scores of the AFSS. In other words, if a patient had a high level of symptoms they would also have a lower HRQoL score. This result would support convergent validity (see Table 4.1).

As a low score on the WHOQOL-BREF indicates poor QoL, and a high score on the AF PROM would indicate a low HRQoL, it was hypothesised that there would be a negative correlation between the scores of the AF PROM and the WHOQOL-BREF, further supporting convergent validity. It is anticipated that domains which are considered unrelated, such as physical symptoms of AF (using the AF PROM) and environment (in WHOQOL-BREF), will show a lower negative correlation, supporting discriminant validity (see Table 4.2.

Table 4.1 Hypothesised correlations between components of the AF PROM and AFSymp.

AFSymp domains	AFSymp items in domains	Hypothesised relationship between domains of the AF PROM and AFSymp (direction and strength)
Heart symptoms	Q1 Q3 Q7 Q8	Stronger Positive Correlation than WHOQOL-BREF (Moderate = >0.2 - <0.7)
Tiredness	Q4 Q5 Q9	Stronger Positive Correlation than WHOQOL-BREF (Moderate = >0.2 - <0.7)
Chest discomfort	Q2 Q10	Positive correlation but treated cautiously

Table 4.2 Hypothesised correlations between components of the AF PROM and WHOQOL-BREF		
WHOQOL-BREF domains	**WHOQOL-BREF items in domains**	**Hypothesised relationship between domains of the AF PROM and WHOQOL-BREF (direction and strength)**
Physical domain	Q3 Q4 Q10 Q15 Q16 Q17 Q18	Negative correlation (weak to moderate correlation = >0.2 <0.4)
Psychological domain	Q5 Q6 Q7 Q11 Q19 Q26	Negative correlation weak to moderate correlation = >0.2 <0.4)
Social relationships domain	Q20 Q21 Q22	Negative correlation (weak to moderate correlation = >0.2 <0.4)
Environment domain	Q8 Q9 Q12 Q13 Q14 Q23 Q24 Q25	Negative or lower correlation to indicate divergent validity (weak correlation <0.3)

4.10 Conclusion

This chapter has presented the proposed method for the development of a PROM for patients with AF. This research study aims to involve patients throughout development to ensure that aspects of HRQoL that are important to patients are captured, a concept that has been emphasised throughout this thesis. The following chapters will present the results of these studies.

Chapter 5: Item Generation for a Novel AF-PROM Questionnaire: A Focus Group Study

Previous chapters have described the negative impact AF can have on the quality of the lives of people with this condition. Qualitative research studies have explored the impact of this AF in further detail compared to quantitative studies. While AF-specific questionnaires are available, many have been developed with limited PwAF input. The need for a questionnaire developed with PwAF input to improve the content validity of such a measure has been presented.

5.1 Introduction

As outlined in Chapter Four, the first step in developing a new measure of condition-specific HRQoL for AF is to generate an over-inclusive pool of potential questionnaire items. To begin to address this step, the current chapter reports on a series of focus groups with key stakeholders: people or person with AF (PwAF), relatives or carers (RoC) and healthcare professionals (HCP). The aim of these focus groups was to understand the impact of AF on day-to-day living (Study 1; see Figure 5.1).

The main findings from Study One are presented as themes identified from the qualitative analysis of data from eight focus groups with PwAF (asymptomatic, paroxysmal and persistent AF), RoC and HCPs. Each theme and subtheme will be discussed and will be supported by quotes from PwAF to reflect the impact of AF on HRQoL. Further supporting PwAF quotes are presented in Appendix D.

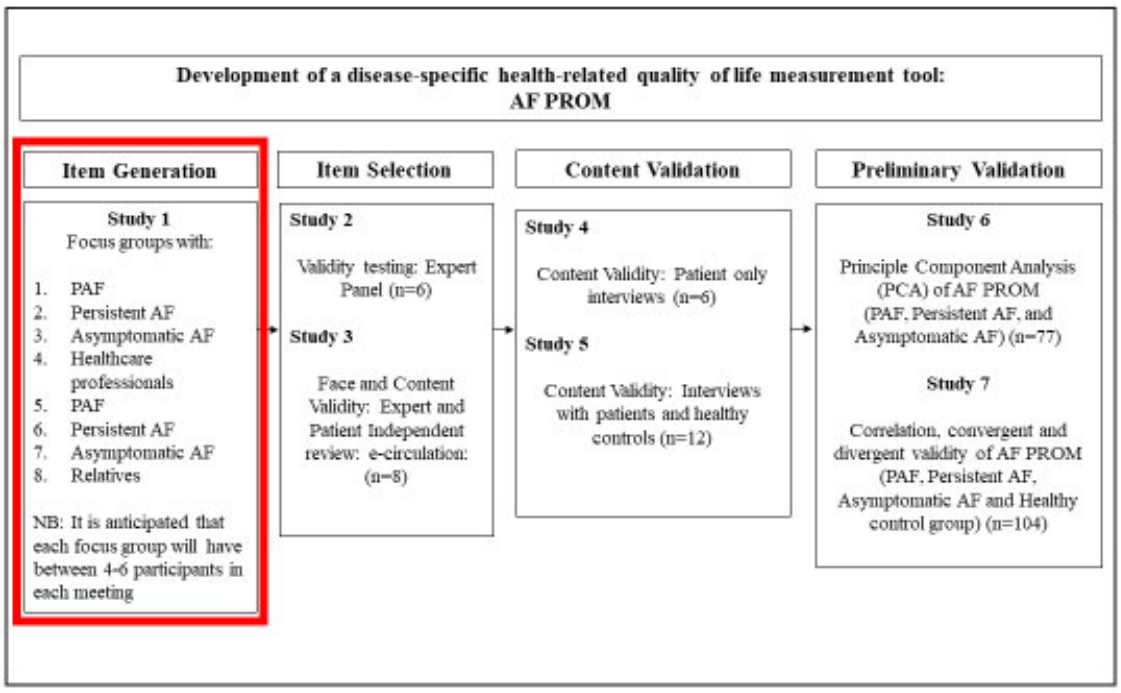


Figure 5.1 AF PROM study overview.

5.1.1 Aims

The aim of this chapter is to identify the main aspects of HRQoL which are impacted by PwAF to enable the item generation of a new PROM for people with AF.

5.1.2 Objectives: Study One

The objectives of Study One are to:

1. Explore the lived experiences of PwAF to identify areas of HRQoL which are affected by AF.
2. Additionally, explore the perception of relatives and healthcare professionals of the impact of AF on the HRQoL of PwAF.
3. Consider the main qualitative findings from the focus groups, to allow the identification of domains which will form initial items in Study Three.

5.1.3 Focus Groups

Although the involvement of PwAF or stakeholders throughout development of PROM is promoted and considered critical at initial stages to increase content validity (Brédart et al., 2014), involvement

is considered inconsistent throughout the literature, with only 16% (31/198) of studies including such representatives (Gargon et al., 2014). To achieve objective 1 and 2, Study One used focus groups to explore the lived experiences of those with asymptomatic (AS), paroxysmal (PA) and persistent (PE) AF, with the additional perspective of RoC and HCPs. Involvement of these groups was sought to provide a more comprehensive assessment, allowing similarities and differences between perspectives to be explored to improve the content validity of the measure.

Although other methods such as individual interviews were considered for data collection, focus groups were considered more appropriate for this stage of the study as they allow a larger number of PwAF the opportunity to reflect on how AF has affected their HRQoL. In the current context, a key benefit of using focus group discussions to collect data is that they allow individuals to report their experiences of AF to others who may have had similar experiences. Shared experiences and shared understanding can help to create a safe environment that enables PwAF to discuss sensitive topics. Focus groups allow for sensitive exploration of any differences of experience that emerge. Against these advantages, focus groups can be difficult to manage and challenging to analyse. In some cases, some PwAF can feel unwilling to offer views that contradict dominant voices within the group. Despite these challenges, on balance, it was felt that focus groups were the most appropriate approach for the study aims.

5.1.4 Methods

Forming a positive environment for discussion by building a rapport among participants was considered important to enable the exploration of the lived experiences of PwAF. Therefore, introductory open-ended questions encouraged PwAF reflecting and elaborating their experience of the initial presentation or diagnosis of AF. These introductory questions allowed each PwAF the possibility to share their experiences whilst having the opportunity to note similarities between experiences to create an environment suitable for later sensitive questions. Sensitive questions were avoided in the early stages of the focus group discussions as they had the possibility of highlighting differences between PwAF which could have had a negative impact on building an initial rapport.

The implications of AF on PwAF HRQoL from qualitative and quantitative literature were presented in Chapter Three. Although much of available quantitative literature focuses on the impact of treatments on HRQoL, qualitative literature has further explored the impact of physical symptoms, the limitations on or implications for activities, social life, relationships and psychological implications (Deaton et al., 2003; Thrall et al., 2006; McCabe et al., 2011; Ekblad et al., 2013; McCabe et al., 2015). Such qualitative literature which described how devastating AF can be for individuals led researchers (SH, MH) to form open-ended questions and prompts (shown in Figure 5.2 below) based

on these concepts. This also permitted the exploration of unanticipated concepts, allowing PwAF to generate the overall content of discussion in each focus group.

To further engage PwAF, generate discussion and reaffirm content covered, the main implications or aspects of HRQoL affected as stated by the PwAF during the focus groups were listed. Final closing questions allowed PwAF the opportunity to reflect on areas of HRQoL identified and voice any other areas which may not have been covered. Questions were adapted for the RoC and HCP focus groups.

I1: How did you first notice your AF?
I2: What was the main thing that made you see your GP about it?
C1: What are the main ways that you find AF affects your QoL?
Prompt/clarify:

- activities of daily living;
- independence;
- psychological well-being;
- physical/symptom-related effects;
- social/relationship-related activities
- burden of treatment/side effects**.**

➢ Can I confirm these with you? – list on the board ... individual verbal ranking – most/least important.

➢ Provide opportunity to go through each point in turn and ask to expand on these areas.

C2: Are there any ways in which AF stops you doing the things you would like to be doing? Which ways? (Activities at home/ Activities of daily life [ADL] or recreational activities)

➢ Which of these do you think is the most important for you?

➢ Can you expand on this?

➢ Do you ever not do things, for instance going out or taking part in an activity, because of your AF?

➢ Do you ever change your plans because of AF? How often?

C3: Do you feel AF interferes with your social life and relationships? If so, how? (social relationships and social activities)

➢ Are there any ways in which AF prevents you from being involved in social activities?

➢ Has your AF, or worry about AF, affected your personal relations?

C3: Does AF affect your mood ... cause you worry (… affect your sleep … limit your concentration)? (psychological well-being – anxiety, worry, acceptance, enjoyment, concentration)

➢ Do you have any worries about the future because of your AF?

➢ Do you feel down or depressed because of AF?

We've covered several different areas in relation to how AF may affect you. Brief summary ...
S1: Is there anything else anyone would like to say?
S2: Are there any things we haven't covered that you think are relevant or important about how AF affects you?

Figure 5.2 Study One: Focus group: PwAF group: Questions

5.1.5 Sample Characteristics

PwAF were recruited directly from Barts Health NHS Trust and indirectly via the Atrial Fibrillation Association (AFA). Convenience sampling methods were used to ensure sampling of PwAF with all types of AF (asymptomatic, persistent, paroxysmal), RoCs and HCPs. A total of 31 participants were enrolled into the study. This was smaller than the target number of 32-48 (with 4-6 PwAF for each group) due to several PwAF, RoC and HCPs withdrawing their initial verbal consent (n= 7). Despite this, the eight focus groups generated a wealth of data relating to the impact of AF on HRQoL and recruitment was halted at this point.

As shown in Table 5.1, twenty-one of the participants enrolled had a diagnosis of AF, as follows: persistent AF (29%), paroxysmal AF (22%) and asymptomatic AF (16%). Participants with AF were mostly female (n=13) and ranged in age from 26 to 88 years old. The mean age of those with paroxysmal AF was 59 years old, with a median age of 58 years. The mean age of those with persistent AF was 63 years old, with a median age of 64 years. The mean age of those with asymptomatic AF was 68 years old, with a median age of 70 years old. Most PwAF reported themselves to be Caucasian (n=17) with either British or other White background. Other PwAF reported themselves to be Black British with Caribbean heritage (n=1), Asian (n=2) and other mixed ethnic background (n=1). Most were employed (n=14) and a smaller number retired (n=7). None of the PwAF had a catheter ablation for AF. Most (n=17) were on a rate or rhythm control medication for their AF.

Comorbidities or relevant past medical history are presented for PwAF in Table 5.1. Only two PwAF reported having no other relevant medical history. The most commonly reported comorbidities in the PwAF groups included hypertension (high blood pressure) (n=7); hypercholesterolemia (high cholesterol levels) (n=5); diabetes mellitus (n=4); and stroke, TIA or thromboembolic event (n=4). All of these are considered risk factors of stroke and may lead to the need for anticoagulation. Most of the participants enrolled were on an anticoagulant, either a vitamin K antagonist (VKA) (n=12) or non-vitamin K antagonist oral anticoagulant (NOAC) (n=4).

A small number of PwAF reported having insomnia (n=1), depression (n=1) and sleep apnoea (n=1), all of which are reported to negatively affect HRQoL. These comorbidities may have had potential implications on their view of HRQoL.

The focus group involving RoC was composed of one female and two male participants. All relatives described themselves as White British. Two relatives were currently employed, and one was retired. Two RoC conveyed their spouses' experiences of living with AF and one participant described her

father's experience of living with AF. Although the relatives' past medical history was not recorded as requested, during the focus groups one RoC explained that he had previously had AF and received a catheter ablation for his AF.

The focus group involving HCPs included those with a range of roles at a specialist centre, including cardiac consultant (n=1), cardiology registrar (n=2), pre-assessment nurse (n=1), arrhythmia nurse specialist (n=1), cardiology ward nurse (n=1) and pharmacist (n=1). Demographic details such as age and past medical history were not recorded for individuals who were relatives or HCPs at their request.

Table 5.1 AF PROM Study One: Sample Characteristics						
Patient group (n)	**PA***	**PE***	**AS***	**RE***	**HP***	**Total**
Total number of participants	7	9	5	3	7	31
Sex (n)						
Female	6	6	1	1	3	17
Male	1	3	4	2	4	14
Ethnic background (n)						
White English/Welsh/Scottish/Northern Irish/British/ Irish	7	5	4	3	4	23
Other White background	0	1	0	0	1	2
Other Asian background	0	1	1	0	1	3
Other Black African/Caribbean background	0	1	0	0	0	1
Mixed/Multiple ethnic groups	0	1	0	0	1	2
Employment status (n)						
Employed	7	5	2	2	7	23
Unemployed	0	0	0	0	0	0
Retired	0	4	3	1	0	8
Treatment for AF (n) (NB: only includes patients with diagnosis of AF)						
Previous catheter ablation treatment for atrial fibrillation	0	0	0	NA	NA	0
Currently only on a heart rate controlling medication(s)	1	7	1	NA	NA	9
Currently only on a heart rhythm controlling medication(s)	1	0	2	NA	NA	3
Currently on both a heart rate and rhythm controlling medication	3	2	0	NA	NA	5
No current pharmaceutical management of AF symptoms	2	0	2	NA	NA	4
AF-related stroke preventive medications (n) (NB: only includes patients with diagnosis of AF)						
Currently taking vitamin K antagonist (VKA)	2	7	3	NA	NA	12
Currently taking non-vitamin K antagonist oral anticoagulant (NOAC)	1	1	2	NA	NA	4
Comorbidities/relevant past medical history (NB: only includes PwAF)						
None reported	1	1	0	NA	NA	2
Oncology						
Cancer - (previous) breast	0	2	0	NA	NA	2
Cancer - (previous) gastrointestinal tract	0	1	0	NA	NA	1
Respiratory						
Ex-smoker	1	3	0	NA	NA	4
Sleep apnoea	0	1	0	NA	NA	1

Table 5.1: AF PROM Study One: Sample Characteristics (continued)						
Sleep Disorders						
Insomnia	1	0	0	NA	NA	1
Depression	0	1	0	NA	NA	1
Cardiac						
Hypertension	3	3	1	NA	NA	7
Hypercholesterolemia	1	3	1	NA	NA	5
Coronary artery disease	0	1	0	NA	NA	1
Mitral regurgitation	0	1	0	NA	NA	1
Stroke/TIA/Thromboembolic event						
Previous blood clot	0	1	0	NA	NA	1
Stroke	0	0	1	NA	NA	1
Transient ischemic attack (TIA)	0	0	1	NA	NA	1
Subarachnoid hemorrhage	0	0	1	NA	NA	1
Endocrinology						
Diabetes mellitus	3	1	0	NA	NA	4
Hyperthyroidism/Graves' disease	0	0	1	NA	NA	1
Hypothyroidism	0	0	1	NA	NA	1
Multinodular goiter (MNG)	0	1	0	NA	NA	1
Hypoparathyroidism	0	1	0	NA	NA	1
Orthopaedics						
Osteoarthritis	1	0	0	NA	NA	1
Rheumatoid arthritis	0	1	0	NA	NA	1
Osteoporosis	0	2	0	NA	NA	2
Gastro						
Gastric bypass	1	0	0	NA	NA	1
Diverticulitis	1	0	0	NA	NA	1
Previous inguinal hernia	0	0	1	NA	NA	1
Glaucoma	1	0	0	NA	NA	1
Rheumatic Fever	0	1	0	NA	NA	1
Skin condition: Eczema	0	1	0	NA	NA	1
Erectile dysfunction	0	0	1	NA	NA	1

*PA = Paroxysmal Atrial Fibrillation (PAF)
*PE = Persistent Atrial Fibrillation
*AS = Asymptomatic Atrial Fibrillation
*RE = Relatives
*HP = Healthcare Professionals

NB: Heart rate controlling medications include beta blockers, calcium channel blockers and digoxin; heart rhythm controlling medications includes sodium channel blockers and potassium channel blockers

Please note: all quotes will be followed by the participant's number which also indicates their AF subgroup. For example, PA001 indicates a quotation from a PwAF with paroxysmal AF.

5.1.6 Results

Each focus group was transcribed by an independent transcriber. The Framework Method was used to code, theme and analyse the results for each focus group separately. These results are discussed in Section 4.5

Although SH was the moderator of the focus groups, and therefore acquainted with the data, this process of analysis involved SH becoming more familiar with the content of the focus groups by reading the transcripts, listening to the audio recording and reflecting on field notes taken by both moderators. All transcripts were read and coded line by line by SH. This process was also completed by an independent nurse researcher (AM) for two focus groups (25% of data). Following AM reviewing and analysing the data, the researchers (SH and AM) met on several occasions in August 2015 to discuss and confirm the main themes and subthemes noted from this data to develop a diagram using the software NVIVO (version 11). Any disagreements were discussed, and it was decided main theme and subtheme names would only be included if agreed by both researchers. This process allowed comparison of the consistency of analysis.

Five main themes relating to HRQoL were identified in the focus group data:

1. Physical or symptom-related effects
2. Psychological effects
3. Activities of daily living
4. Relationships
5. Treatment

Each major theme and subtheme will be considered in this chapter. These are shown in Table 5.2. Other themes can be reviewed, along with supporting quotes, in Appendix D. As this study aimed to identify the lived experiences of PwAF, findings from focus groups with PwAF will provide the basis for the main analysis of the impact of AF on HRQoL. Additional analysis of this impact from the perspectives of RoC and HCP will be presented for each of the five themes.

Table 5.2 AF PROM Study One: Focus Group Themes	
Theme	**Subtheme**
Physical or symptom related effects	Pain / discomfort
	Heart rate or rhythm
	Feeling unwell, tired or short of breath
	Interaction with other medical conditions
Psychological effects	Anxiety and worry
	Coping
Activities of daily living	Diet
	Housework
	Medications
	Sleep
	Travel
	Hobbies
	Washing and dressing
	Work
	Socialising
Relationships	Lack of understanding
	Being a burden to others
	Causing friends and family to worry
	Socialising
	Avoidance
	Sexual Relationships
Treatment	Anticoagulation
	Symptom management
	HCPs, online and other support

5.2 Physical Sensations and Symptoms

One theme which was identified as being affected by AF was physical sensations and symptoms. This theme had four main subthemes: pain or discomfort, heart rate or rhythm, feelings and interaction with other medical conditions. Most of these subthemes related to pulse and sensations (such as feeling tired or shortness of breath). An overview of the main symptoms identified in the focus groups is shown in Table 5.3. Each subtheme considered will be supported by a selection of quotes from participants to illustrate the theme.

In some instances coded text has been used to support more than one subtheme. For example, a quote reporting a PwAF experience of an episode of AF which described physical symptoms may also describe the psychological implications of this experience. Additional quotes for each subtheme are presented in Appendix D.

Table 5.3 AF PROM: Physical sensations and symptoms of AF

Theme	Subtheme
Physical sensations and symptoms	Pain or discomfort
	Heart rate or rhythm
	Feeling unwell, tired or short of breath
	Interaction with other medical conditions

5.2.1 Pain or Discomfort

Chest pain or chest discomfort was described by those with persistent and paroxysmal AF (PA001, PE008, PA021, PA022, PE023, PE024). This was referred to as *'pressure'* in their chest (PA005), a *'bruised'* feeling (PE023), a *'tight'* (PE024) feeling in their chest, and also a *'constant chest pain'* (PA021).

Although chest discomfort is a recognised common symptom of AF (NICE, 2014), the exact cause of the discomfort is not currently understood. The length and severity of this symptom varied between PwAF. The impact of these symptoms affected PwAF physically but also led to psychological or emotional effects.

As PwAF reported a number of concurrent symptoms, they expressed difficulty in identifying which symptoms were causing reduced HRQoL. For example, one PwAF PE008 explained feeling *'very*

breathless', 'terribly, terribly unwell' , 'a terrible pressure in my head [and] *in my chest'.* This PwAF also described how AF *'changed [her] life overnight'.* It left her *'physically… completely winded'* and unable to walk due to the sensation of having a *'hand pushing [her] back the other way'.* This restricted her physically and reduced her ability to complete tasks or activities. This PwAF also described the psychological implications of these symptoms, describing feeling *'so vulnerable'* that she needed to have her husband to be with her *'just to do stuff outside'* (PE008)**.**

5.2.2 Heart Rate or Rhythm

Some PwAF described various symptoms relating to their heart rate or rhythm. Some described this rhythm as being irregular, some described what is clinically known as bradycardia (a slow heart rate), some described what is clinically known as tachycardia (a fast heart rate) and some described having palpitations. These palpitations were described by some as a pounding sensation, or an awareness of the heartbeat or rhythm. One person with paroxysmal AF (PA022) described ectopic beats (i.e. harmless changes in the heartbeat which are sometimes referred to as premature atrial or ventricular contractions). Some described dizziness (PE009, PE024, PA022, PA021), falls and blackouts (PE008, PE009, PE006) because of rate or rhythm symptoms. The severity, duration and location where the sensation was experienced appeared to influence the impact on HRQoL, which varied significantly between individuals.

Although only a small number (n=5; PE006, PE008, PE009, PA02, PE024) of PwAF reported experiencing dizziness, having a history of falls or blackouts. During analysis, the researcher (SH) considered this aspect important to present, as these symptoms caused fear in some individuals and if experienced could be devastating. One PwAF reported her experience as follows:

> *I noticed it [referring to AF] because I fell down three times, so I was a bit worried. I went to my GP... I just found myself on the floor. Before it happened, I didn't feel any dizziness.... Since then the journey began. What this lady said, I have been feeling that and even more, to the extent that, when I really feel that, I just sit in a corner and cry. When did it become like this?* (PE006)

One PwAF (AS020) who was asymptomatic experienced concern or anxiety about having a diagnosis of an irregular rhythm despite not experiencing any sensations. Some PwAF described that sensations relating to their heart rate or rhythm either caused a feeling of anxiety or were affected by anxiety (AS020, PA021, PA022, PE026). It was reported that either the symptoms (i.e. sensations from the heart) or the fear of the symptoms increasing resulted in some PwAF exhibiting behaviour changes. For example, one PwAF reported that heart rate or rhythm sensations brought her to a standstill: '*I*

couldn't get up, I couldn't move' (PA022). This resulted in this PwAF having to leave work and seek medical attention. Another PwAF described avoidance and reduction of activities due to fear of these symptoms:

> *I loved walking up in the mountains … I am scared to go off walking on my own [now]. …So, yes, it has had quite an impact in that way… It is whether it will exacerbate symptoms or whether I would collapse and not have anybody around … Also, I don't want to stop other people.* (PA021)

Although the impact of these sensations is dependent on their severity, their unpredictability could result in PwAF regularly having to take sick leave from work. One PwAF described having to stay in hospital '*for a whole week'* (PE008) because of AF symptoms. There also may be psychological implications such as fear and reduced independence because of being admitted to hospital even for a short period, as one PwAF explained:

> *I was feeling unwell. Then they found the irregular heartbeat and then I was really sick. A week from finding I had an irregular heartbeat, my life changed completely. I was so ill. I can't say mentally, but I was suddenly like a different woman. I suddenly felt very vulnerable, I was scared to be far from the hospital, I was shaking all the time. It was just awful.* (PE008)

This PwAF further describes how the AF symptoms she experienced at home left her feeling her mobility was restricted:

> *I could hardly walk to the hospital, which is at the end of my road. I was completely breathless. It was really scary … I was so ill … So, that's when it started, so it's been four years.* (PE008)

Although it is accepted by researchers that the length of time since the episode could impact perception, this PwAF continues to refer to this event four years later as an episode which was *'really scary',* suggesting that this was negative memorable event associated with fear.

Some people with paroxysmal AF (PA001, PA021, PA022, PE006, PE023, PE024, PE025, PE026) also noted problems with sleep because of heart rate or rhythm sensations. The impact of these symptoms on sleep varied and the symptom severity and length of symptoms could influence sleep. Some PwAF described these symptoms as being more severe at times of rest or sleep, with some causing wakening. Some (PE025, PE024, PE026) also described how reduced sleep affected their ability to cope and concentrate.

Another implication of heart rate or rhythm symptoms may be the need to take medications at the time of these episodes which may be considered an inconvenience and lead to potential associated side effects. This is an implication which would also be influenced by other symptoms of AF and is not restricted to the heart rate or rhythm effects.

5.2.3 Feeling Unwell, Tired or Short of Breath

Those with AF described experiencing AF symptoms which included feeling unwell, tired or short of breath. Some PwAF described feeling one or a number of these sensations during an episode of AF.

Feeling '**unwell'** (PE008) was a symptom described by those with paroxysmal (PA002, PA021) and persistent AF (PE008). One PwAF described the onset as '*all of a sudden'* and the sensation as feeling '*really, really ill'* (PA002). This was associated with concern or anxiety about the symptoms which led to seeking urgent medical attention. Another PwAF described how her '*life changed completely'* and described this experience as *'just awful'* following a diagnosis of AF which was accompanied by feeling '*unwell'* (PE008). This PwAF went on to describe feeling '*like a different woman'* (PE008). The psychological implications of feeling like this included feeling '*very vulnerable*' and fear about being far from *'the hospital'*, which left this PwAF '*shaking all the time*' (PE008).

Feeling **tired** was another noted subtheme, and although mostly discussed by those with persistent (PE007, PE008, PE009, PE010, PE023, PE024, PE025, PE026) and paroxysmal AF (PA001, PA003, PA004, PA021, PA022), some who were asymptomatic (AS020, AS027) also mentioned feeling more tired than normal. The severity ranged between PwAF. Some described *'extreme tiredness bordering on fatigue'* (PA004) or '*crushing tiredness'* (PA001), while others described the symptoms to a lesser degree of tiredness but noted being '*more tired than tired should be* [for] *the activity level'* (PA003).

Those who described more severe tiredness commonly described the occurrence of these feelings as being '*all the time'*, and the impact of this as being '*overwhelmingly'* (PA004). Apart from the described psychological implications such as reduced concentration levels and ability to *'cope'* (PA004) and lost enthusiasm (PE007), these feelings of tiredness also had implications for daily life, such as an impact on work and home life. One PwAF described needing to '*lay down for half an hour'* after work to '*recharge*' (PE025). This also had an impact on hobbies and social interaction as one PwAF described not being able to '*do the exercises I used to do'* (PE009).

PwAF appeared to have much difficulty assessing what was causing these symptoms, especially tiredness. Some considered these symptoms to be potentially influenced by age, activities or the side

effects of medications needed for AF such as '*Metoprolol*' (PE007). For example, **shortness of breath** was discussed by those with persistent (PE006, PE007, PE008, PE009, PE010, PE023, PE024, PE025, PE026) paroxysmal (PA001, PA004, PA005, PA021) and asymptomatic AF (AS020). Some PwAF (PE008, PE009, PE010, AS020, PE024) described this sensation as occurring at the same time of the sensation of feeling tired. It is not clear if one symptom was causing the other i.e. shortness of breath was causing the tiredness. Some PwAF described that the cause of shortness of breath was often confused with other comorbidities or conditions such as a '*chest infection'* (PE010) *and general 'fit[ness]'* level (PE025).

5.2.4 Interaction with Other Medical Conditions

As AF mainly affects those of an older age (Chapter One) who are also more likely to suffer from other medical conditions which share similar symptoms to those of AF, there can be confusion about which condition is responsible for which symptoms. For example, some PwAF can also experience chronic obstructive pulmonary disease (COPD) and both conditions can cause symptoms such as shortness of breath. The theme entitled "other medical conditions" related to experiences mostly reported by those with persistent AF (PE008, PE009, PE010, PE023, PE024, PE026) and by one person who was asymptomatic of their AF (AS020). These medical conditions were described as either interacting with AF or as resulting in AF.

Confusion about which condition is causing symptoms may have an impact on the lives of the PwAF leading to delayed treatment. For example, one PwAF described being *'very, very breathless and [having] a very, very tight chest. [Not] know[ing] whether [it] is AF or whether [it] is [another] problem. They* [referring to HCPs] *have talked about sending me to a respiratorist, [but] haven't done that yet'* (PE024). This PwAF went on to describe the impact on her day-to-day activities, noting that *'even picking up a cup and saucer can feel jolly heavy to carry'* (PE024). The interaction of these symptoms also had an impact on her sleep, causing her to *'drop off to sleep at the drop of a hat'* (PE024).

5.2.5 Additional Analysis: Physical Symptoms: Perspective of Relatives and Healthcare Professionals

RoC reported similar symptoms of AF to those reported by the PwAF focus groups. Although RoC may not have personally experienced the sensation of heart rate or rhythm-related symptoms, they reported how the symptoms of AF, especially at the time of the episode, were *'the frightening part'* (RE030) and were associated with negative psychological emotions such as anxiety. Those in this

group were aware of some of the negative implications of living with AF and its associated treatments. For example, some described how AF symptoms (such as tiredness and shortness of breath) limited a PwAF's ability at home and working life, meaning daily tasks (such as cooking, housework and travelling) would require more planning and regular breaks:

> *[S]he could only do, maybe peel the potatoes or make the dinner, and then she would have to have a sit down; or do the hoovering or something, and then she was washed out for the day and she'd come and have a sit down*. (RE031)

Although this was not described by the PwAF group, the symptoms of AF (particularly shortness of breath) also negatively impacted those who had physically active jobs. For example, RE030 reported that their relative '*is a builder and he just wasn't able to go up the ladders'*.

Healthcare Professionals (HCP) view the symptoms and implications of AF on HRQoL from another perspective. HCPs are often most likely to hear from PwAF either at the time of an AF event (for example, when attending hospital) or following an event at an outpatient clinic or when in hospital for an intervention. Although HCPs can lay claim to 'expert' knowledge, this knowledge is highly selective and often acquired during acute clinical episodes, rather than the day-to-day lived experience of the condition. Despite these different perspectives, HCPs listed and described a similar range of AF symptoms as reported by PwAF. However, the information they provided had less depth and richness regarding the broader implications of AF on HRQoL. Information provided was often succinct and to the point. For example, one HCP when asked about the symptoms of AF listed *'palpitations, feeling very unwell, dizzy, sick, breathless*' (HP011). From the focus groups, the knowledge and understanding of these symptoms of AF is profound, however the implications of AF on HRQoL, required prompts and further probing.

5.3 Psychological Effects

Analysis of focus group data from PwAF, RoCs and HCPs identified negative psychological effects of AF and complications. Three main subthemes emerged related to anxiety and worry and coping (Table 5.4).

Table 5.4 AF PROM: Psychological Effects	
Psychological effects	Anxiety and worry
	Coping

5.3.1 Anxiety and Worry

> *One of the things with AF is it does affect your mental health … and it has certainly affected my anxiety levels.* (PE025)

Anxiety and worry were dominant themes throughout the focus groups, reported to some extent by all but two PwAF (PE010, AS028). Anxiety or worry appeared to be experienced along with the symptoms of chest pain or discomfort. For example, one PwAF (PA021) described how the continued chest pain led to a '*constant awareness'* of having AF. She further described feeling more '*worried and anxious … when the pain comes'* which led to a *'huge difference'* in her QoL (PA021). This anxiety was also echoed by another PwAF who described how the concern and anxiety caused by chest pain has led to awakening from sleep (PA022).

Concerns about the future progression of AF was mainly related to (i) worsening of symptoms (PA002, PA003, PA005, PE006, PE007, PE009, PA021, PE023, PE025), (ii) concerns about treatment (PA003, AS018, AS019, AS020, AS027) and (iii) anxiety about the complications of AF (PA001, PA003, PA004, PA005, PA021, PA022, PE025, PE026) such as blood clots, stroke or death. These concerns led to some PwAF reporting limitations on their ability to complete daily activities, including travelling, which in some led to a sensation of a loss of control. For example, one PwAF reported:

> *I live alone, so in the past what I used to do, when I didn't want to stay in or have friends in, I go window shopping and I have lunch outside. I enjoy myself and then come back in. Now I'm not able to do that, because I'm afraid. So, I'm kind of becoming isolated because I don't want to go down. Walking in the park, I don't want to do that, because*

> *I'm afraid what might happen. So, it makes me very sad sometimes to say, is this how life is going to be from now on?* (PE006)

Anxiety relating to symptoms and future progression of AF was expressed by those with paroxysmal and persistent AF (PA005, PE007, PE006, PE009, PA021, PE023, PE025). Those with paroxysmal AF reported increased anxiety due to *'the unexpectedness'* (PA005) of AF. Along with the unexpectedness, PwAF reported the severity of symptoms may have impacted their level of anxiety. PA021, for example, felt strongly that '*it did, especially when the symptoms were really bad … very much so … [I felt] very stressed, very anxious, quite emotional at times, tearful, which isn't normally me*'. For some, anxiety led to behaviour changes such as limiting or avoiding activities (PA005, PE006). Although those with persistent AF expressed anxiety, this appeared to be related to concerns about the implications of the symptoms. As one PwAF expressed it, '*I can remember being in bed at night thinking, "Am I going to make it through the night?" … You think you're going to die, but you're not; you just feel like you are'* (PE025).

PwAF expressed concern over the diagnosis and treatment of AF (PA003, PE007, PE009, AS018, AS019, AS020, PA021, PE025, AS027). Those PwAF described how a presentation at a hospital for something unrelated led to a diagnosis of AF, immediate referrals to cardiologists and discussions which PwAF described as being *'a bit of a shock'* (AS020). This led to a fluctuation of feelings where '*your mood can go from "I'm happy to live with it" to "it's scary and apprehensive"'* (AS020).

The degree of anxiety or worry varied amongst asymptomatic PwAF. One (AS027) felt the term worry was '*a bit over the top'*, describing it more as *'an awareness and concern',* although treatments such as the *'dreaded Warfarin'* were a reminder of a diagnosis of AF and the only time in which some PwAF felt anxious.

Some described anxiety about experiencing episodes of AF or complications of AF whilst being in a different country (PE023, PE024, PE026), *'particularly if you are travelling on your own …. And, if something did go wrong, who are you going to tell? Who is going to do something about it?'* (PE026). Particularly worrying complications included thromboembolic events, stroke (PA001, PA004) and death (PA001, PA003, PA004, PA005, PA021, PA022). This concern is reflected in the quote below.

> *So, with me, I think stroke is even more of a worry than death, quite honestly, because [when] you're dead, you're dead, that's it, but with a stroke you can lay there for years; you could be so affected by stroke. That, for me, is one of the biggest worries.* (PA005)

This is echoed by another PwAF, who explained how better communication may have reduced anxiety related to AF diagnosis.

> *I found that, being told that I had AF, but also that I'd got an underlying condition* [referring to 'Infra-Hisian Disease'] *that they couldn't treat me for, left me with a great deal of apprehension and fear, which had a huge impact on my QoL. I was too frightened to live in my own flat on my own for about 18 months, and I stayed with my elderly parents, because I was just so scared. Nobody explained things to me and I thought, when they said to me, 'There's nothing we can do to treat you, we're just going to monitor you,' I thought that meant I could just drop dead at any time.* (PAF021)

The awareness of the risk of stroke was discussed by three PwAF with paroxysmal and asymptomatic AF (PA003, PA004, PA005, AS020). Concern about the potential impact and burden caused by AF-related stroke was also reported (PA005). Others suggested that the risk of stroke was a reason why they avoided or paced certain tasks, as one PwAF explained:

> *I still do all the things I want to do, but I am aware that I have to take it a little bit steadier, because I don't want to trigger anything that puts me in a remission of massive AF and I end up having a stroke or something*. (PA003)

Feelings of fear and anxiety about receiving a diagnosis of an AF-related stroke accompanied anxiety from a diagnosis of AF. As one PwAF reported, *'the fear of stroke is really quite strong, I think'* (PE0025). This was echoed by another PwAF who described shock at diagnosis but also anxiety because of risk of a thromboembolic event.

> *Yes, I was shocked when I got the diagnosis… it was a hammer blow, I have to say. But you quickly get over that. You just have to accept it and that's it. … I'm more frightened and fearful now that they've discovered a blood clot in the left atria … They did say to me … that parts or the whole thing could have come away at any time and you would've been a stroke victim. So that scared the living daylights out of me…. So, I'm more fearful now in the last month to six weeks of, perhaps, will I get a heart attack on the Tube? Will I feel unwell? Cross fingers, I've been OK.* (PA004)

5.3.2 Coping

Although not anticipated, ability to cope with a life with AF and its implications was a theme that arose across the focus groups (PA002, PA004, PA005, PE008, PE023, PE024, PE025, PE026). Some

described difficulty coping with the symptoms of AF: *'I would say they were my feelings, actually, total fatigue and, overwhelmingly so that I couldn't cope'* (PA004). Coping may be influenced by various factors such as the impact of disturbed sleep, personality traits, available support, education, previous experiences and the degree of impact of the condition. The influence of some of these aspects was noted by some PwAF and will be mentioned below.

Some PwAF (PE023, PE024, PE025, PE026) described the impact of AF on sleep and how this affected their ability to cope with AF and their day-to-day activities and how it sometimes resulted in negative psychological feelings. The quotation below explains how AF symptoms result in poor sleep.

> *I am a reasonable sleeper, but, like you, I wake up early in the morning and, very often when I wake up, that is when the symptoms are worse. You wonder why because you are resting, if you like; you are lying in bed and all of a sudden thud, thud, thud. But I think now, like you, I am in AF all the time. I don't feel I have a break … But sometimes, when I wake up and, perhaps, have had, not a bad night, but a night where the AF, obviously, I assume, has been really kicking in badly, when I get out of bed it is a case of, can I put one foot before the other? You really have to force yourself, which is quite debilitating really, because, if you have got a job – it is not a paid job, it is voluntary, but I like to feel I keep up to my promises – some days I really feel as if I could just say, 'I'm going back to bed.' Whether I would sleep or whether I wouldn't, I don't know, but I do wake up very early in the morning, like you do.* (PE023)

Some PwAF reported that it was more difficult to cope with AF after poor sleep:

> *I find that lack of sleep means I don't cope with it* [referring to AF] *as well; I don't cope with anything as well, if I have a really bad night.* (PE025)

However, another PwAF (PE026) suggested that '*it is not that the AF is any worse than usual or that your mind is really that different about it, but it is just because you are tired and drained'.* The impact of this was described as leading to a reduction in ability to cope and negative psychological feelings.

> *[I]t brings on a wave of depression when I wake up, which I have to shake myself out of. But it is the lack of sleep that is causing this wave of downness or depression, if you want to call it that, rather than the AF, but they are all related.* (PE025)

Two PwAF (PA003, PA005) described trying to manage by using avoidance coping (e.g. mental disengagement; denial), although this was not always effective:

> *It's strange, but I won't let it affect me, really. I try to put it to the back of my mind, but I know, in my heart, I'm still waiting for that next time, because of the little prep things I do*. (PA005)

Four PwAF (PA003, AS018, AS019, AS020) described how support and reassurance from HCPs reduced initial anxiety from their diagnosis. Having a variety of treatment options was described by some PwAF as reassuring (PA001, PA003, PA005). Three PwAF with paroxysmal AF discussed the reassurance derived from medications reducing symptoms and anticoagulants reducing the risk of stroke (PE023, PE025, PE026). One (PE008) saw the need to provide reassurance to another PwAF during the focus group. Another (PA022) described how talking to others provided reassurance

5.3.3 Additional Analysis: Psychological Effects: Perspective of Relatives and Healthcare Professionals

RoCs appeared to be aware of the negative psychological implications of living a life with AF. One RoC, describing how anxiety and worry were experienced before the diagnosis of AF, described her father explaining that '*it was actually relief, because they* [referring to her mother and father] *had really wound themselves up'* (RE029).

The RoC focus group reported that the person's attitude and past medical conditions may impact the PwAF's ability to cope. For example, one RoC described his wife's experience as follows:

> *But I think that is also part of her personality, because she has had bowel cancer, 15 odd years ago now. She has had a colostomy for 15 years and I think she got very sort of, 'Oh well, there are a lot of people worse off than I am.' And I think that actually makes a difference to the way the person reacts to what they have got.* (RE029)

As well as the other participant groups, HCPs were aware of the negative psychological implications of living with AF. One HCP, for example, described

> *get[ting] as many calls from PwAF that just need psychological support as we do PwAF calling about their symptoms. Sometimes, actually, the phone call about the symptoms is just a mask for them wanting to talk to somebody*. (HP011)

Another described how PwAF

> *don't generally say they're depressed, but the way they describe how the impact is going to be on their life, it's not in a positive way; it's something that's kind of happened to them, they don't know why, they don't understand, really, and they just feel like it's a little bit unfair. I've heard the word 'unfair' a lot.* (HP017)

As one HCP put it, *'there's the fear of having an attack, but also people have read up on AF; there is a fear of having strokes as well'* (HP015).

All HCP discussed the impact that AF can have on anxiety or worry. They discussed that this was related to symptoms of AF (HP012, HP013, HP014, HP015, HP016), medications for AF (HP017), stroke (HP011, HP015, HP016, HP017), activities (HP013, HP016, HP017), travelling (HP012, HP014), financial implications (HP014), access to medical care (HP012, HP016), long-term effects on their heart (HP011), death (HP016) and effect on relationships (HP014, HP016). The quote below reflects some of these statements.

> *Although they don't necessarily admit to how much of an impact it has on them psychologically, I get PwAF who still call me every week. So, there is definitely a psychological need to talk about their symptoms, even though they're not admitting that they're feeling depressed or anxious, particularly PwAF who become very focused on their symptoms, exactly when they happen and what, potentially, triggers them*. (HCP011)

Three HCPs (HP011, HP015, HP017) described how PwAF experienced an awareness of AF. Four HCPs (HP011, HP012, HP013, HP016) described how PwAF often avoided certain foods or activities which were viewed by the PwAF as having the potential to trigger an episode of AF. This is supported by the quote below.

> *[T]here are lots of young people who, because they're so young and healthy, they think there must be a cause for this, that it's outside of me. So they keep thinking of certain things they do might be a trigger and they avoid certain foods*. (HCP012)

> *Yes, they eat certain things at certain times of the day and then lay down afterwards instead of sitting up.* (HCP013)

> *Yes. Very analytical of their symptoms and can become quite obsessive, really, and that, in itself, is limiting, because their entire focus becomes on their AF and how it affects them.* (HCP011)

One HCP (HP013) described how anxiety led to behaviour changes such as avoiding '*work, exercise, anything they see as precarious*' if the PwAF considered them to exacerbate symptoms or anxiety. This anxiety was additionally reported by another HCP, who reported that in some cases this led to isolation and to reduced HRQoL.

> *Quite often my PwAF [say] that they're really scared about travelling or going out of the house, particularly when they've got paroxysmal AF and they've got the episodes really bad. They say that they are scared being abroad somewhere that, if something happens to them, they might not have medical care or something.… I had a case where the guy hadn't left the house for two years, because he was so scared to go out.* (HCP012)

Ability to cope with AF was considered by one HCP (HP014) to impact HRQoL. Others (HP011, HP016) stated that factors such as age, sleep and attitude may influence the ability of PwAF to cope:

> *[T]here are quite a few PwAF I speak to whose symptoms are more apparent at night … So it has a massive impact and, obviously, lack of sleep, then, has an impact on their ability to go to work and function as a parent or a wife or a husband.* (HP011)

HCPs (HP016, HP017) reported that some patients' HRQoL was negatively affected due to a feeling of loss of control over their AF symptoms and their overall health. This was reported as being caused by having AF symptoms and by the failure of treatments to control these symptoms, as the following statements indicate:

> *I find there are PwAF who are on Warfarin, who regularly have to have INR checks. I think that's just a constant reminder for them on a regular basis that they're unwell. I think that that's quite psychologically negative for them, just that they can't take control of that themselves; they have to put their trust in a healthcare provider on a weekly basis.* (HP017)

> *I think accepting the diagnosis, because I get a lot of phone calls from PwAF who have been through the system and had ablations and, when they get a recurrence of symptoms, it's quite devastating for them and it's that kind of loss of control; they've been on medication and their AF has been controlled and now they're getting symptoms and they*

> *can't understand why and are very sort of questioning as to why is this happening now, why is the medication not working, why hasn't my ablation worked. I think it's not only accepting the diagnosis, but accepting that, sometimes, some long-term treatments aren't always going to cure them, basically, which is quite hard, particularly saying* [that to*] the younger population who don't actually have anything else wrong with them.* (HP011)

One aspect which was noted by some HCPs (HP016, HP017) which was not expressed by other PwAF groups was how PwAF often expressed disappointment or devastation relating to the limitations of treatments, as one HCP recalled:

> *I remember we had a military PwAF who was still active in the military. Those have been the ones that I've heard and taken note of because it's one of their passions, it's one of their hobbies and now they're worried that they won't be able to do it, because, obviously, their heartrate is going to be slowed and they want to know precisely what heartrate they can get to. They're very into their training and, to try and tell them that they need to aim for a different heartrate, that's big for those and those are the ones that always stick in my mind, the people who seem to be the most disappointed about being limited in terms of aerobic capability, I guess.* (HP017)

This HCP further explained how disappointment was expressed if the PwAF misinterpreted the aims of the treatment:

> *I think, unless they're believing that that is going to be the end of their problems, they're going to be fixed, I've had quite a few people in here come in and say, 'I thought it was going to fix me,' and then they just go really down because it's come back. …But I've had a couple that have misinterpreted what I think their aims are.* (HP017)

The need for psychological support was noted by HCPs (HP011, HP014), but due to time and work constraints they considered providing this was often difficult, as one HCP explained:

> *I think patients sometimes feel really discouraged when they feel symptoms, like palpitations after their ablations. I've heard the arrhythmia nurse say to me that they often need reassurance from us on the ward, that that might happen quite soon after their procedures and sometimes they don't expect it and then they're really anxious….*
> (HP014)

5.4 Activities of Daily Living

The PwAF involved in the focus groups described how activities of daily living (ADLs) were affected by AF. This appeared to depend on the symptoms of AF and the psychological implications of AF of individuals. Nine subthemes of ADLs were noted as being affected: diet, housework, medications, sleep, travel, exercise, hobbies, washing and dressing, work and socialising (Table 5.5).

Table 5.5 AF PROM: Activities of Daily Living	
Activities of daily living	Diet
	Housework
	Medications
	Sleep
	Travel
	Hobbies
	Washing and Dressing
	Work
	Socialising

Many PwAF (PA001, PA003, PA005, PE006, PE007, PE008, AS018, AS019, AS020, PA021, PA022, PE025, PE026, AS027) described feeling *'aware of living with AF'* (PE008). This was reported as being associated with the symptoms of AF, increased risk of stroke and the need for and consequences of taking regular medications for AF and stroke risk. This awareness appeared to impact PwAF in various ways, leading to changes in diet (PE025), greater caution when carrying out normal activities, avoidance, reduction and pacing of activities (PA001, PA003, PA005, PA021, PA022, PE026) which were viewed as some as being triggers of AF.

5.4.1 Diet

Two PwAF (PA001, PA002) reported concerns that certain foods or activities may trigger or cause symptoms of AF. This led to behaviour changes. One PwAF, for example, described wondering *'if there's anything I'm doing in my lifestyle that's triggering this… So, I decided to cut out any caffeine and any alcohol altogether'* (PA001). Another (PA002) reported it was *'better not to[referring to drinking] than have the symptom'.* The impact of this behaviour change (abstaining from certain foods or drinks) was not directly reported as affecting HRQoL by these PwAF. However, one PwAF (PE008) expressed lack of pleasure in things she used to enjoy, and another (PE009) suggested concern over medication and alcohol interaction:

> *I really love wine, I don't drink too much. But I'm not interested now in wine, which is scary. That scared me. Now, if we're having people and I have a glass, I will drink it, but not enjoy it. That's a big loss to me.* (PE008)

> *There's the worry in your mind that it might affect the medication.* (PE009)

> *Yes, I wouldn't be able to drink much anyway, but it's just I love very nice wine, the taste of it, and that has gone. I know it's stupid, but I used to enjoy it. …* (PE008)

Some PwAF discussed the impact of AF on diet (PA001, PA002, PA004, PA005, PE008, AS020, PA021, PA022, PE025, AS027). Some (PA005, PE006, PE024, PE023) described that the overwhelming tiredness from AF affected daily tasks such as eating and drinking. Those who felt their ability to cook was restricted by their AF explained that even the smallest of cooking tasks such *'picking up a cup and saucer'* (PE024) felt exhausting. Others described the extreme effort required for normal tasks such as '*standing for a long time at the cooker'* (PE006) whilst cooking. Some described how this tiredness affected their eating habits because of the extreme effort required, how it reduced their motivation and how, despite having a desire to eat or drink, they felt too exhausted to *'move'* (PA005). Some restricted certain foods or drinks for fear that these might trigger symptoms of AF (PA005). Others described this restriction was placed on certain foods (such as vegetables) or drinks (such as coffee or alcohol) because of concern that these foods may interact with treatments needed for AF stroke prevention (i.e. warfarin). This constant awareness resulted in '*more of a focus'* (PA005) on diet which some described as *'tak[ing] over your day'* (PE025), as in the case of the PwAF quoted below:

> *I think Warfarin does [affect my HRQoL] to an extent ... having to think about, I feel, what you eat all the time. If I have eaten a lot of this, I shouldn't eat much of that. It is this constant looking at things that you are doing. It takes over your day sometimes ... like we are going on holiday in two weeks… So, I won't have my vegetable intake, so is my INR suddenly going to go up because I am not eating as many vegetables?... I think one of the things with AF is it does affect your mental health, I would think, and it has certainly affected my anxiety levels.* (PE025)

5.4.2 Housework

PwAF with persistent AF described housework activities such as shopping, cooking (as previously discussed) and cleaning being affected (PE008, PE023, PE024, PE025, PE026). This was mainly due

to the feelings of extreme tiredness and shortness of breath which led to a feeling of having *'no energy'* (PE024). Some expressed a fear that tasks such as shopping were unattainable without support from others (PE008):

> *I just thought, the journey hasn't been that long that I am not able to go downstairs,* ***because I'm afraid to go shopping because I can't carry it all. If I go shopping I have the mini cab which helps me take my things upstairs.*** (PE006)

PwAF expressed feeling rest was needed following normal housework tasks. For example, one PwAF described doing '*a little bit of washing up, which is not much – a cup, saucer and plate – I've got to sit down*' (PE024). Others described needing to pace activities to allow them to be completed. One PwAF, for example, despite still feeling able to '*do all the things I want to do',* remained aware of the need '*to take it a little bit steadier, because I don't want to trigger anything that puts me in a remission of massive AF and I end up having a stroke or something'* (PA003).

5.4.3 Medications

The reduction of symptoms due to taking regular medications caused reduced vulnerability but left an element of awareness of AF and its impact. This is reflected in the following quote.

> *Now I've lost that feeling of being vulnerable… but I'm someone else. I am not what I used to be, that is for sure. I have six different tablets, including, obviously, the warfarin, but digoxin, bisoprolol … The only thing I don't really feel is the heart palpitations … I do feel better than I did, but I'm certainly aware of living with AF.* (PE008)

Other PwAF described how taking medications for AF or its complications was a reminder of their risk of stroke and living with this condition: *'It is an awareness and concern. … I mean 99% of the day I never think about it. I think about it at dreaded warfarin time' (*AS027). However, another described feeling reassured by being on an anticoagulant: '*I always console myself with the thought, well, if you are on an anticoagulant, you are much less likely to have a stroke'* (PE026).

The impact of medications appeared to affect two areas of HRQoL, ADLs and treatment, and will therefore be discussed under both subthemes. The impact of taking medication was viewed by some as an inconvenience (PE010, AS019, AS020), the level of which may be influenced by the length of time since starting medication and whether the PwAF is taking other regular medications. Although this inconvenience was only noted by a small number of symptomatic individuals (PE010), others who were asymptomatic of their AF described feeling that AF *'hasn't affected [their] QoL, so to*

speak, apart from having to remember to take these drugs at certain times' (AS020). Another felt the regular times for medications left them feeling *'frightened'* (AS019).

> *Medication, I'm not that keen on. This flecainide, they said you've got to take it on an empty stomach, so I've got to work out when I have my breakfast. I take my pill about nine o'clock in the morning and have my breakfast at about 10. So, I'm trying to work out. Then I've got to finish my supper at a certain time to take it again at nine. It was all this. I thought to myself, 'She's driving me up the wall.'* (AS019)

5.4.4 Sleep

The disruptive impact of AF on sleep was experienced by those with paroxysmal AF and persistent AF. Some PwAF felt that the symptoms of AF, mainly palpitations and shortness of breath, would be exacerbated during periods of rest or sleep. These symptoms interrupted their sleep and led them to feel '*very anxious'* with the result that they found it *'difficult to get back to sleep'* (PA021), and despite feeling *'really tired all the time*' (PE010), found difficulty getting to sleep. Some PwAF reported experiencing dreams which were considered to be caused by the side effects of medications for AF (for example, PE026 '*was getting a lot of nightmares and I mentioned that to the GP and he said, "We'll change you onto a different beta blocker*"'), which led them to not *'feel refreshed'* after sleep. This impact on sleep was reported by PwAF as *'inevitably ... affect[ing] your mood the next day; it makes you feel down'* (PE026) which additionally affects *'focusing'* (PA022) and ability to work. However, one PwAF described feeling that '*it is the lack of sleep that is causing this wave of downness or depression, if you want to call it that, rather than the AF, but they are all related'* (PE025).

5.4.5 Travel

The implications of AF for travel were discussed mainly by those PwAF with paroxysmal and persistent AF (PA004, PE006, PE008, PA021, PE023, PE024, PE026). Difficulties or concerns were voiced about travelling both small distances, for example, when going to the shops, and longer journeys such as holidays abroad. The impact of AF whilst travelling by car was mentioned by two PwAF (PA001, PE026). One of these (PA001) described experiencing symptoms of AF whilst driving but they had '*been able to stop the car quite easily'* and therefore this did not cause concern. The other (PE026) was advised by the medical team to restrict their driving following an electrical cardioversion for AF (see Chapter One for details of the procedure).

Feeling *'frightened'* (PE023), '*particularly if you are travelling on your own'* (PE026) abroad, was mainly due to the symptoms of AF and concern over the thromboembolic implications of AF such as '*blood clots'* (PE024) which would require medical attention. This resulted in some travelling in Europe rather than outside of Europe or even avoiding travelling *'for several years because it is too much bother to get it ready and then getting there'* (PE024), and because of the fear that in the *'end, you think it's not going to be worth it'* (PE026). Others restricted such travel based on medical advice (PA021), and although higher travel insurance costs did not affect this PwAF (PA021), they reported others facing higher costs when travelling, this is supported by the statement below.

> *One thing that has affected my HRQoL, at the moment the consultant said I can travel to Europe but I can't travel beyond Europe. I used to love travelling in the Far East and Australia, so, at the moment that may be a no-go forever, it may be just a no-go for a few years. I just think, because they have told me I can't, that is frustrating, but yet I will follow advice…* (PA021)

Some PwAF were concerned that travelling is '*too much of a risk'* (PA004). This has meant some have *'had to cancel a holiday… literally [at] the last minute'* (PA004), which led to financial consequences. One PwAF described that *'fear* [of being a burden] *... stop[s] you doing things ... you [would] love to be with them [referring to travel companions], but…don't want to impinge on their lifestyle'* (PE023).

5.4.6 Hobbies

Some PwAF described how the awareness of AF, its implications and need for medication led them to avoid or reduce or pace certain activities (PA001, PA002, PA003, PA005, PA021, PA022, PE026). This appeared to be either due to the fear that this may trigger symptoms or related to the implications of being on certain medications such as anticoagulants (which can lead to increased bleeding, bruising). This appeared to affect other domains of HRQoL, such as hobbies, and to impact relationships with others. As one PwAF recalled, '*I stopped walking, as well, for a while and I stopped doing yoga and I stopped going to evening classes'* (PA021). With other hobbies such as *'gardening',* however,

> *I just have to pace much more what I do, which is a pain, but it hasn't stopped me completely. It is just having to rethink before I do anything: What am I doing and how long can I do it for?* (PA021)

It could be suggested that this may be impacted by the length of time since diagnosis and the degree of support which is available. For example, this PwAF stated that she *'feel[s] more confident in what I'm doing, I'm better at pacing, perhaps because I don't want to go back to the AF symptoms again*' (PA021). Another described how this awareness of the need to pace activities has impacted her relationships, as she no longer feels she has the same ability as previously, causing her to prefer to '*go out on my own where I can set my own pace, rather than try and keep up with normal speed*' (PE024).

Others (PA005, PE009, AS020) described how this led them to be more *'cautious'* when carrying out activities as an accident could lead to *'bigger consequences when you're on* [an anticoagulant such as] *warfarin'* (PA005). This view is shared by another PwAF who stated that when *'I'm doing physical activity … [I need] to be consciously aware that… I need to let my friends know… I'm carrying my card; I'm letting them know that I'm taking these drugs… in case I fall unconscious'* (AS020).

Hobbies, sports and recreational activities were described by PwAF as being impacted by AF. The different activities which were affected varied between PwAF. Some described exercise, DIY and gardening being impacted. Some PwAF felt the unpredictability of their condition caused concerns and frustration as they *'just don't know when it's going to strike'* (PA005) and *'you can be breathless one day and the next day you are fine'* (PE023). Some felt that the *'lack of energy … That is the bit that concerns you'* (PE007). Others expressed how these limitations were lessened by *'pac[ing] … [or] 'tak[ing] a break …which is a pain'* (PA021).

Although some PwAF expressed no limitations associated with physical activity (PA004, PE025, AS027, AS028), others who had paroxysmal AF (PA003, PA004, PA005, PA021, PA022), persistent AF (PE006, PE007, PE009, PE023, PE024, PE025, PE026), and those with asymptomatic AF (AS018, AS020, AS027, AS028) reported limitations. Difficulty with low intensity activities such as walking or gardening (PA003, PA005, PE009, PA022, PA021, PE024) was reported, which led some to need to compensate by pacing activities and not talking during activities (PE024); others described *'trying to explore other things and …[finding] other interests'* (PA021). Some acknowledged variability between individuals with AF in exercise (PE023, PE025).

Some acknowledged physical activity was accompanied by anxiety (AS020, PA021). One PwAF with asymptomatic AF (AS020) described taking precautions (such as carrying an identification card and informing friends or family of being on an anticoagulant) when doing exercise activities because of risk of bruising and bleeding being on an anticoagulant.

> *For me, at the back of my mind I just have to be careful when I'm doing physical activity or when I'm psyching myself up to be consciously aware that, if I cut myself and like with*

> *the snowboarding that I'm going on, that I bruise quite easily and that I need to let my friends know in case I fall unconscious. I'm carrying my card; I'm letting them know that I'm taking these drugs.* (AS020)

Others (PE026 and PA021) echoed this anxiety, but also described anxiety relating to the inducement of symptoms:

> *Again, you were saying about swimming, I am scared to go off walking on my own. Whether that will change or not, I don't know. So, yes, it has had quite an impact* [on HRQoL] *in that way…. It is whether it will exacerbate symptoms or whether I would collapse and not have anybody around.* (PA021)

Three PwAF (PE006, PE007 and PE009) described how the lack of energy had a negative impact on recreational activities such as gardening and DIY, causing them to stop or limit these activities.

> *Your piece about not wanting to DIY, I'm the same. I love my DIY. I haven't touched it. My back garden is half done and it hasn't been touched for about the last seven years.* (PE007)

> *The problem is you miss it as well, not being able to do it.* (PE009)

5.4.7 Washing and Dressing

Although the impact of AF on normal activities such as washing and dressing was mentioned by only a few PwAF (PA004, PA005, PE006), some experienced severe difficulty from symptoms of shortness of breath and tiredness when '*bending down … getting into my bath… dressing … lifting my legs … so many things like that'* (PE006). Another PwAF (PE024) described tiredness causing difficulty but did not clearly indicate if washing and dressing were a problem.

5.4.8 Work

Although, not all PwAF were working or studying, a number of PwAF (PE006, PE007, PE009, PA021, PE023, PE025, PE026) with persistent AF noted the effect of AF on their work. The symptoms of AF (such as tiredness and shortness of breath) were one aspect which impacted work or study. For example, one PwAF (PE025) described how tiredness affected concentration levels and how this snowballed throughout the night and affected sleep and created anxiety about working the

next day. Another PwAF felt that anxiety related to AF and its symptoms '*affected how I related to other people'* and expressed concern about not *'pulling my weight'* (PA021). One way PwAF described overcoming these symptoms and anxiety was to pace activities and to say no to certain activities (PA021, PE023):

> *I suppose I have to stop and think about what am I going to do much more before I do it than I ever did before, and pacing myself. I am very much aware, for example, the last few weeks I have been doing a lot and I am looking at the diary thinking, I am actually probably going to have to say 'no' to some things, because I feel like I am pushing myself too hard. I am getting a few symptoms that are telling me, 'You need to ease back.'* (PA021)

However, such coping mechanisms were not always successful. For example, one PwAF (PE006) felt she needed to give up a volunteering job because of the severe symptoms of AF. Another (PE007) explained the inconvenience of essential hospital appointments affected their work (i.e. having to take days off work at short notice). Although these statements only portray a negative impact of AF on work, it is important to consider the positive effect mentioned by two PwAF who felt that work shifted their focus from AF:

> *I find, if I am feeling, perhaps, it is difficult to put one foot in front of the other, when you actually go and you are doing something* - (PE023)
>
> *You perk up.* (PE026)
>
> […] *I say, 'forget it', but you do forget it.* (PE023)
>
> *Yes, you do.* (PE026)

5.4.9 Socialising

Some PwAF (PA003, PA005) described how the awareness of AF led to a feeling of *'still waiting for that next time*' (PA005) and preparing '*just in case'* (PA005) they were alone and experienced symptoms of their AF. Another expressed a loss of control (PE008). This suggests that PwAF feel a sense of dependence on others which potentially could affect relationships. This is supported by the following quote:

> *You just said and mentioned about being on your own with the phone. I also have that. If I'm walking the dog and I'm going somewhere remotely on my own, have I got my phone*

> *with me, because it does trigger the fact that, potentially, you might be caught off guard and think you're absolutely fine.* (PA003)

PwAF described how these AF-related restrictions on day-to-day living led to negative emotions such as feelings of embarrassment (PE006, PE025), guilt (PE008, PA021), lost independence (PA003, PE023, PE024, PE025, PE026), increased vulnerability (PA001, PA003, PA004, PA005, PE006, PE008, PE023, PE024, PE025, PE026) and a sense of isolation (PE006, PE007, PE008, PE024). Some additionally expressed how these negative psychological implications, such as loss of motivation (PE023, PE024, PE025, PE026), loss of enthusiasm (PE006, PE007, PE008, PE009, PE010) and lost interests (PE007, PE008, PE009), led to feeling unable to carry out tasks, further leading to PwAF either not undertaking activities previously enjoyed or being initially reluctant to attend activities such as parties or social gatherings. This led to a change of lifestyle which some described as '*a big loss'* (PE008). This is reflected in the following quote who describes his previous social life and compares to his life now.

> *So, over the months we got into meeting at five and leaving the pub at 11. Good or bad, it was a social life, it was good fun. Everybody would have a laugh. We might then meet up on a Saturday lunchtime, Monday we used to play cards in the evening in the pub, then Tuesday to Thursday it was quiet … I haven't done that now for years and, yet, it was the focal point. It just shows how it* [referring to AF] *does affect you*. (PE007)

One PwAF described how her symptoms led to changes in the way which she engages with the world, leading her to feel *'like a different woman'* (PE008). Describing how AF had *'changed* [her] *life overnight'*, this PwAF stated that '*what [she] wasn't prepared for'* was how this had changed her physically and psychologically, she described as leaving her feeling '*suddenly like a sick woman'* (PE008):

> *I'd never been sick before. I felt so vulnerable and I'm not a control freak – only my husband calls me that – but I was always in charge. I just felt like I couldn't make any decisions, I couldn't think clearly... (*PE008)

Some PwAF expressed mourning over lost ability (PE006, PE007, PE008, PE009, PA021, PE026) a sensation highlighted in the following statement.

> *It is like having to accept that I should be grateful I can get up and just do these things, but there is that wanting to do a bit more because it has been taken away from you, if that*

> *makes sense, and you, perhaps, mourn that you can't do those things anymore, or perhaps not as much as you would like to. Is anyone else like that?* (PE026)

However, a few PwAF (PA003, AS020) described a positive impact of their perspective changing: *'when you've been affected … you kind of do re-evaluate your life a bit and you want to make the most of life'* (AS020).

Some of those with asymptomatic AF (AS018, AS019, AS020) reported that the condition had no impact on socialising. The negative impact on socialising was mainly described by PwAF with persistent AF. One PwAF reported that symptoms left her feeling *'not able to do [things], because I'm afraid … I'm afraid what might happen'* (PE006). This left her feeling *'very sad sometimes to say, is this how life is going to be from now on?'* and also resulted in a feeling of '*becoming isolated'* (PE006). Others (PE007, PE008, PE009, PA021, PE025) described how symptoms such as reduced energy resulted in not attending usual social events.

> *I went away for a few days recently and, if I do get a bit of chest pain or discomfort, I sort of think, 'Oh gosh, how much am I going to be able to do today? Am I going to have to tell my friend, 'Look, actually, you're going to have to go to this museum on your own or do that walk on your own, because I don't feel up to it.' The holiday I have just booked in Ireland, I am a little bit worried about and I have said to my friend, 'I am just concerned I might not be able to socialise with you in the evening or if I've had enough or it's too much, I won't be able to join in on the things we're planning on doing.' So that's quite hard. I do find that hard …* (PA021)

Some (PE023, PE025) did not allow their AF to have an impact because colleagues and friends were unaware of their AF; but others (PA022) mentioned that if their symptoms increased in severity then socialising would be reduced.

5.4.10 Additional Analysis: Activities of Daily Living: Perspective of Relatives and Healthcare Professionals

RoCs were aware that activities relating to daily life and exercise (RE031) were negatively affected. Aspects of HRQoL such as the impact of food and alcohol were noted by some relatives (RE030). Others noted that limited ability to carry out normal daily tasks would require the PwAF to 'plan more'. For example, one RoC explained how their relative

> *could only do, maybe peel the potatoes or make the dinner, and then she would have to have a sit down, or do the hoovering or something, and then she was washed out for the day and she'd come and have a sit down.* (RE031)

RoC were also aware of the implications of taking regular medications and how carrying extra medications and notification cards reduced anxiety (RE031). One RoC (RE031) also described the anxiety which was related to travel and the cost implications such as increased travel insurance fees. No RoC was aware that their relative's social life was impacted because of AF. One RoC (RE030) noted how symptoms (shortness of breath) caused difficulty for the PwAF at work (climbing ladders) and described the PwAF expressing worry about the consequences of being on an anticoagulant and having an accident at work.

Concern about the impact on a physically demanding job was not reported by any PwAF in the focus groups.

Various HCP (HP011, HP014, HP015, HP016, HP017) described the impact of medications on PwAF. Some (HP015, HP017) noted that the side effects of medications may impact their daily activities. One HCP described a PwAF expressing concern that '*he was scared, he was anxious…* [about having] *to take medication that is going to limit [him]'* (HP017). Some (HP014) described the consequence of taking these medications such as INR checks because of taking warfarin. Some HCPs (HP014, HP016) suggested that the age of the person and other comorbidities may impact how much taking medications impacts HRQoL. One HCP (HP014) expressed the view that *'the regular appointments and the pill burden'* would negatively impact the HRQoL of PwAF; a similar subtheme emerged from the focus groups with PwAF themselves. Although three HCPs (HP011, HP012, HP013) claimed that PwAF reported avoiding certain foods and eating at specific times because of fear that this may trigger episodes, none of the HCP described the ability to cook or reduced energy as aspects of HRQoL affected.

HCPs reported that the ability of PwAF to travel was affected: '*[Q]uite often … they're really scared about travelling or going out of the house … [or] being abroad somewhere … [where] they might not have medical care or something … particularly when and they've got the episodes really bad*' (HP012). The HCPs also noted negative implications such as travel insurance costs and travelling to areas where healthcare facilities were not nearby (HP012, HP014, HP015, HP016, HP017).

Five HCPs (HP012, HP014, HP015, HP016, HP017) stated that the impact of AF on exercise, hobbies and recreational activities was an area often asked about during clinical assessments, during which PwAF often reported that AF affected their ability to carry out recreational activities because of uncertainty of what activities are safe to do: '*[T]hey're worried that they won't be able to do it … because it's one of their passions, it's one of their hobbies'* (HP017). HCPs (HP011, HP012, HP016, HP017) noted the potential impact of AF on work and occupational activities, noting symptoms such as *'fatigue, [which] can interfere with work'* (HP016). Another HCP (HP013) reported that occupational and recreational roles may be impacted but had the view that the degree of impact would depend on their age.

5.5 Relationships

Some PwAF expressed that since receiving a diagnosis of AF, relationships with others had changed for various reasons. Themes such as increased vulnerability, lack of understanding from others and expressed worry from others were reported as leading to a fear of being an increased burden, further leading to changes in the amount of socialisation and relationship dynamics. An overview of the subthemes identified from the focus groups can be seen in Table 5.6.

Table 5.6 AF PROM: Relationships	
Relationships	Lack of Understanding
	Being a burden to others
	Causing friends or family to worry
	Socialising
	Avoidance
	Sexual Relationships

5.5.1 Lack of Understanding

Some PwAF reported that relatives, friends and colleagues had a lack of understanding of AF and its impact on HRQoL such as increased fear and behaviour adjustments and limitations, which led to some PwAF reporting negative psychological feelings (PE006, PE007, PE008, AS018, AS020, PA021, PA022, PE023, PE025). Some PwAF reported that relatives or colleagues appeared to have difficulty understanding that AF was '*something you're going to manage [long-term], it's not something that you have it or don't have it'* (PE008). This is supported by the two quotations below.

> *The anxiety affected how I related to other people. Some people seemed to not understand where I was coming from, sort of, 'Well, you've seen the consultant, they've said they're just going to monitor you, you'll be alright.' Didn't understand the fear that went with that and that, when I went back to work on a phased return and I was saying things like, 'I need to take breaks,' because normally we didn't and worked through lunch and everything, and I just said, 'I need to pace myself.' And they just didn't get that, and then I got guilt feelings that I wasn't pulling my weight.* (PA021)

> *It affects your relationship because it is also about what people expect of you and that all changes. You hope that people are tolerant of your condition and some people really don't understand it and you end up feeling a bit pathetic.* (PE025)

There was an additional fear of the unpredictability of symptoms which led to avoidance of activities with other people (PE006). Some PwAF explained that the lack of understanding from others led to feelings of a '*need to lie to people'* so that others would not *'see how vulnerable [you are]'* (PE006). One PwAF described worry that if others heard constantly the true impact that AF had on one's health, '*they probably wouldn't call anymore'* and the PwAF would be viewed as a burden on others. Becoming more withdrawn by the avoidance of activities has the potential of causing isolation and increased anxiety because of lack of support from others. These quotes suggest a sense of shame or stigma for some PwAF; however, another reported no stigma.

> *So, if I'm going on a date, I'd be happy to bring it up. For me, there's no stigma with what I have. I'm not having a heart bypass or having a pacemaker fitted. For me, it's more about spreading that news. It's not like cancer.* (AS020)

5.5.2 Being a burden to others

Although no PwAF expressed that they felt they were a burden on friends or relatives, some PwAF (PA001, PE006, HP014, HP015, PA021, PE023, PE026) voiced concerns about becoming a burden. One concern was of the lasting effects of a potential AF-related stroke, which could lead to *'be[ing] a burden to your children [or others]'* (PA001). Limited ability due to the unpredictability of AF symptoms which may cause PwAF to become a burden on others was a concern for some. Some PwAF avoided activities such as family holidays because of an '*awful feeling that you are holding them back*' and a fear of what their relatives *'are going to say in the future'* about them '*imping[ing] on their lifestyle'* (PE023). There was also concern from PwAF that managing symptoms by '*tak[ing] breaks…[or] pac[ing] myself*' may be viewed negatively by colleagues who were not aware of the condition or did not have a good understanding of the impact of AF on their daily lives.

5.5.3 Causing friends or family to worry

Although some PwAF (PA001, AS027, PA022, AS028) reported that friends or family expressed worry about them, this had no negative impact on their relationship; others (PA002, PA003, PA005, HP016, PA021) reported that their RoCs expressed concern about morbidity because of AF, symptoms and the side effects of medications, which negatively impacted their relationship with others. PwAF were aware that some relatives were *'more worried'* (PA005), *'so they panic more than you'* (AS018) and this caused relatives to be '*always checking in'* (PA003), which can have *'an effect on the family … and your friends'* (PA002). This concern '*begins to grate a little bit because [PwAF]*

just want to get back to normal, whatever [their] normal is going to be' (PA021). By contrast, other PwAF seemed to be reassured by this, suggesting *'that's what happens in families, isn't it? When you love someone, they're important, you want to make sure they're alright'* (PA001).

Some PwAF described relying more heavily on friends or family members for support (PA003, PE006, PE008, HP011, HP014, HP014, HP016, PA021, PE023, PE024, PE025, PE026), either because of AF symptoms or for psychological support because of AF. For example, one PwAF explained how a *'neighbour called in to look after'* her (PE024), while another described having '*the mini cab [driver] … help … take … things upstairs'* when shopping (PE006). One PwAF described not being able to travel alone anymore as she felt she did not *'have the confidence'* and so required her husband to travel with her to reduce this vulnerability (PE025) but expressed concerns that she had '*become far too reliant on him'* (PE025). This need for additional support led to some noting a change in *'what people expect of you'* (PE025), which can lead to a change of role among friends or in family settings. However, some expressed a desire to maintain independence (PE023, PE024, PE026), so when support is no longer available they are able to manage. For example, one PwAF described how when *'[you] want to get in touch with someone, they are not there; they are out. So, you just have to cope'* (PE024).

5.5.4 Socialising

AF symptoms reduced and limited social interaction in some PwAF, as the quote below illustrates.

> *But social interaction, like what we are doing now, in the evening it is like, 'I can't do this, I am just too tired.' But, again, I try and adapt by having a rest before we go. I don't do big meals anymore. We used to have five or six people round for dinner, but I have stopped doing all that, because, by the time I have cooked it all, I am like, 'Can I go to bed now, please?' So, it definitely affects me in that respect, but that is basically evenings, I guess.* (PE025)

One PwAF suggested the degree of effect on relationships and socialising may be influenced by '*personality*' type:

> *[S]ome people are like that anyway; they don't like to go out, so not a problem. But it's the thing that makes you change from being somebody who is very sociable to somebody who just can't bear the idea of doing something. Eventually, if you do it, like you say, you'll enjoy it, but it's just everything seems to be an effort. That can be very isolating.* (PE008).

Those who were asymptomatic (AS018, AS019, AS020, AS027, AS028) felt that AF did not impact their social life and did not feel there *'is a social stigma'* (AS027). Some PwAF with symptomatic AF (PE006, PE007, PE008, PE009, PA021, PA022, PE023, PE025, PE026) explained that socialising was more difficult because of change of ability due to physical symptoms. For example, some PwAF described thinking, *'I can't do this, I am just too tired'* (PE025). Others described the psychological cause of reduced socialisation: *'[O]nce again, we're back to that enthusiasm thing, you're just not up for it'* (PE007). This left some PwAF feeling a loss of a previous ability: '*[Y]ou, perhaps, mourn that you can't do those things anymore, or perhaps not as much as you would like to'* (PE025). Although some felt unable to socialise as much as previously, others appeared to avoid certain social activities for fear of inducing symptoms.

5.5.5 Avoidance

Across the focus groups, some PwAF with persistent AF (PE006, PA021, PA022, PE023, PE024) described avoiding talking or spending time with family or friends, which had a negative impact on their relationships with others. Reasons offered for avoidance included: 1) a fear of experiencing symptoms when doing activities; 2) a fear of relatives seeing their increased vulnerability because of these symptoms ('*I don't want them to see how vulnerable I am, with gasping and so on'* (PE006)); and 3) a desire to '*set my own pace, rather than try and keep up with normal speed*' as it is '*very difficult to keep up'* (PE024) when carrying out activities.

5.5.6 Sexual Relationships

Loss of libido and its potential negative impact on relationships was reported to be caused by the symptoms of AF (mainly tiredness) or side effects of medications (e.g. tiredness).

> *It may just be me but sexual relations, lost interest, and that was brought up in the early stages with the doctor, because I thought it might have been the drugs.* (PE007)
>
> *Yes.* (PE008)
>
> *Sure.* (PE009)
>
> *But at the end I said, 'Do any of these prevent anything?* [Referring to the medications impact on sexual relations] *I said, 'I don't really feel up to it.' He said, 'No, it's not the drugs.' So, once again we're back to that lack of energy. I can't be bothered.* (PE007)

> *Me too … Your tiredness has a huge impact. I live with my husband and I'm very lucky he's very understanding and very helpful. But that would definitely impact on relationships*. (PE008)

The impact of a '*lost interest'* (PE007) in sexual relations with their significant other concerned PwAF, one of whom voiced concern about '*What's my Mrs thinking because I'm not interested in her?'* (PE007). Another explained how this loss of libido would '*would definitely impact on relationships'* (PE008). However, she does not suggest this has had a negative impact on her HRQoL, as she describes feeling '*very lucky*' that her husband is '*very understanding'*.

A letter from a PwAF (Appendix D.5.6) received following the focus group explained the severe impact this aspect can have on HRQoL. This PwAF felt this information was too sensitive to be shared in the presence of other members of the group. In this letter she explained how the impact on sexual activity changed from when she was first diagnosed with PAF, when she noted a fear that sexual activity may induce AF symptoms, to a *'terrible tiredness'* and *'loss of libido'* when later being diagnosed with persistent AF.

5.5.7 Additional Analysis: Relationship: Perspective of Relatives and Healthcare Professionals

Although the FG with RoCs did not articulate an impact of AF on relationships, one RoC acknowledged that '*relationship[s had] changed slightly'* (RE029) since a diagnosis of AF (RE029).

HCPs (HP011, HP012) acknowledged that the symptoms of AF and the possibility that '*lack of sleep has an impact on their ability to go to work and function as a parent or a wife or a husband'* (HP011) caused PwAF to feel their '*various roles'* within relationships were impacted (HP012)**,** which was not expressed by any PwAF. HCPs acknowledged there was a concern about '*becoming more dependent on other people*' (HP015) because of the symptoms of AF or because of the lasting effects of stroke (HP014, HP015). HCP acknowledged that PwAF are concerned that '*they're so reliant on their partners and they're really anxious that [this] will put strain on their partners'* (HP014). HCPs noted the *'effects on sexual function … alongside [the symptom of] fatigue'* (HP013) *… as well [as], medications that are used to treat [AF]*' (HP016). Although HCPs noted the impact on relationships, they did not acknowledge the psychological impact that a lack of understanding from others had on PwAF or the impact of family or friends' worry on the PwAF. They also did not acknowledge that PwAF avoided social activities or the reasons behind this.

5.6 Treatment

Treatment for AF was a theme discussed by PwAF which appeared to improve and decrease HRQoL in different individuals. This theme had three main subthemes which were: anticoagulation, symptom management and support (as shown in Table 5.7).

Table 5.7 AF PROM: Treatment	
Theme	**Subtheme**
Treatment	Anticoagulation
	Symptom management
	HCP's, Online and Other Support

5.6.1 Anticoagulation

The impact of anticoagulation on HRQoL was associated with stroke risk concern and the implications and concern about the side effects of anticoagulants. Concerns of stroke were raised by those with paroxysmal (PA001, PA004, PA005) and persistent AF (PE023, PE025, PE026). This subtheme was also identified as being an important aspect of HRQoL in the psychological domain. PwAF (PA004, PA005, PA001) stated that *'one of the biggest worries'* (PA005) is a '*fear of stroke … even more than death, actually'* (PA005), mainly because of fear of '*what strokes leave in their wake'* (PA005), so that they *'might not be in a position to be able to communicate'* (PA001), and the impact that this could have on them and their families. However, taking anticoagulants such as warfarin or non-vitamin K antagonist oral anticoagulants (NOAC) appeared to reduce this fear of stroke in some PwAF (PE023, PE025, PE026).

Implications of taking regular anticoagulants were discussed by PwAF with paroxysmal (PA001, PA002, PA003, PA004, PA005, PA021), persistent (PE008, PE024, PE025, PE026) and asymptomatic AF (AS019, AS020, AS027, AS028). PwAF with paroxysmal AF appeared to be more severely affected by taking warfarin and discussed the implications for a longer period of time compared to other groups. Although taking medications on a regular basis may be considered troublesome, PwAF expressed that the side effects of warfarin appeared to *'impact more, sometimes, than'* other drugs such as '*beta-blockers'* (PA005).

Across the focus groups, it become apparent that the perceived impact of warfarin on HRQoL amongst PwAF may be influenced by knowledge and understanding of the medication and the length

of time spent on it. The perception that warfarin was a '*poison*' was reported by two PwAF (PA001, PA005). One PwAF described *'accepting warfarin'* as being the '*biggest thing'* for them (PA005), and three PwAF (PA001, PA003, PA005) described feeling anxiety and taking a long time to get '*their head around*' taking this medication (PA001). One of these PwAF (PA001) reported that warfarin caused her to *'confront [her] mortality'* and others agreed (PA003. PA005). The perception of warfarin from one PwAF (PA005) was influenced by observing others on this medication: *'It's like 20 years ago, but it stayed with me that warfarin was the thing that you didn't really want to go to'* (PA005). Although this PwAF (PA005) was *'very reluctant'* when starting warfarin, this fear reduced over time.

Warfarin requires regular blood tests to allow monitoring and alterations of doses. Seven PwAF (PA003, PA021, PE024, PE025, PE026, AS027, AS028) discussed the implications of this. Some PwAF described a change in HRQoL due to getting regular blood tests (PA021). However, some had opposing views, stating that INR tests did not affect their HRQoL anymore because of alternations to their lives (AS027, AS028). For example, one participant (AS027) overcame the implications of regularly travelling abroad by acquiring a personal INR testing machine which allows the results to be sent via email to health professionals for advice regarding dosage of warfarin.

Dietary restrictions resulted in some PwAF placing *'more of a focus on it'* (PA005), which for many PwAF (PA001, PA002, PA004, PA005, PE008, AS020, PA021, PA022, PE025, AS027) was initially a constant reminder of AF and its implications. PwAF noted that avoiding or reducing their intake of foods such as '*cranberries'* (PA005) or drinks such as alcohol (AS027) was necessary to *'manage'* their INR, the implications of which were discussed in Section 5.4.

One of the side effects of anticoagulants is an increased risk of bleeding and bruising; this was a noted side effect of warfarin and NOACs by various PwAF (PA001, PA005, AS020, PA021, PE023, PE025, PE026). These concerns resulted in some PwAF (AS018, AS020, PA021) making lifestyle changes in case of an accident. One PwAF described getting a '*bracelet made up that [says], "I am in AF and I am on an anti-coagulant", and I have got a little card in my purse'* and also the need to *'have plasters in my bag'* (PA021).

Although the risk of bleeding at accidents is viewed as a risk for those on any anticoagulant, those on a non-vitamin K antagonist oral anticoagulant (NOAC) (PE023, PE025, PE026) acknowledged that not having a reversible medication for some NOACs was a significant *'downside'* of this medication (PE026). However, one stated that they assessed this risk by asking themselves, '*how many major traumas have I been through in my life? One'* (PA021). Having a substantial reduction in the number of blood tests per year was viewed as a major advantage by some PwAF:

> *I just thought the benefits outweigh the risks … not being on Warfarin and having to go for lots of blood tests, just, again, has really improved my [HR]QoL against what I think it could have been.* (PA021)

5.6.2 Symptom Management

Some with paroxysmal AF (PA001, PA003, PA004, PA005, PA021) discussed the implications of being on medications such as having dietary restrictions and the '*side effects of medications [which] are very important'* (PA001). However, some with persistent AF explained that not '*know*[ing] *if* [the impact on QoL is] *from the tablets or the AF itself''* (PE008) and other factors such as age (PA004) made it '*very difficult to separate'* (PA001) and identify the cause. Having other comorbidities may influence this perception. Almost all (AS018, AS019, AS020, AS027) PwAF who were asymptomatic discussed the implications of medications on their HRQoL. One (AS027) found taking medications for years had become a habit, which could suggest that the length of time taking medications could affect the degree of impact on HRQoL.

The severity of effect was dependent on the individuals. Some PwAF described severe side effects which in one case resulted in a hospital admission (PA001), while in others (PA001, PA003, PE008, PE009, PE026) caused the treating healthcare providers to alter the medications to reduce or stop side effects. Some PwAF described how either new medications or adjusted doses reduced the symptoms of their AF (PA001, PA003, PA005, AS019, PE023, PE025, PE026).

Those with persistent AF (PE006, PE007, PE008, PE009, PE023, PE024, PE025, PE026) also discussed side effects of medications. Two of these PwAF described digoxin causing negative side effects such as a rash (PE006) or constipation (PE023). One PwAF (PE026) described beta blockers causing sleeping problems such as nightmares and anxiety during sleep which caused tiredness the following day. This same PwAF described side effects from another drug called amiodarone, which was described as being 'extremely unpleasant'. One PwAF (PE007) discussed having a lost interest in sexual relations because of the side effect of medications. Three PwAF (PE023, PE024, PE025) mentioned experiencing nasal drip, which was '*embarrassing*' (PE025).

As suggested in Section 5.6.1, perception of the impact of medications on HRQoL may have been influenced by observing the use of these medications by relatives or friends (PA005). Some PwAF (PA005, AS018, AS019) described a fear, anxiety or awareness about some of their side effects. Three PwAF mentioned the side effects of amiodarone (loss of sight and skin sensitivity to light) which lead to anxiety or non-adherence. For example, an asymptomatic PwAF who was worried

about developing sight problems from his medication stated, '*I read about the side effects with amiodarone and I thought, "I don't fancy this." It affects your eyesight and everything else. Because I drive for a living, so I refused to take them'* (AS019). This view was echoed by another PwAF who refused the medication as she *'won't risk [her] sight'* (PA005).

One PwAF taking a medication that increased sensitivity to sunlight explained how simple tasks became more complicated as total exposure time had to be calculated in advance and precautions planned:

> *One of the side effects of the amiodarone was the sunbathing … I've just got to remember, if I've gone out and I'm out for an hour, it's going to take me an hour to get back. My daughter-in-law used to phone me up and say, 'Dad, it's very sunny out there.' 'But I'm not sunbathing.' That's going back to the family again – when you turn round and say about your medication, it can do this, so they panic more than you*. (AS018)

Symptom management including hospital admissions and catheter ablations were noted by three PwAF with paroxysmal AF (PA001, PA003, PA005), one with persistent AF (PE023) and three who were asymptomatic (AS018, AS019, AS020). None of the PwAF who took part in the focus group had received an ablation, which perhaps may influence their perception. All PwAF who discussed the ablation appeared to have a good understanding of the procedure. The ablation procedure appeared to be a *'last resort'* for some (PA001). However, another PwAF reported feeling reassured that *'if things got worse'*, there were more *'treatments available'* (PA003).

5.6.3 HCPs, Online and Other Support

Support was mentioned as being immensely important to some PwAF (PA001, PA004, PE007, PE008, PE009, PA021, PE025). Those who received little support highlighted that poor communication, '*mixed information, mixed opinions about things … undermines your confidence in what you should and shouldn't be doing'*, *w*hich can leave a negative impact (PA021). The importance of knowledgeable HCPs who communicate effectively with *'good explanation[s]'* was highlighted and viewed as '*helpful'* (PA001).

The need for support was noted by PwAF (PE007, PE008) and appears to stem from the vulnerability and fear that accompanies AF. One described how *'you think you're going to die, but you're not; you just feel like you are*' (PE025). Another PwAF describes how she *'felt very vulnerable, I didn't want to leave my street … but nobody warns you. I think they should. They should really touch on it, because that's probably one of the things that has the biggest impact; you're by yourself'* (PE008).

The support received from charities such as *'the British Heart Foundation' and* AFA, BHF and Health Unlocked was for some '*more information … than [they had] …ever been given from any healthcare professional'* (PA021). This was described by one PwAF (PA021) as making the '*biggest difference to helping [her] cope psychologically and start improving [her] [HR]QoL'.*

5.6.4 Additional Analysis: Treatments: Perspective of Relatives and Healthcare Professionals

All RoC noted that treatment and therapies had an impact on their relatives with AF (RE029, RE030, RE031). Concerns were expressed by PwAF (RE029, RE031) relating to a fear of procedures and therapies and the progress of AF. Although, the impact of medications related to symptom control and risk of stroke was expressed, this appeared to be expressed in less depth compared to the PwAF accounts (RE029, RE030).

The implications of symptom management and associated therapies were discussed by all RoC (RE029, RE030, RE031) in the focus group. Concerns about the side effects of medications were discussed. One PwAF expressed concern there was a negative view of some anticoagulants because of the increased risk of bleeding when using anticoagulants, especially in relation to working life, the need for regular blood tests and its impact on alcohol intake, which led this PwAF refusing anticoagulants.

> *I think the issue that will affect him is the issue of anticoagulation. I think he thinks that will affect his quality of life ... If he has an accident at work, it is going to be a problem; drinking; having to go for blood tests. I think, in his mind he is quite negative about the image of warfarin.* (RE030)

Difficulty tolerating some medications for symptom control led to one PwAF feeling '*no, he didn't tolerate the beta blocker at all … he felt even worse than he did before'* (RE030). Two of the RoC (RE029, RE031) expressed that their relative had had an AF ablation and described how admission to hospital caused distress and anxiety. This was not discussed by the PwAF group. Although experience of treatment and care varied between RoC, one RoC clearly explained the positive impact that good care, communication and support had on the PwAF's HRQoL (RE029). Communicating clearly led to reduced negative emotions caused by AF symptoms and associated treatments, as one RoC explained:

> *The chap we saw … was absolutely brilliant. He kept coming back and sat down, and out came the pad and the pen, 'This is the problem,' and he is drawing pictures. It made*

> *such a difference, it really did. 'That's your heart, this is the problem, this is what's causing it.' Alright, we had already been through it with [the consultant] once, but this chap wanted to go through it again, to reassure, and it did reassure her. She was really reassured that, 'Don't worry, you're here and it's going to be OK.'* (RE029)

Like the PwAF, HCP (HP011; HP015; HP016; HP017) noted that some PwAF voiced deep concern about the increased risk of stroke, '*especially the ones who have had family members who have had strokes and know people who have had strokes'* (HP015). Another (HP016) described having *'one or two, though, that are desperate or want to take anti-coagulation even though their risk was zilch'* (HP016). HCPs (HP011, HP017) described concern that INR control when on warfarin varied:

> *[T]he majority just turn up, 'Oh, it's a little bit high.' They don't really seem to be concerned, but you do get a certain amount of the population that, if it's 1.8 or 1.9, they don't know what they've done. 'What have I done?' 'Why has this happened to me? I thought I'd been so good.'* (HP017)

The implications of taking an anticoagulant drug on QoL were discussed by some HCPs (HP011, HP014, HP016, HP017). One HCP described the regular blood tests as being

> *a constant reminder for them on a regular basis that they're unwell... I think that that's quite psychologically negative for them, just that they can't take control of that themselves; they have to put their trust in a healthcare provider on a weekly basis*. (HP014)

One HCP (HP017) described PwAF raising concerns about bleeding when taking anticoagulants, especially when doing leisure activities, which demonstrates the importance of certain leisure activities to HRQoL. Furthermore, it suggests that AF medications can lead to a decrease of HRQoL through their impact on valued ADL. The risk of bleeding also had the implication of causing PwAF to reduce or stop higher risk activities such as rugby.

> *I had a PwAF who was a rugby player and we had a 20-minute conversation of, 'OK, so what if I just don't get hit? What if they hit my body but not my head? Is that OK?' I was just trying to tell him that it probably wasn't a good idea, but he went through various options that he could still play rugby as long as he dodged really well. It was really, really tough.* (HP017)

HCPs (HP011, HP016, HP017) suggested regular appointments for anticoagulation could provide social benefits for some PwAF as it was an opportunity for them to meet other PwAF, *'especially if you take a lot of PwAF and they come in groups, because most of that age and generation, they're all on Warfarin so it's almost like a social visit down to the clinic'* (HP017).

Although HCPs did not mention specific medications, they (HP012, HP017) did imply that PwAF *'don't want to take any drugs'* (HP017), leading the PwAF to prefer an ablation as an alternative treatment option. While health professionals did not discuss in detail why PwAF prefer not to take medications, some (HP012, HP015, HP017) suggested that PwAF often opt for an ablation procedure to avoid taking medications *'that [are] going to limit me'* (HP017).

HCPs (HP011, HP012) were aware of the need of support and *'reassurance'* (HP012). One HCP described receiving '*as many calls from PwAF that just need psychological support as we do PwAF calling about their symptoms. Sometimes, actually, the phone call about the symptoms is just a mask for them wanting to talk to somebody'* (HP011). This was noted (HP011, HP012, HP014) to some degree as being provided by *'arrhythmia nurses and the preadmission nurse'* (HP014) and charities and websites often provided support for PwAF.

5.7 Findings: Study One

The aim of this chapter was to identify the main aspects of HRQoL which are impacted by AF to allow the item generation of a new PROM for PwAF. The qualitative analysis of data from eight focus groups involving PwAF, RoC and HCPs has allowed the identification of five domains which are impacted or were reported as causing a change in HRQoL. The provisional names of these domain themes are (i) physical or symptom-related effects, (ii) psychological effects, (iii) activities of daily living, (iv) relationships and (v) treatment. A summary of the findings from the different groups follows.

5.7.1 Summary of Results: PwAF

Personal reflections from PwAF provided an insight into how the symptoms of AF and associated negative emotions led to restrictions and limitations on daily activities. Severe symptoms of AF (such as fatigue or shortness of breath) and the unpredictability of symptoms led to some being unsure or unable to keep usual commitments. Activities which were reported as being limited included washing and dressing, diet, sleep, housework, work, travel (short and long distances) and hobbies.

Furthermore, interference during sleep and resting due to AF symptoms made coping with AF and normal activities more difficult for some.

Limitations on ability led to negative emotions (such as embarrassment, guilt and isolation) which affected relationships due to an increase in vulnerability and dependence on others. Loss of libido which was related to the symptoms of AF (mainly tiredness) was reported by a small number of PwAF. Although this was not reported as affecting HRQoL, it was acknowledged this may impact sexual relationships in others. Some with more severe AF symptoms hinted at feeling a stigma attached to this condition which led to further negative feelings and less social interaction. Others expressed clearly feeling that there is no stigma attached to this condition and that they would be happy to discuss it with others.

PwAF expressed fears over the future progression of AF and concerns about the treatments for AF, although some expressed that the variety of treatment options was reassuring. Anxiety and fear about experiencing thromboembolic events or the implications thromboembolic events such as death or increased dependence on others were expressed by most PwAF. The need for treatments or therapies either to reduce the risk of thromboembolic events or to control AF symptoms was reported as negatively affecting HRQoL. Other side effects, although not limiting HRQoL, were reported as being inconvenient and led to some behaviour changes (such as carrying identity cards or being more cautious when carrying out higher-risk activities such as cycling to work). The need for medication that required regular hospital appointments was the only cause of anxiety in some who were asymptomatic of their AF (AS028). Negative psychological implications of living with AF such as anxiety became clear throughout this study and the importance of seeking support from various avenues was reported. The benefit of receiving such support was highlighted.

5.7.2 Summary of Results: RoC

RoC reported similar symptoms as those reported by the PwAF focus groups. RoC reported AF symptoms led to behaviour adaptations, meaning normal daily tasks required more planning and regular breaks. Activities of daily life reported as being limited or negatively affected included diet, cooking, work and travelling (small and large distances). This group highlighted the financial implications of travelling (such as increased travel insurance costs) and access to medical facilities. Although this group overall stated that socialisation was not affected, some noted their *'relationship changed slightly'* (RE029) but were not able to articulate how this impacted HRQoL.

Fear about the progression of AF and about the future treatments of AF was also relayed by this group. They additionally reported the inconveniences associated with treatments or therapies either

for symptom control or for reducing the risk of stroke; the side effects of medication also caused worry. Their perception of the severity of impact on overall HRQoL was reported as being less severe compared to that expressed by PwAF. However, the RoC group suggested that the time since diagnosis, past medical history and personality influenced the PwAF ability to cope with diagnosis of AF. They acknowledged how good communication from knowledgeable staff reduced this anxiety and led to reassurance.

5.7.3 Summary of Results: HCP

HCPs reported similar physical symptoms to those expressed by the PwAF and RoC focus groups. Anxiety related to activities which were perceived as potential triggers of symptoms of AF and fears about thromboembolic events were also reported. This group relayed how PwAF expressed concern or anxiety related to various aspects of their lives (such as travelling, the financial implications of AF, access to medical care, progression of AF treatments and the impact of AF on other relationships) which led to increased dependence on others, including HCPs.

HCP reported how treatments and therapies, particularly the burden of taking medications, side effects and regular hospital appointments caused limitations on activities of daily life mainly because of negative emotions. Although HCPs reported how diet was affected due to taking medications, the impact of this on HRQoL was not clearly expressed.

Although HCP expressed a deeper insight than the RoC group about the impact of AF on relationships, they were unable to provide an insight into why PwAF avoided social activities. HCPs reported that sexual relationships were impacted due to the symptoms of AF and the side effects of medications associated with AF which was also reported by the PwAF focus groups. In addition, the HCPs did not report the influence that a lack of understanding from RoC had on the anxiety experienced by PwAF.

5.8 Study One: Discussion

As far as the author is aware, this is the first study to explore the impact of AF and associated treatments from the perspective of PwAF, relatives and healthcare professionals qualitatively in a London population. One of the main significant findings is the described impact of AF on those who are asymptomatic of AF. Although it might have been anticipated that being asymptomatic would mean there is no impact on HRQoL, this study suggests that some PwAF who are asymptomatic expressed worry about treatments and the associated increased risk of stroke.

Chapter Two describes how disease-specific measures which measure HRQoL in this population reduced HRQoL compared to the general population (Yamamoto et al., 2014); however, one limitation of this study population was that they had previously had symptoms of AF. The patients included in this population were unaware of having AF previously and were diagnosed either because of a stroke or due to opportunistic screening as part of their routine care. There has been a recent emphasis on screening for AF after a stroke due to the increased risk of further stroke. Asymptomatic screening is recommended in all individuals above 65 years and in those who have had a stroke (NHS, 2014; ESC, 2016). Results of this research study complement such guidelines, allowing further insight into the experiences of individuals following a stroke or following diagnosis using newer, home-based technologies such as blood pressure machines which identified an irregular rhythm and led to further investigations in one PwAF. AF-related thromboembolic events such as AF-related stroke can be an important factor leading to a diagnosis of AF (NICE, 2014). Although this theme had a limited number of supporting quotes compared to other themes, this was an important area of consideration because of the potential impact on HRQoL and psychological implications.

Although the responses of the healthcare professionals did not differ significantly from that of the relatives, It could be suggested that the HCPs understanding may be positively influenced by working in a specialist centre. Some of the research studies presented in Chapter Two highlighted that interventions in a specialist centre may have provided biased results (Fiala et al., 2016). Similarly, the results of this study may be biased by the experience and knowledge in this specialist centre. An area of future research may be to investigate if HCPs understanding of the impact of AF on HRQoL is affected by working in a specialist or non-specialist centre. Further to this, investigating if the PwAF understanding of AF is impacted as a result of care received in each specialist or non-specialist centre would be an area of future research.

Physical or symptom-related effects reported by PwAF included chest pain, feeling unwell, fatigued, short of breath and symptoms related to rate or rhythm control such as palpitations. Guidance documents (NICE, 2014; ESC, 2016) and other qualitative studies have identified participants expressing similar symptoms of AF, for example, Medin et al. (2014) identified four main themes (shortness of breath, heart symptoms, chest discomfort and dizziness) in the qualitative analysis of the interviews of participants (n=91) with AF.

When the results of this theme were compared to existing AF-specific questionnaires, all four measures (AFEQT, AFQoL, AFQLQ, QLAF) considered appeared to cover various aspects of this theme. However, there is some inconsistency between the depth of information collected for this domain. For example, the AFEQT does not include an item about chest pain or discomfort but QLAF

asks four additional items about this symptom (if experienced) (in relation to accompanied symptoms and impact on daily activity). Although most of the themes are covered in this domain by existing measures, none of these measures included items related to the themes feeling unwell or the interaction with other medical conditions.

Some measures attempt to capture some of the complex concepts highlighted in qualitative research such as the link between symptoms and concerns surrounding their unpredictability (AFEQT, AFQoL). Such concepts were reported by McCabe et al. (2011), who identified such a theme and its impact on limiting functional ability. The results of Study One have further highlighted how PwAF, especially those with PAF, experience such concepts. Although the results of this domain are similar to existing guidance and literature, the physical symptoms of AF are only one aspect of the impact on HRQoL.

Although prevalence of depression and anxiety in the general AF population is high in several studies, the prevalence of diagnosed depression in the population of Study One is small (n=1). None of the participants enrolled in the study had a diagnosis of anxiety. Literature has examined the link between AF, depression and anxiety (McCabe, 2010; Patel et al., 2013; Galli et al., 2017), with some literature (Schnabel et al., 2013) suggesting that anxiety or depression may affect the haemodynamic function of the heart, leading to increased risk of AF. The results of one literature review suggest further longitudinal research in this area (Galli et al., 2017). Regardless of the exact cause in this complex interaction, those who are asymptomatic of AF have been found to have lower levels of HRQoL, including in mental domains, suggesting the symptoms of AF are not the only cause of reduction of HRQoL (Savelieva et al., 2001; Yamamoto et al., 2014).

Another research study (Thompson et al., 2013) suggests that depression or anxiety may influence the perception of symptoms. As already described elsewhere in this thesis, the length of time since an episode or negative experience surrounding AF may have also impacted perception.

The psychological implications of AF in this study related to anxiety and coping with AF. Implications of this domain were complex and related to other domains of HRQoL, for example, limiting daily activities and impacting relationships with others. Although anxiety was a prominent theme discussed across these focus groups, a recent review of literature on older people with AF highlighted that general mental health was a subdomain least affected by AF and suggested that age and life experience may impact an individual's perception of AF (Zhang et al., 2015). Findings from the RoC group acknowledge experience may impact perception.

Although limited in size, findings presented in several of the qualitative studies were similar to the findings from Study One. For example, McCabe et al. (2011) reported that participants expressed anxiety related to the unpredictability of AF symptoms, limitations on daily activities and anxiety about increased stroke risk.

One study suggests that treating the symptoms of AF alongside the treatments of other comorbidities such as depression or anxiety would be of benefit (Thompson et al., 2013); this is also in keeping with NICE guidance (2014). In addition to anxiety surrounding AF, negative feelings such as 'not feeling like myself' or feeling down or depressed were reported in Study One. HCP reported that AF impacted PwAF's lives, and *'not in a positive way'* (HP017) overall. HCPs acknowledged the negative impact that AF can have on the psychological well-being of PwAF, with some suggesting more emphasis was needed to be placed on this aspect of HRQoL. Although coping with AF is considered important by qualitative literature, this is not covered in any of the other measures considered.

Qualitative literature has also highlighted participants' ability to cope and need for support. For example, McCabe et al. (2011) report some participants felt 'uninformed and unsupported'. The impact of a lack of information and poor communication was also highlighted by Aliok et al. (2015), who reported poor coping, especially in relation to the management of essential anticoagulants and dietary implications. This is highlighted in other literature also (Corbi et al., 2011). The qualitative study by Altiok et al. (2015) furthermore highlights some positive methods participants used to cope with AF. Such recommendations are also noted in guidance documents such as NICE (2014), which outlines that further psychological support should be provided if needed. Most of the measures considered mention anxiety to some degree but this is not the primary focus of any of the measures, most of which focus on symptoms and treatments.

Activities of daily living, often referred to as functional ability, is a key aspect of HRQoL (Bowling, 2004; Andersson et al., 2014). Bowling (2004) describes that measures of HRQoL focus on various aspects of activities of daily living such as mobility (for example, ability to walk), self-care (for example, washing and dressing) and instrumental activities (for example, ability to work) but often measures ignore other aspects such as emotional, social and financial needs which may be considered more important depending on the individual. Furthermore, Bowling (2004) suggests that the impact on ability to perform household chores (such as cooking) is also largely ignored in measures. This variability in focus may be due to clinicians developing such measures and has been noted when reviewing existing AF-specific measures.

From the qualitative data, the symptoms of AF directly limit activities but also restrictions can be self-imposed due to the perceived impact of AF. A study by Altiok et al. (2015) reported activities (such as housework and exercise) which were self-associated with triggering symptoms of AF were often limited or avoided. This study also reported the symptoms of AF were reported as restricting activities of daily life in twenty-four participants interviewed (total n=32). Similarly, findings from the semi-structured interviews (n=11) with participants with AF reported activities were limited or individuals adjusted their lives to cope with AF symptoms (Deaton et al., 2003). This was reported as being so severe in some individuals that some sought early retirement or alternative employment. This study produced a similar finding.

Although literature solely focusing on the activities of daily life domain in the AF population appears to be limited, one study compares treatment by catheter ablation to antiarrhythmic drugs and records the impact on aspects of daily activities. This study included a questionnaire which recorded the perceived impact and the impact of AF on performance. This questionnaire appears to be developed solely for this study and included items regarding the impact of AF on everyday activities and additionally the impact of AF on vacations, fears and the physical difficulties of driving due to AF (Bubien et al., 1996). The findings of this study report significant self-reported improvement in activities, such as driving at one and six months post catheter ablation. This study highlighted that 'self-imposed restrictions' on activities were related to negative HRQoL scores as measured by the SF-36 (Bubien et al., 1996).

Some AF symptom classifications such as the European Heart Rhythm Association classification (EHRA, 2010) note the importance of this domain by measuring the level of impact of AF-related symptoms on normal daily activities in three of four AF symptom classifications. A later study of the measures modification (Wynn et al., 2014) led to the subdividing of one classification, allowing the clinician to indicate whether the symptoms are affecting activities of daily life and whether or not the symptoms are troublesome to the patient. Such a modification highlights the variability between individuals i.e. how some individuals may be troubled by mild symptoms and others may not; this is also highlighted by some guidance documents (ESC, 2010). The perception of the degree of impact and level of adjustments made by the individual to perform usual activities may be impacted by the length of time since adjustments commenced (Bowling, 2004).

Although symptom questionnaires have highlighted that that AF symptoms can impact activities of daily life, restrictions on activities of daily life may also be due to associated medication, as has been highlighted by guidance documents (European Society of Cardiology, 2010). For example, athletes commencing some anti-arrhythmic medication are recommended to avoid sports for a period to allow these medications to become effective. Those on anticoagulants are recommended not to perform

high-risk sports (European Society of Cardiology (ESC; 2010). This could mean athletes may have to have an appendage occlusion device inserted, a costly and invasive procedure whose use in the NHS is restricted to those unable to take anticoagulants, or avoid high-risk sports which could have financial and work implications. Disappointment about such restrictions was highlighted in this study (Chapter Five).

Disease-specific HRQoL measures were reviewed (Appendix E 6.3.3) and although each of the measures include various items relating to activities of daily life affected, none are consistent in the number of items or specific areas of activities of daily life recorded. For example, three measures include items regarding the impact of AF on exercise (AFEQT; AFQoL; AFQLQ), two of the measures reviewed include items regarding diet (AFEQT; AFQLQ) and one includes items regarding hobbies (AFEQT).

Although disease-specific measures include items in this domain, these items are often broadly phrased. For example, item seven in the AFEQT (Appendix B.3.2) asks, "How much difficulty have you had in doing any activity because you felt tired, fatigued, or low on energy?" The inclusion of broadly worded items may be to increase the generalisability of items. However, none of the measures reviewed clearly ask participants about the impact of AF on sleep, work, washing and dressing which have been highlighted as important in this study.

Although qualitative literature (Altiok et al., 2015) noted the negative impact of AF on cooking, none of the reviewed measures includes any items that clearly record the impact of AF on cooking. Differences in perception of impact between healthcare professionals and individuals with AF is highlighted in the findings of Study One. As already reported, ability to cook was reported as being negatively affected because of AF symptoms by some individuals with AF. However, this was not reported by the HCP focus group. Such inconsistencies may further highlight differences between perceptions of PwAF and HCP and the importance of including people with the condition in the development of measures.
Although the importance of the impact of AF on activities of daily life has been highlighted in qualitative and quantitative literature, available measures do not appear to include detailed items about the impact of this condition on such activities. The variability in focus between measures could be argued as highlighting the need of inclusion of participants with AF in the development of this measure.

Limited studies report the impact of AF on the relative or the relative's perception of a PwAF. However, one study (Dalteg et al., 2014) explored the impact that uncertainty surrounding AF had on their relationship. Only two measures (AFEQT, AFQOL) included any items regarding relationships,

and only one of these measures (AFQOL) included the impact on sexual relationships. It is understood that such items may be viewed as taboo depending on the culture; however, such concepts may be important to explore if such a limitation or impact is affecting the HRQoL of a PwAF.

McCabe et al. (2011) reports patients expressed emotional distress related to disappointment relating to treatment effectiveness which is similar to the views expressed by the HCP in Study One. As outlined in Chapter Two, most of literature surrounding AF are quantitative studies which investigate the impact of AF treatments or interventions such as anticoagulants, catheter ablation or drug therapies on HRQoL. Many of the measures used are generic measures but there appears to be an increase in the number of disease-specific measures which are used. The main findings of interventions and treatments on HRQoL have already been presented in Chapter Two. Most of the measures considered have attempted to capture some of this domain. However, the amount recorded is inconsistent between measures. Although some of these measures include items which attempt to capture the side effects of such treatments such as bleeding in those on anticoagulants, only one attempts to capture the inconveniences associated with attending appointments or the potential food interactions associated with taking VKAs. However, at the time of the development of these measures, NOACs either were not available or were only recently available and therefore the impact that these may have may not be captured by current measures. With recent focus on comparing such therapies, this study has added to the body of knowledge and allowed the exploration of the views of individuals with AF who are on NOACs.

5.8.1 Study One: Limitations

There are several limitations to this study. One is the number of participants recruited. As the study was advertised online, it is impossible to know how many PwAF considered taking part in this study. Although 31 participants were enrolled into this study due to PwAF withdrawals, enrolment numbers were slightly smaller than anticipated (n=32-48). This left some focus groups with small numbers (i.e. n=2 or n=3). Proceeding with focus groups with such small numbers was less than ideal. However, cancellation due to the last-minute withdrawal of some PwAF was considered unprofessional and unfair to the others participating with travel arrangements in place. The withdrawal and refusal of PwAF may have been influenced by the burden which was potentially placed on PwAF or RoC. Some PwAF and RoC who were approached appeared to show passive interest regarding the study. However, upon realising that participation would involve travelling to London to attend a focus group with no financial incentive, interest in participation was lost and viewed as inconvenient. It is possible that individual interviews arranged at a convenient time and place for each participant (e.g. at the hospital on the day of an existing appointment) may have increased the number of participants, but this was impractical. In addition, this change of methodology may have reduced the range of topics

discussed. Although this potential limitation is acknowledged, even with a smaller number of participants, this methodology allowed a range and depth of data to be captured, allowing the aim of this study to be achieved.

Recruitment for the focus groups relied upon the convenience sampling methodology, which was considered the most appropriate methodology. Upon reflection, capturing the view of PwAF who have had an AF ablation may have been beneficial to provide an additional viewpoint. The focus groups included volunteers who were happy to voice their experiences in a group setting in the English language. Therefore, PwAF enrolled needed to have a level of English sufficient to communicate with others about their experiences and the impact of AF on their HRQoL. The location and times of the focus groups along with these being completed in the English language may have influenced who had opportunity to participate.

Following the focus groups, the limitation of this methodology was further highlighted to the researcher. One PwAF in the focus group explained by letter (Appendix D.5.6) the severe impact that AF can have on sexual relationships. However, this PwAF felt this information was too sensitive to be shared in the presence of other members of the group. Therefore, it should be considered that some PwAF may have experienced similar fears regarding expressing this sensitive topic in the presence of others, potentially leading to the true impact of this theme not being fully captured. Upon reflection, this could have been overcome by individual interviews.

5.9 Conclusion

This study has presented the results of eight focus groups involving participants with AF (paroxysmal AF, persistent AF, asymptomatic AF), relatives of those with AF and HCPs who care for PwAF. The main themes identified were:

1. Physical or symptom-related effects
2. Psychological effects
3. Activities of daily living
4. Relationships
5. Treatment

The above identified themes are supported by quotes from the participants throughout. Additional supporting quotes can be seen in Appendix D. Items in a new HRQoL measure will be based on the results presented in this chapter. The next chapter will describe the next stages of this overall study, which involve item selection and the initial content validation process of the AF PROM development.

Chapter 6. Item selection and content validation of AF PROM: expert panel (n=6), expert and patient independent review (n=8), interviews with participants with atrial fibrillation (n=6) and interviews with participants with AF and healthy participants (n=12).

The development of a HRQoL measure suitable for use in an AF population with patient involvement throughout was the overall aim of this study. Eight focus groups allowed the identification of the main domains of HRQoL which were affected by AF. These focus groups involved PwAF (n=21), relatives of PwAF (n=3) and healthcare professionals with specialist knowledge of AF (n=7). Chapter Five presents the impact of AF or its treatment on patients' HRQoL from the perspectives of patients, relatives and healthcare professionals. Although each experience of AF was unique to these individuals, clear commonalities in experiences were evident. Analysis of the focus groups' content indicated that five main themes or domains were affected by the condition: Physical or Symptom-Related Effects, Psychological Effects, Activities of Daily Living, Relationships and Treatment. The degree of impact of AF on HRQoL was variable between participants with AF; some expressing the impact as being severe and others describing it as minimal. The symptoms of AF as well as the risks of other comorbidities associated with AF led to some participants with AF expressing negative feelings such as increased anxiety, hopelessness and despondency. To manage living with AF and its impact on HRQoL, participants with AF noted modifying their behaviour and activities such as pacing activities or reducing social activities. The direct impact of the symptoms, associated emotions and modified behaviour was expressed as negatively impacting activities of daily living at home, work, social life and relationships. Some PwAF expressed that the treatments of AF and associated therapies caused negative feelings such as increased anxiety or concern. This chapter (Six) will describe the next four stages of the development of AF PROM which are focused on item selection and initial validation of this measure.

6.1 Aims and Objectives

The overall aim of Chapter Six is to describe the process of item selection and content validation of the initial AF PROM.

The objectives of Chapter Six are to:

6.1.1 Assess face validity of the five domains of HRQoL affected by AF identified by the focus groups in this study.

6.1.2 Identify suitable items based on the five domains presented in Chapter Five to form a preliminary HRQoL measure suitable for use in an AF population.

6.1.3 Assess content validity of items in the preliminary HRQoL measure and remove redundant items.

6.1.4 Assess the content and face validity of this preliminary measure to assess its suitability for the preliminary validation stage.

6.2 Methods

Addressing these objectives involved a series of structured consultations with clinicians, people with atrial fibrillation (PwAF) and relatives (these are outlined in Figure 6.1). The method, sample characteristics and results of each of these studies will be presented in this chapter.

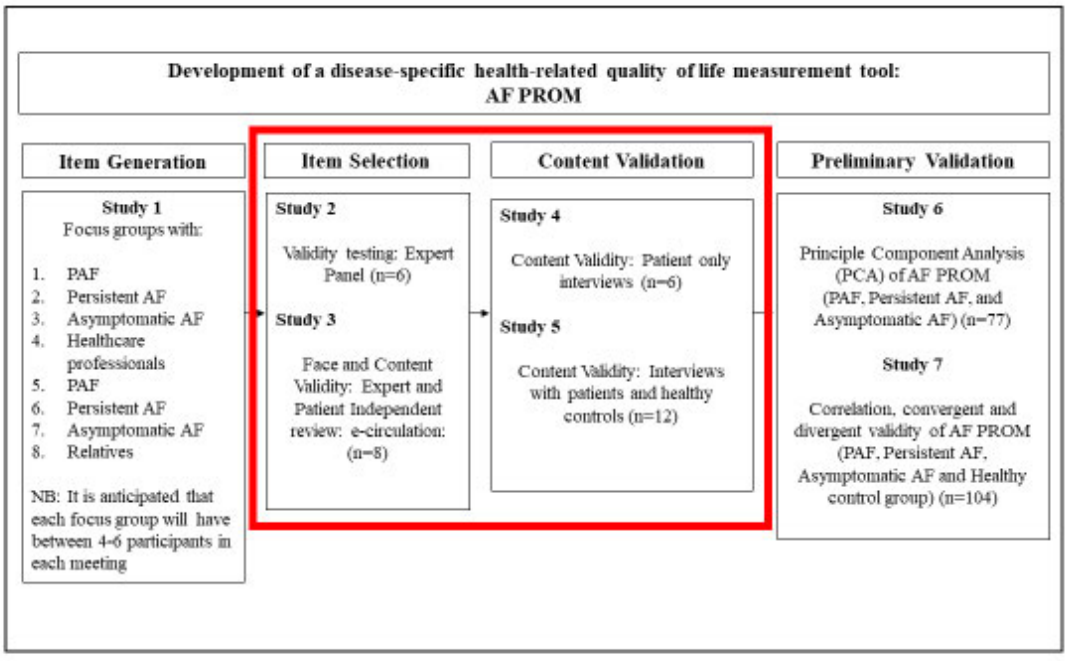


Figure 6.1 AF PROM Overview

6.3 Item Selection: Study Two

To achieve the initial objective (6.1: assessment of face validity), an expert panel (n=6) met on one occasion (90 minutes) to consider the face and content validity of the five themes of HRQoL that had emerged from the focus-group analysis. The expert panel rated the themes based on importance and relevance and commented and discussed the suitability of these themes and individually rated each of them in relation to importance and relevance – with specific consideration given to the different subgroups of AF (asymptomatic, paroxysmal and persistent AF). The panel members individually rated the importance and relevance of each theme using a four-point rating scale (1= not relevant or important, 2 = somewhat relevant or important, 3 = quite relevant or important and 4 = very relevant or important).

Following this expert panel meeting, researchers (SH, MH and MC) met to review the experts' ratings and comments. The content validity index (CVI) was calculated based on the experts' quantitative responses (CVI = number of experts who gave a rating of three or four divided by the total number of experts). CVI allows the assessment of the content validity of AF PROM by calculating the agreement of the relevance and importance of items or domains amongst the expert panel and has been used in other studies (Polit and Beck, 2006). This method works on the principle of reducing the rating options from four to two; resulting in items or domains being classed by the panel as relevant or not relevant and meaning the probability of being rated relevant or irrelevant is fifty per cent. Although Lynn (1986) proposed that the number of panel members should be between three and ten, in practice this method has been used with smaller numbers of experts (such as two in the study by Fowles and Feucht (2004)) and higher numbers (such as fifteen in the study by Zamanzadeh et al (2015) or by Roberts et al (2017)), with some researchers suggesting that larger numbers should be used so to reduce the probability of chance factors (Zamanzadeh et al, 2015). Lynn (1986) further proposed that validity is dependent on the number of experts, and in studies where there are five or less experts there should be unanimous agreement (CVI score of 1.0). Although used in many studies, this method has received much criticism, with some researchers viewing it as the '*most primitive approach*' (Cohen, 1960 pp. 38) for not allowing insight into the levels of agreement with others and suggesting that further statistical analysis to assess probability (such as kappa coefficient) be used in addition or instead of CVI (Wynd et al, 2003; Polit and Beck, 2006).

Although this methodology may have limitations, it was considered appropriate as part of the development process and important as a systematic, repeatable and feasible approach for capturing the face and content validity assessments of the expert panel members.

6.3.1 Methods: Study Two

The expert panel (n=6) included the research team, comprising of a research nurse (SH); a mental health nurse academic (MH); and an academic health psychologist (MC), together with three additional members: an EP cardiac consultant with a research interest in AF, a research nurse manager who coordinates several AF-specific research studies and an AF patient charity lead.

6.3.2 Results: Study Two

Overall the feedback from the expert panel (Table 6.1) supported the relevance and importance of all five domains. Most discussion focused on three domains concerning 'Psychological', 'Activities of Daily Living' and 'Treatments' and related to the domain names and relevance to the asymptomatic AF population.

Table 6.1 Study Two: Expert panel theme CVI rating

	Theme 1: Physical (total n= 6)	Theme 2: Psychological (total n= 5)	Theme 3: ADL (total n= 5)	Theme 4: Relationships (total n= 4)	Theme 5: Treatment (total n= 4)
1a: How important is this domain of HRQoL for patients with: Paroxysmal AF?	1	0.83	0.83	0.83	0.66
1b: How important is this domain of HRQoL for patients with: Persistent AF?	1	0.83	0.83	0.83	0.66
1c: How important is this domain of HRQoL for patients with: Asymptomatic AF?	1	0.66	0.66	0.66	0.66
2: How closely do you feel the participant quotations shown reflect this domain?	1	0.83	0.83	0.83	0.66
3: How well do you feel the domain name reflects this area of HRQoL?	1	0.33	0.33	0.83	0.66
4: How closely does this domain reflect the concerns of the patients that you work with?	0.83	0.83	0.66	0.83	0.66
5a: In your setting, how relevant do you feel this domain is in: Paroxysmal AF?	0.83	0.83	0.83	0.83	0.66
5b: In your setting, how relevant do you feel this domain is in: Persistent AF?	0.83	0.83	0.83	0.83	0.66
5c: In your setting, how relevant do you feel this domain is in: Asymptomatic AF?	0.83	0.83	0.66	0.66	0.66

Please note, one member (003) of the expert panel had to leave early and could not complete the responses regarding treatment. Therefore, this data is missing.

Please also note, another panel member (007) only completed one domain section (Physical).

The expert panel reported that overall the themes in the 'Physical' domain were consistent with the focus-group content derived from PwAF. The relevance and importance of this domain had the most agreement amongst the panel with a CVI score of 1 or 0.83 for all theme statements relating to this domain.

There was agreement amongst researchers for most of the questions regarding the importance and relevance of the 'Psychological' domain with CVI scores (mostly 0.83) supporting this statement. The importance of this domain was highlighted by the qualitative statements reported. For example, a panel member recalled a PwAF reporting that '*AF* [was worse than] *than death*' (EP1003). However, one member (EP1002) indicated that this area is not important to PwAF who are asymptomatic with their AF. This domain was the focus of much discussion and this led the panel to suggest that the domain title 'Psychological' should be further considered. This was supported by the qualitative feedback and by the low CVI score (0.33). Based on the expert feedback, the name of the domain 'Psychological Effects' was updated to 'Your Feelings'.

The CVI scores (0.83) for the relevance of the domain concerning 'Activities of Daily Living' reflected agreement amongst the panel that the focus-group findings supported the inclusion of this domain; however, the panel suggested that the domain title 'Activities of Daily Living' required further consideration. This feedback and the low CVI score for the domain name (0.33), led to the name being updated to 'Your Activities'. Although one participant (EP1001) rated this domain as important and relevant (four out of four) for all PwAF, they reported, 'However, I don't think the patient has the opportunity or the time to ask in clinic'. Another participant (EP1002) reported that this domain was not very important or relevant to those with asymptomatic AF but rated it as more important for those with paroxysmal or persistent AF.

Although there was agreement amongst most of the expert panel that the 'Relationship' domain was an important aspect of HRQoL (CVI score 0.83 agreement in relevance in paroxysmal and persistent population), one panel member (EP1002) suggested this would be less important or relevant for people with asymptomatic AF. There appeared to be some agreement about this as the CVI scores for items relating to relationships in this population was lower (CVI 0.66). Furthermore, another member suggested that this aspect should be dealt with sensitively as 'this may off put some patients' (EP1001) answering questions.

Most participants agreed that domain four (Treatment) was an important and relevant domain relating to all those with AF, and the quotations presented adequately reflected this domain. Although all who responded suggested a score of three or four, resulting in a CVI of 0.66 for the suitability of the current title, two panel members additionally reported the term '*therapy*' might be more suitable.

Following the panel group meeting, SH, MH and MC reviewed the qualitative and quantitative results. The five domain names were updated to:

1. Physical or Symptom-Related Effects
2. Your Feelings
3. Your Activities
4. Relationships
5. Treatment

6.3.3 Discussion: Study Two

The use of expert panels to assess the face and content validity is commonly used in questionnaire development (Fayers and Machin, 2016). The feedback from members of the expert panel was a key part of ensuring the face and content validity of the five domains of HRQoL allowing objective 6.1.3 and 6.1.4 of this chapter to be achieved. Although this stage did not include any PwAF, the panel composition included five members who were very familiar with AF, its impact on HRQoL, its treatment and treatment pathways. One of these experts was a patient representative (with an authoritative position in an AF charity). One member of this panel was less familiar with AF, but was able to prepare for this meeting by considering the impact of AF on HRQoL by reviewing the literature review (Chapter Three) and the main themes identified from the focus groups (Chapter Five) prior to this panel meeting. Including a panel familiar with AF encouraged focused and constructive discussions to take place which is a benefit of this stage. A potential limitation of this stage was the variability of number of responses (responses n=4–6) with two of the panel not completing all feedback items for the domains, which has impacted results (see Table 6.1). Although the formal meeting was conducted over 90 minutes, which could be considered a limitation, further discussions and email correspondence occurred between all members of the expert panel to clarify statements and conclusions.

6.3.4 AF PROM: Item Generation

Following the results of Study Two, researchers (SH, MH and MC) met on two occasions. SH generated draft items associated with the five main themes noted in Study One in preparation for these meetings. Aspects of the development of AF PROM (such as the phrasing of stems and number of item response options) that were discussed during the meetings can be seen in Table 6.2. The first meeting focused on constructing an initial version of AF PROM (version one [see Table 6.3]) with items that mapped onto the derived themes (noted in column three of Table 6.4). Following

development, main themes covered in existing AF-specific measures (AFEQT, AFQoL, AFQLQ, QLAF) were discussed by the researchers and the results are presented in Appendix D 6.3.1–6.3.5. In addition to the two meetings, email correspondence allowed a series of reviews of AF PROM leading to the development of several versions (version 2 to version 6 (highlighted in Table 6.5)) in preparation for Study Three. The final meeting between the researchers allowed the face validity of AF PROM to be assessed, which involved comparing initial items to the focus-group content and comparing the draft scale to the other available measures of HRQoL for this patient group.

Table 6.2. Generation of items: Points for consideration during discussions

Aspect of PROM	Under consideration during discussion	Was this achieved in AF PROM (v1) or not achieved?
Disease specific	Specific to those with AF (asymptomatic, PAF and persistent AF).	Only three items included a statement which referred to the PROM being specific to AF. Upon reflection of version one, this was not achieved sufficiently in version one and led to the inclusion of atrial fibrillation (AF) in an opening statement to make this specific to AF in later versions.
Question format	Aim: create items which are worded clearly, brief, easy to understand and easy to answer. Potential use of stems? Avoidance of double negatives. Use of bold and underline to highlight instructions or time frame.	Several main stems were used to reduce the word count in the measure, reducing patient burden and making it more aesthetically pleasing for participants.
What is the stem trying to measure?	The relevant use of phrasing of bothered/extent ability. Affected/impact/affect/burden/occurrence of symptoms.	The appropriateness of the phrasing of each stem was considered. The first stem aims to measure the impact of bother of physical symptoms, treatments and feelings. The second stem records the extent of effect on activities. The final stem measures the negative effect on social life and relationships. Initial items were listed under potential stems. It was aimed to list items in a relevant order to make most sense to the reader: for example, physical symptoms were listed together. These were listed under the domain titles for initial development but titles were removed in later versions.
Length of period of time for questionnaire?	Hours/day(s)/week(s)/month(s)/year(s).	Although each option was discussed, it was decided to use the phrasing one month, as it is more likely to capture occurrences those with less occurrences of AF (i.e. asymptomatic or PAF).
Response options	Open or closed items? Use of binary format (yes or no)? Ordinal scales (i.e. ranking/grading: low to high)? Use of sub items? The use of statements (degree of agreement/disagreement)? The use of visual analogue scales (VAS)? Use of Likert scales? Use of Guttman scales (although mostly used in items relating to activities)?	The benefits of the use of closed and open items was discussed, however, to reduce patient and clinician burden it was decided to use closed items. Several versions of individual items were drafted to investigate the potential use of: items with binary responses, statements, Ranking items, VAS and Gutman scales. In version one, the use of statements was further investigated, however it was removed in future versions to allow consistency between items and reduced patient burden.
If ordinal, how many response options?	Odd or even number of responses? Between 3–7 options?	Researchers discussed an argument that suggests by having an even number of response options this leads participants being forced to respond, removing their option of a don't know category. Researchers also discussed the implications of having more than five options with some studies suggesting participants cannot reliability discriminate between the response options (Fayers et al, 2012). Throughout discussions, items were drafted and included a number of various number of responses options (between 3-7). After discussion, it was considered that a five-point Likert scale would be sufficient, providing less options, therefore reducing patient burden and be more aesthetically pleasing.
Phrasing of Likert items?	No/not applicable/not at all/a little bit/a bit/ moderately/quite a bit/a lot/extremely.	It was decided to use 'Not at all, a bit, moderately, quite a bit and extremely'. Such phrasing was considered appropriate to use for each of the stem items.
Reading level	Low/medium/high reading level.	It was hoped to use terminology that was appropriate to the layman to improve understanding of the PROM and improve the number of responses.
Number of items?	Sufficient to capture impact but considerate of the impact of patient burden.	It was hoped to have an initial maximum of 30–35 items at this early stage to allow removal of items which were irrelevant or inappropriate at a later stage.
Format	Paper/electronic version? Font size?	It was hoped the initial draft would be suitable for both paper and electronic format. Large enough font size to aid reading.
Content/themes covered in existing AF-specific measures	Themes covered by existing measures discussed.	Themes missing from existing questionnaires (AFEQT, AFQoL, AFQLQ, QLAF) were discussed by the researchers and the results are presented in Appendix D 6.3.1–6.3.5.

Table 6.3 AF PROM (Version One)						
Items	**Version 1 (original)**	**Response options**				
Stem	**During the past 4 weeks, how much have you been bothered (by the following)?**	**Not at all**	**A bit**	**Moderately**	**Quite a bit**	**Extremely**
Domain Title: Physical Symptoms						
1	Pain					
2	Palpitations (heart fluttering)					
3	Fast heartbeat					
4	Slow heartbeat					
5	Feeling unwell					
6	Tiredness					
7	Feeling light-headed/dizziness					
8	Blackouts					
9	Shortness of breath					
Domain Title: Your Treatment						
10	Side effects of medications					
11	Side effects of anticoagulants					
12	Attending medical appointments (outpatients, check-ups, investigations or admissions)					
Domain Title: Your Feelings						
13	Feeling anxious or worried about the future					
14	Feeling anxious or worried about my treatments					
15	Feeling down or depressed					
16	Feeling I can't cope					
17	Not feeling like myself any more					
18	Not being able to do things I used to (like sports or hobbies)					
19	Not being able to eat or drink the things I used to (like drinking coffee, alcohol, particular foods)					
Stem	**Over the past 4 weeks, to what extent has your ability been affected in relation to:**					
Domain Title: Your Activities						
20	Your daily needs (such as washing and dressing)?					
21	Your household chores (such as cooking and cleaning, shopping)?					
22	Your usual leisure activities (such as gardening, sports)?					
23	Your usual study or work?					
24	Your sleep and rest?					
25	Your day-to-day travel?					
26	Going on longer journeys (like holidays)?					
27	Getting about (at home and inside)?					
Stem	**How much would you agree with the following statements: 'I feel that since diagnosis AF has …'**					
Domain Title: Social/Relationships						
28	Since diagnosis AF has negatively affected my relationships with friends and family.					
29	Since diagnosis AF has negatively affected my sexual relationships.					
30	Since diagnosis AF has negatively affected my social activities.					

Table 6.4 Generation of items: Amendments of AF PROM leading to Version Seven for Study Three

Theme	Sub theme	AF PROM Items (version one)
Physical or Symptom-Related Effects	Pain/discomfort	1
	Thromboembolic events	11, 13
	Heart rate or rhythm	2, 3, 4
	Feeling unwell, tired and shortness of breath	5, 6, 7, 8, 9
	Interaction with other medical conditions	13
Psychological effects	Anxiety and worry	13, 14
	Implications of AF-related restrictions on day-to-day life	15, 16, 17, 18, 19
	Coping	15, 16
Activities of daily living	Diet	19, 21
	Housework	21
	Medications	10, 11
	Sleep	24
	Travel	25, 26, 27
	Hobbies	18, 22, 30
	Washing and dressing	21
	Work	23
	Socialising	18, 21, 23, 28, 29, 30
Relationships	Lack of understanding	13, 18, 19, 30
	Being a burden to others	28
	Causing Friends or family to worry	28
	Socialising	18, 21, 23, 28, 29, 30
	Avoidance	23, 28, 29, 30
	Sexual Relationships	29
Treatment	Anticoagulant	11
	Symptom management	10, 12, 14
	HCP's, Online, and Other Support	*Noted: missing in v 1&2

Table 6.5 Comparison AF PROM (Version One) to themes from the focus groups

AF PROM version	Upon reflection: noted potential limitations of this version	Justification or resulting changes
One	Large font size improves reading but content covers three pages in paper format.	Font size reduced. Questionnaire content reduced to two pages.
Two	V2 does not include introduction section with context/aim of the measure. Review wording of stems. The inclusion of domain titles may be a distraction and may not be beneficial for the reader. After comparing draft items to domains, it was noted v2 did not include an item to cover sub-domain support. The use of statements in the relationship domain was reconsidered.	Introduction with context and aim drafted and included in v3. Stem (1) reworded to improve readability. Domain titles removed in v3. One item was added to attempt to capture the domain support in v3. Agreement statements removed. All items in the measure used stem questions to maintain consistency and improve readability of measure. As a result of this change, one item (normal social activities) was relocated under stem two to improve the readability of the measure.
Three	Make more aesthetically pleasing. Introduction (aim and context section) require editing and formatting changes.	Addition of City, University of London and Barts Health NHS Trust logo in v4. Formatting and editing changes to Introduction (aim and context section).
Four	Make more aesthetically pleasing in paper format.	Further formatting and editing changes to Introduction (aim and context section) and logos. Online AF PROM draft developed based on v4.
Five	No changes to the content of AF PROM but v5 was edited to allow feedback focused on relevance and clarity of each item (electronic and paper format).	Upon reflection, this should have been referred to as another title and not referred to as another version of AF PROM.
Six	Final checks of the measure to improve measure prior to sending to experts.	Final formatting changes prior to sending to experts i.e. font size altered to improve readability in paper version of v7 which is presented to the experts.

6.4 Item Selection: Study Three

To allow the content and face validity of preliminary items of AF PROM to be assessed, experts and PwAF (total n=8) independently reviewed initial items of AF PROM (version seven, version eight and version nine). This stage enabled improvements to be made to the content and phrasing of items. Participants were sent the questionnaire drafts as an electronic format (n=5) or a paper format (n=3), dependent on their preference, together with a rating form. Following their review, items were rated on relevance and clarity using a five-point rating scale (1= very relevant or very clear, 2 = relevant or clear, 3 = neutral, 4 = not relevant or clear and 5 = irrelevant), and they had the opportunity to elaborate with comments and suggestions for changes and additions. Agreement of the panel was assessed in relation to the items' relevance and clarity for each version. Quantitative and qualitative data was reviewed for each version by researchers (SH, MH and MC). Proposed amendments were discussed and only occurred when all three researchers unanimously agreed that such a change was appropriate and consistent with the original data presented in Chapter Five.

Response rates during Study Three were variable. AF PROM version seven was sent to five participants with a response rate of five; however, one response was completely qualitative and not consistent to the quantitative format requested. Version eight was sent to three PwAF with a response rate of one. Version nine of AF PROM was sent to three participants with a response rate of two.

6.4.1 Methods: Study Three

Version seven was reviewed individually by three EP cardiac consultants with a research interest in AF (one of whom was involved in the HCP focus groups in Study One and another who was involved in the expert panel in Study Two), a research nurse (who was involved in coding 25% of the data presented in Chapter Five) and one research nurse manager (who was involved in the expert panel in Study Two). Version eight was reviewed by a PwAF who had persistent AF and was involved in the focus groups. Version nine was reviewed by one PwAF with paroxysmal AF who was involved in the focus group in Study One and a nurse academic who has an interest in chronic conditions and has been involved in the development of several questionnaires. Characteristics of the healthcare professionals are kept vague in this thesis to respect their confidentiality.

6.4.2 Results: Study Three

Three different versions of AF PROM were reviewed by individuals who were considered by the researchers as being experts. Feedback regarding each version was reviewed by SH, MH and MC and amendments were made after discussions between the researchers. Disagreements were discussed and amendments were made if all researchers agreed that an amendment was appropriate and was consistent to the data collected from the focus groups.

6.4.2.1 Results: Study Three: Version Seven

Three cardiac consultant specialists, one cardiac research nurse manager and one cardiac specialist nurse, all with much expertise and research interest in AF, provided written feedback on version seven (n=5). The feedback from one participant was completely qualitative, focusing mainly on formatting changes which was not consistent to the quantitative format requested. Although reviewed by researchers and considered beneficial, these results could not be tallied or presented in this section. The additional four healthcare professionals rated the thirty-one draft items for their relevance and clarity. Feedback at this stage led to several amendments of version seven that are highlighted in Table 6.6.

Column one of Table 6.6 shows the quantitative responses from the participants. Overall, members rated 32% (n=10) of the items as being both very relevant and very clear. Only one member rated that two items (1 and 4 in version seven) were irrelevant or meaningless. One member indicated that some items (21, 25, 26 and 29) relating to the domain 'Your Activities' were not relevant or were unclear; however, no comments were made relating to these items for further explanation apart from item 29 (in version seven) in which one member suggested '*could do with examples …*' (EP2003).

All comments were reviewed and carefully considered with some amendments occurring due to this feedback. For example, one expert panel member (EP2002) suggested amending the phrasing of some items to '*such as*' rather than '*like*'. This was completed for items (16, 17, 18, 19, 20, 24 and 25 (version one)). Another suggestion led to the inclusion of '*blood thinners*' in the phrasing of one item (item 9 in version eight) as one member suggested this may be '*clear to me but perhaps not to all patients*' (EP2004). Amendments to the phrasing of the items in AF PROM occurred from version one to version eight. These changes resulted in AF PROM being reduced from 31 items to 28 items. Items were redrafted to be more personal and specific to the PwAF with the addition of statements such as '*due to my AF*'. An example of this is shown in item 6 (in version eight) (seen in Table 6.6).

Table 6.6 Amendment of Version Seven to Version Eight of AF PROM

Item	Item (Version Seven)	Expert Feedback (n=4) (a) relevance and (b) clarity				Amendment	Feedback/Justification	Item	Version Eight (updated to)
		Rating	I-CVI	Pc	K*				
Stem: Over the past 4 weeks, how much have you been bothered by the following?		NA for stem				No change	NA for stem	**Stem: Over the past 4 weeks, how much have you been bothered by the following?**	
1	Pain	**A**	0 5	0 38	0 19	Reworded	Expert feedback suggested item 1 (v7) had low relevance and perhaps was considered by the experts as being unclear Qualitative feedback suggested amending this item, becoming more specific to AF and *'indicat[ing] chest pain'* (*EP200*3) This was amended based upon this feedback	**1**	Chest Pain
		B	0 5	0 38	0 19				
2	Palpitations (heart fluttering)	**A**	1	063	1	Reworded	Although experts considered this item to be relevant (CVI=1), its clarity could be improved One expert suggested amending this item to '*palpitations (an awareness of your heart beating)'* as '*strictly palpitations are simply an awareness of the heart beating. Fluttering is often ascribed to ectopics' (EP2004).* This was amended upon review of the feedback by researchers	**2**	Palpitations (being aware of my heart beating)
		B	75	0 25	67				
3	Fast heartbeat	**A**	1	063	1	Reworded from version one and items (3 and 4) merged	Although experts considered this item to be relevant (CVI=1), the experts considered its clarity could be improved (CVI=0 75) Feedback from one expert highlighted that *'some patients may get confused with questions 2, 3, and 4 as they are similar (especially 2 and 3)' (EP2005).* Therefore, 2 items (items 3 and 4) were merged together improve clarity	**3**	My heart rate (fast or slow)
		B	75	0 25	67				
4	Slow heartbeat	**A**	0 5	0 38	0 19	Reworded from version one and items (3 and 4) merged	The relevance (CVI=0 5) and clarity CVI=0 5) of item 4 was lower than other items As already indicated, feedback from one expert highlighted that *'some patients may get confused with questions 2, 3 and 4 as they are similar (especially 2 and 3)' (EP2005)* Therefore, two items (items 3 and 4) were merged together improve clarity	**4**	Irregular heartbeat (skipping, chaotic or missed beats) **(+)** *
		B	0 5	0 38	0 19				
5	Feeling unwell	**A**	1	063	1	Reworded	Although feedback highlighted the relevance of the item (CVI=1), its clarity was rated lower (CVI=0 5) with one participant suggesting this was not specific and *'could cover anything' (EP2004).* This item was reworded to make this more specific to AF	**5**	Feeling unwell due to my AF
		B	0 5	0 38	0 19				
6	Tiredness	**A**	1	063	1	Reworded	Although experts considered this item to be relevant (CVI=1), feedback indicated the clarity of this item (CVI=0 75) could be improved, and one expert suggested using the term "*fatigue*" *as this has a slightly different connotation*' *(EP2004).* This item was updated to record the individuals' tiredness or fatigue due to their AF to make it more specific and clearer	**6**	Feeling tired or fatigued due to my AF
		B	75	0 25	67				
7	Feeling light-headed/ dizziness	**A**	1	063	1	Reworded	Feedback indicated this item was relevant, but its clarity could be improved No written comment was provided Researchers (SH, MH and MC) updated this item to improve the readability to this measure by adding the word 'or'	**7**	Feeling light-headed or dizzy
		B	75	0 25	67				
8	Blackouts	**A**	0 5	0 38	0 19	**Removed**	**Study Three aim:** Researchers (SH, MH, MC) intended this stage to remove items to reduce patient burden Although the wording of this item was rated clear by all experts, the item level content validity was rated low on relevance (CVI=0 5) (see Table 6 5) One expert explained blackouts were *'not really a common symptom of AF. You can have slow AF, but you can have any rhythm slow'* (*EP2004*), which suggest that the relevance of item 8 (v7) may be limited to a small number of the AF population Expert feedback was reviewed by all researchers and after discussion it was decided to remove this item	**8**	Shortness of breath*
		B	1	063	1				
9	Shortness of breath	**A**	1	063	1	No change	After review of the item and feedback by researchers, no changes occurred to item 9	**9**	Side effects of anticoagulants (blood thinners) *
		B	75	0 25	67				

Table 6.6 Amendment of Version Seven to Version Eight of AF PROM continued (1)

10	Side effects of medications	**A**	1	063	1	Reworded	This item (item 10) was reworded to be more specific towards the individual and to AF Its location within the questionnaire was also changed	**10**	Side effects of my other medications for AF *
		B	75	0 25	67				
11	Side effects of anticoagulants	**A**	1	063	1	Reworded	Although feedback indicated this item was relevant (CVI=1), it was suggested its clarity could be improved (CVI 0 75) with one expert stating this may not be clear to '*all patients*' *(EP2003).* Therefore, item 11 was reworded to improve its understanding The location of this item changed due to the removal and alteration of other items	**11**	Feeling anxious or worried about the future *
		B	75	0 25	67				
12	Attending medical appointments (such as outpatients, check-ups, investigations or admissions)	**A**	1	063	1	**Removed**	This item was considered by all experts to be relevant (CVI =1); however, was not considered clear (CVI=0 75) with one expert asking '*does this include INR checks?*' (*EP2004*) Therefore, after discussion, it was decided to remove item 12 (v7) as the impact of attending such appointments could also be captured by item 14 (v7), which measures the impact of treatment	**12**	Feeling anxious or worried about my treatments *
		B	75	0 25	67				
13	Feeling anxious or worried about the future	**A**	1	063	1	No change	Feedback indicated good relevance (CVI=1) and clarity (CVI=1) No written comment provided No change to the content of this item NB: The location of item 13 within AF PROM was altered in future versions due to the removal of other items	**13**	Feeling down or depressed *
		B	1	063	1				
14	Feeling anxious or worried about my treatments	**A**	1	063	1	No change	Feedback indicated good relevance (CVI=1) and clarity (CVI=1) No written comment provided No change to the content of this item NB: The location of item 14 within AF PROM was altered in future versions due to the removal of other items	**14**	Feeling I can't cope *
		B	1	063	1				
15	Feeling down or depressed	**A**	1	063	1	No change	Feedback indicated good relevance (CVI=1) and clarity (CVI=1) No written comment provided No change to the content of this item NB: The location of item 15 within AF PROM was altered in future versions due to the removal of other items	**15**	Not feeling like myself anymore *
		B	1	063	1				
16	Feeling I can't cope	**A**	75	0 25	67	No change	Feedback indicated this item was clear (CVI=1) and had some relevance (CVI = 0 75) in relation to AF No written comment provided No change to the content of this item NB: The location of item 16 within AF PROM was altered in future versions due to the removal of other items	**16**	Not being able to do things I used to (such as sports or hobbies) *
		B	1	063	1				
17	Not feeling like myself anymore	**A**	75	0 25	67	No change	Feedback indicated this item was clear (CVI=1) and had some relevance (CVI = 0 75) in relation to AF One comment from an expert further supported its relevance stating, '*people often say they feel like thy have aged quickly* [with AF]' (*EP2004*)	**17**	Not being able to eat or drink the things I used to (such as coffee, alcohol, particular foods) *
		B	1	063	1				
18	Feeling I need more support	**A**	0 5	0 38	0 19	**Removed**	All experts considered item 18 (v7) to be clearly worded (CVI=1); however, its relevance was questionable as indicated by experts (CVI = 0 5) Before reviewing the items and feedback, it was decided there must be unanimous agreement between researchers about the relevance of items to allow their inclusion into the next version of the measure The need of this item was discussed in detail with one researcher considering its relevance to be low and the other two researchers suggesting this item was highly relevant After much discussion this item was removed as it was highlighted that item 16 (v7) could capture a similar concept	**Stem: Over the past 4 weeks, how much have the following activities been affected? ***	
		B	1	063	1				
19	Not being able to do things I used to (like sports or hobbies)	**A**	1	063	1	Reworded	Although expert feedback indicated good relevance (CVI=1) and clarity (CVI=1), this item was reworded as one expert suggested using '"*such as*" *rather than like*' (*EP2003*)	**18**	Taking care of my personal needs (such as washing and dressing) *
		B	1	063	1				
20	Not being able to eat or drink the things I used to (like drinking coffee, alcohol, particular foods)	**A**	0 5	0 38	0 19	Reworded	Although this item was considered to be clear (CVI=1), its relevance was noted to be low (CVI=0 5) Upon review this item was retained by researchers but amended to use the term '*such as*' rather than '*like*' (*EP2003*) based on previous expert feedback	**19**	Taking care of my household chores (such as cooking and cleaning, shopping) *
		B	1	063	1				

Table 6.6 Amendment of Version Seven to Version Eight of AF PROM continued (2)

Stem: Over the past 4 weeks, how much have the following activities been affected?		NA for stem				No change	No change to stem; however, its location has changed within the PROM	**20**	Doing my usual leisure activities (such as gardening, sports) *
21	Taking care of personal needs (such as washing and dressing)	**A**	0 5	0 38	0 19	Reworded	Although this item was rated clear (CVI=1), its relevance was reported as low (CVI=0 5) Upon review, this item was amended to be more specific to the individual with the inclusion of the word '*my*' As mentioned in previous sections, although retained within this measure, the item changed location in future versions due to the removal of other items	**21**	Doing my usual study or work*
		B	1	063	1				
22	Taking care of household chores (such as cooking and cleaning, shopping)	**A**	75	0 25	67	No change	Feedback indicated this item was clear (CVI=1) and had some relevance in relation to AF (CVI=0 75) Although its location in future versions altered, no changes occurred to the content of this item	**22**	Sleep and rest*
		B	1	063	1				
23	Doing usual leisure activities (such as gardening, sports)	**A**	1	063	1	Reworded	Although expert feedback indicated good relevance (CVI=1) and clarity (CVI=1), this item was reworded to be more specific to the individual by including the word '*my*'	**23**	Getting about indoors*
		B	1	063	1				
24	Doing usual study or work	**A**	75	0 25	67	Reworded	Although expert feedback suggested some relevance (CVI=0 75) and clarity (CVI=0 75), this item was amended to be more specific to the individual by including the word '*my*'	**24**	Day-to-day travel (such as going to the shops) *
		B	75	0 25	67				
25	Sleep and rest	**A**	75	0 25	67	No change	Feedback indicated this item was clear (CVI=1) and had some relevance in relation to AF (CVI=0 75) Although its location in future versions altered, no changes occurred to the content of this item	**25**	Going on longer journeys (such as holidays) *
		B	1	063	1				
26	Getting about indoors	**A**	0 25	0 25	0	No change	Feedback indicated this item was clear (CVI=1) and feedback indicated some relevance in relation to AF (CVI=0 25) Upon review of the patients' comments in Study One, no changes occurred to the content of this item; however, its location in future versions was altered as a result of the removal and amendments to other items	**26**	My normal social activities*
		B	1	063	1				
27	Day-to-day travel (such as going to the shops)	**A**	75	0 25	67	No change	Feedback indicated this item was clear (CVI=0 75) and had some relevance in relation to AF (CVI=0 75) Although its location in future versions altered, no changes occurred to the content of this item	**Stem: Over the past 4 weeks, have the following been negatively affected?**	
		B	75	0 25	67				
28	Going on longer journeys (such as holidays)	**A**	75	0 25	67	No change	Feedback indicated this item was clear (CVI=1) and had some relevance in relation to AF (CVI=0 75) Although its location in future versions altered, no changes occurred to the content of this item	**27**	Relationships with friends and family*
		B	1	063	1				
29	Normal social activities	**A**	1	063	1	Reworded	Item 29 of version seven was rated as being relevant (CVI=1) and was reported as being clear (CVI=0 75) Written feedback highlighted the importance of having such items individualised One expert mentioned, '*what might be a normal social activity for me might not be for you, so there is perhaps an assumption in this question*' (*EP2003*) This item was amended to include the phrase '*my*' to make this more individualised	**28**	Sexual relationships*
		B	75	0 25	67				
Stem: Over the past 4 weeks, have the following been negatively affected?		NA for stem				No change	No change to stem; however, its location has changed within the PROM		
30	Relationships with friends and family	**A**	1	063	1	No change	Feedback indicated this item was clear (CVI=1) and had some relevance in relation to AF (CVI=0 75) Although its location in future versions altered, no changes occurred to the content of this item		
		B	75	0 25	67				
31	Sexual relationships*	**A**	1	063	1	No change	Feedback indicated this item was clear (CVI=1) and was relevant (CVI=1) Although its location in future versions altered, no changes occurred to the content of this item		
		B	1	063	1				

6.4.2.2 Results: Study Three: Version Eight

AF PROM version eight was sent to three participants from the focus groups. Although all PwAF were happy to be contacted, only one PwAF completed the feedback at this stage. This PwAF provided positive feedback, reporting that almost all items appeared relevant (n=26) and all appeared clear (n=28) (column one Table 6. 5) and commenting that (Appendix D 6.5.2) AF PROM version eight is '*a very good questionnaire*' (EP PER 3001). This PwAF further reported two items (items 11 and 23) were not felt to be personally relevant.

6.4.2.3 Results: Study Three: Version Nine

A revised AF PROM (version nine) incorporated these revisions together with formatting changes to make the questionnaire more aesthetically pleasing (which involved reducing the font size slightly and adding City, University of London and Barts Health NHS Trust logos to all three pages). This was sent to two senior nursing academics and a PwAF (who had been a participant of the paroxysmal AF PwAF focus group). One nursing academic and a PwAF rated the items for relevance and clarity. The results of this stage were generally positive with one participant reporting:

> *Overall a very good form/feedback questionnaire. Love the (in brackets) comments! Really helps!! I know it is difficult … designing a form that suits someone like me who has paroxysmal events and someone who has more frequent or continual AF overall – well done!* (EP PAF 4001).

This participant provided further feedback to suggest that several items were particularly relevant, stating '*Very relevant! I had a bleed when the warfarin went haywire …*' [referring to item 10] (EP PAF: 4001).

The CVI scores reported unanimous agreement on the relevance (n=25 items) and clarity (n=20) of most of the items with only one item (3) rated by both participants as being unclear. Three items (items 6, 25 and 26) were rated as being not relevant by at least one participant. Eight items (items 4, 6, 8, 9, 10, 22, 23, 24 and 25) were rated by at least one panel member as being unclear. Both participants reported that PwAF may be unsure how to answer some questions if there is a vagueness over which symptoms or side effects of medications are being caused by AF or their medications for AF. For example, one participant states, '*but how does one know, other than having a bleed, if a side effect … [is] just the AF and not the anticoagulant?*' (EP PAF: 4001*)* and another asks, '*how can they*

know what the cause of any fatigue is?' and suggests researchers '*could take out* [the wording] *due to my AF*' (EP Academic: 4002).

Version nine was further updated to include some formatting changes leading to the formation of AF PROM version ten which can be reviewed in Appendix D 6.4.3 and which will be used in Study Four for the content validation stage

Table 6.7 Study Three: Expert panel: Quantitative feedback

Column 1: Expert Feedback: Version Eight Scores (n=1) *				Column 2: Expert Feedback: Version Nine Scores (n=2)			
Items	I-CVI	Pc	K*	Items	I-CVI	Pc	K*
1a.	1	0.5	1	1a.	1	0.25	1
1b.	1	0.5	1	1b.	1	0.25	1
2a.	1	0.5	1	2a.	1	0.25	1
2b.	1	0.5	1	2b.	1	0.25	1
3a.	1	0.5	1	3a.	1	0.25	1
3b.	1	0.5	1	3b.	0	0.25	-0.3
4a.	1	0.5	1	4a.	1	0.25	1
4b.	1	0.5	1	4b.	0.5	0.5	0
5a.	1	0.5	1	5a.	1	0.25	1
5b.	1	0.5	1	5b.	1	0.25	1
6a.	1	0.5	1	6a.	0.5	0.5	0
6b.	1	0.5	1	6b.	0.5	0.5	0
7a.	1	0.5	1	7a.	1	0.25	1
7b.	1	0.5	1	7b.	1	0.25	1
8a.	1	0.5	1	8a.	1	0.25	1
8b.	1	0.5	1	8b.	0.5	0.5	0
9a.	1	0.5	1	9a.	1	0.25	1
9b.	1	0.5	1	9b.	0.5	0.5	0
10a.	1	0.5	1	10a.	1	0.25	1
10b.	1	0.5	1	10b.	0.5	0.5	0
11a.	0	0.5	-1	11a.	1	0.25	1
11b.	1	0.5	1	11b.	1	0.25	1
12a.	1	0.5	1	12a.	1	0.25	1
12b.	1	0.5	1	12b.	1	0.25	1
13a.	1	0.5	1	13a.	1	0.25	1
13b.	1	0.5	1	13b.	1	0.25	1
14a.	1	0.5	1	14a.	1	0.25	1
14b.	1	0.5	1	14b.	1	0.25	1
15a.	1	0.5	1	15a.	1	0.25	1
15b.	1	0.5	1	15b.	1	0.25	1
16a.	1	0.5	1	16a.	1	0.25	1
16b.	1	0.5	1	16b.	1	0.25	1
17a.	1	0.5	1	17a.	1	0.25	1
17b.	1	0.5	1	17b.	1	0.25	1
18a.	1	0.5	1	18a.	1	0.25	1
18b.	1	0.5	1	18b.	1	0.25	1
19a.	1	0.5	1	19a.	1	0.25	1
19b.	1	0.5	1	19b.	1	0.25	1
20a.	1	0.5	1	20a.	1	0.25	1
20b.	1	0.5	1	20b.	1	0.25	1
21a.	1	0.5	1	21a.	1	0.25	1
21b.	1	0.5	1	21b.	1	0.25	1
22a.	1	0.5	1	22a.	1	0.25	1
22b.	1	0.5	1	22b.	0.5	0.5	0
23a.	0	0.5	-1	23a.	1	0.25	1
23b.	1	0.5	1	23b.	0.5	0.5	0
24a.	1	0.5	1	24a.	1	0.25	1
24b.	1	0.5	1	24b.	0.5	0.5	0
25a.	1	0.5	1	25a.	0.5	0.5	0
25b.	1	0.5	1	25b.	0.5	0.5	0
26a.	1	0.5	1	26a.	1	0.25	1
26b.	1	0.5	1	26b.	0.5	0.5	0
27a.	1	0.5	1	27a.	1	0.25	1
27b.	1	0.5	1	27b.	1	0.25	1
28a.	1	0.5	1	28a.	1	0.25	1
28b.	1	0.5	1	28b.	1	0.25	1

Note: Items in AF PROM were rated on (a) relevance and (b) clarity I-CVI = item level content validity p_c = probability of chance occurrence; calculated with the formula: p_c= [N! /A! (N -A)!] * 5^N (N=total number in panel) (A = the number of panel who rated the item as relevant or clear) (Number of experts is variable; version 7=4; version 8=1; version 9=2) K* = Kappa calculated with the formula: K= (I-CVI- P_C)/ (1- P_C) * CVI score used for single participant for consistency purposes

6.4.3 Discussion: Study Three

The review of successive draft versions of the AF PROM by experts allowed further assessment and improvement of the face and content validity of this measure, allowing improvements to the quality, structure and wording and reduction of the items.

As highlighted in Table 6.6, the review of version seven led to the removal of three items (4, 8 and 12). Although syncope is listed as a symptom of AF alongside dizziness (NICE, 2014), throughout the researchers' (SH, MH and MC) discussion it was noted that item 8 (v7) would fail to fully assess the complexities of syncope; the assessment of which is variable throughout Europe (ESC, 2014). Furthermore, it was considered that if a PwAF had experienced such symptoms, these would likely be noted in the previous item (item 7, referring to light-headedness or dizziness). Upon reflection, the removal of item 8 (v7) may be considered a limitation of this study. To overcome this, item 8, referring to the symptom syncope (blackouts), could have been merged with the previous item, which would have reduced the number of items but not removed the content covered. As already highlighted in Table 6.6, items 3 and 4 were merged. Such an amendment allowed a reduction in the number of items but permitted the content to remain consistent, which was considered beneficial by researchers (SH, MH and MC).

Although it could be argued that the removal of item 12 (v7) was not purely founded upon the feedback from experts but rather upon reflection by researchers when reviewing the items, such an amendment was considered appropriate and reduced the number of items reducing patient burden. Throughout discussion amongst researchers, it was highlighted that the inclusion of item 12 (v7) may lead to an exploration of the concept of various types of support; moving away from measuring the impact of AF on HRQoL.

Review of version eight was completed by a PwAF who had been involved in the focus groups. This was important in ensuring PwAF involvement throughout development. Version nine was also reviewed by one PwAF who was involved in the paroxysmal AF PwAF focus group. Their feedback was also very beneficial in highlighting some aspects of the measure which required further consideration and ensured that content was consistent to that noted in the focus groups. Feedback was sought from two nurse academics who both have had much experience in the development of questionnaires. Although only one academic provided feedback, this provided a different perspective of the potential use of this questionnaire in other settings and how it might be improved. Only two participants with AF were involved in the content validation stage, however, which could be considered a limitation.

6.5 Content Validation: Study Four

Study Four further allowed the content and face validity of the preliminary measure to be assessed. This process involved people with AF (n=6) reviewing the preliminary items and being interviewed individually to ensure that the items were relevant, clear and unambiguous prior to the preliminary validation stage. The interviews were recorded and transcribed by a professional transcriber. These interviews were thematically analysed by SH with the aid of NVivo (version 11) software.

6.5.1 Methods: Study Four

Six PwAF consented to take part in individual interviews to assess the content and face validity of AF PROM (version ten). The results from five of six individual interviews will be presented in this section as one participant withdrew their consent. This involved five male participants (Table 6.8) three of whom had persistent AF, one had paroxysmal AF and one was asymptomatic of their AF. None of the participants had received an ablation for AF; however, most (four out of five) were on medication for their AF. Four were on a heart-rate controlling medication, two of whom were also on a rhythm-controlling medication. Only one participant was currently taking no medications for their AF. Three of the five participants were on an anticoagulant for the prevention of an AF-related stroke.

Table 6.8 Study Four and Study Five sample characteristics		
Sample Characteristics of interview participants (n=17)	**Study Four (n=5)**	**Study Five (n=12)**
Participant group		
PAF	1	3
Persistent AF	3	3
Asymptomatic AF	1	3
Relatives		3
Sex		
Female	0	5
Male	5	7
Ethnic background		
White United Kingdom (UK) and Ireland	5	10
Other White background	0	1
Indian	0	1
Employment status		
Employed	4	8
Unemployed	0	0
Retired	1	4
Treatment for AF (NB: only includes participants with diagnosis of AF)	**(n=5)**	**(n=9)**
Previous catheter ablation treatment for atrial fibrillation	0	0
Currently on heart-rate controlling medication(s)	4	4
Currently on heart-rhythm controlling medication(s)	2	1
Currently on both a heart-rate and rhythm-controlling medication	2	1
No current pharmaceutical management of AF symptoms	1	3
AF-related stroke preventive medications (NB: only includes participants with diagnosis of AF)		
Currently taking VKA	2	1
Currently taking NOAC	1	6

6.5.2 Results: Study Four

Study Four focused on assessing the face and content validity of AF PROM (v10) by means of individual interviews with PwAF (n=5). Two main themes emerged from these interviews concerning the clarity and relevance of items and suggestions for further consideration.

6.5.2.1 Results: Study Four: Theme 1: Clarity and relevance of items included in AF PROM

The PwAF participants reported that items were clear as they '*were all perfectly easy to understand*' *(IPE 034)* and relevant for inclusion. This is supported by the statement that the items of AF PROM '*are all relevant to the atrial fibrillation … as I say, I think all the questions obviously relate to the AF. There was not one I would single out and think that is not ideal*' (IPA 033).

The relevance of items to AF such as those which considered travelling, sleep, rest and items relating to the heart rhythm or rate were highlighted in this stage of the process. One PwAF expressed the relevance of some items (items 2 and 22).

> *I liked the questions about sleeping and 'Did you notice your heartbeat?' That was the first thing that I noticed there was something wrong, when I was lying in bed and I could feel my heartbeat when I was resting in the quiet of the day* (IPE 034).

Another participant noted the relevance of specific items (item 25) based on their experience of the impact of AF and describing the impact of symptoms of AF (shortness of breath) restricting their ability or, as they state, '*being able to do things*' (IPE 032), and reported the restriction as being most noticeable when travelling on holiday, which led to negative feelings described as *'disappointing'* (IPE 032).

6.5.2.2 Results: Study Four: Theme 2: Suggestions or aspects requiring further consideration

One PwAF (IPE 034) suggested the addition of two items: a statement at the beginning of AF PROM which focuses on past treatments, suggesting '[Perhaps AF PROM should] *say "post-atrial fibrillation [or] after success of your procedure" or something. It is implying that I still have AF'* (IPE 034). This PwAF (IPE 034) also proposed the addition of another item regarding leisure

activities which indicated the *'different levels of fitness you do'* further elaborating that *'you could say "very high, stressful impact" like weightlifting, rowing machines, things like that'*.

Although most (four out of five) of participants reported that none of the items in AF PROM were considered rude or off-putting, one PwAF (IPE 036) highlighted that the phrasing of one item (item 28: relationships) '*might be* [considered rude or off-putting] *... Not for me personally, but I can see, maybe for some people*' *(IPE 036).* However, when further probed on suggestions about how to improve the wording, the PwAF responded, '*I am not sure, to be honest*'.

6.6 Discussion: Study Four

This study aimed to assess the face and content validity of items that have been generated based on the five domains of HRQoL that were derived from analysis of the series of focus groups presented in Chapter Five. Interviews were conducted to confirm if selected items were unambiguous and to ascertain whether items required removal or amendment.

Although some suggestions regarding alterations to the content of AF PROM moved away from the main purpose of this stage of the study, these suggestions were reviewed and considered in-depth.

Although the first two participants in Study Four had adequate time and support to review and evaluate AF PROM, a lack of depth was noted in the responses in the first two interviews in Study Four (n=5). There were several potential causes of the PwAF brief responses that might have been because changes were not required, time restraints or to limited engagement in the activity. To overcome these limitations, further PwAF participants were asked to complete and evaluate AF PROM, and additionally advised to make notes prior to the interview to aid understanding of the content.

Upon reflection, a think-aloud study prior to this stage could have provided further in-depth understanding of the wording and interpretation of the items and would have overcome some of the limitations of this stage. Following this stage, an amendment to include a think-aloud study prior to Study Five was considered in-depth; however, this could not be completed to a high-quality due to time limitations. Therefore, it is recommended that the use of a think-aloud study following the preliminary validation stage of AF PROM would further support the face and content validity of this measure.

6.7 Content Validation: Study Five

Participation in Study Five of the development of AF PROM included participants with AF (n=9) and relatives of those with AF (n=3) completing the newly developed AF PROM (v11), WHOQOL-BREF (generic QoL questionnaire) and AF-symptom questionnaire (AF-symptom questionnaire), and then being individually interviewed. Interview questions focused on participants assessing the quality of the content and relevance of the items in AF PROM. Interviews were thematically analysed by SH.

6.7.1 Methods: Study Five

The characteristics of those included in Study Five can be seen in Table 6.9. Slightly more participants in this stage of the study were male (n=7) than female (n=5). Most described their ethnic background as white British, one reported other white background and one participant described her ethnic background as Indian. Most participants were employed (n=8) and some were retired (n=4). Of the participants with a diagnosis of AF, four were on a heart-rate controlling medication, one was only on a rhythm-controlling medication and one was on both rate and rhythm-controlling medication. Three participants were currently on no medications for their AF. Six of the nine participants with AF were on a NOAC and one was on a VKA.

6.7.2 Results: Study Five

Two main themes were reported from the interviews (n=9) with PwAF relating to the clarity and relevance of items included in AF PROM, and providing suggestions or areas for further consideration for AF PROM.

6.7.2.1 Results: Study Five: Theme 1: Clarity and relevance of items included in AF PROM

None of the participants (n=9) reported problems with the clarity and relevance of items included in AF PROM, and overall the feedback appeared positive or constructive. Participants highlighted how AF PROM *is* '*very comprehensive and it's actually very clear, the questions, and very well written … [and] all the questions are relevant*' (IAS 099), and reported that the questionnaire covered a range of aspects of HRQoL including '*physical and emotional, and activities of daily living and leisure … [which are] all fairly important*' (IPE 053) and led to PwAF feeling treated as '*a person, not just a heart*'. This is supported by the below statement.

> *I think it [referring to AF PROM] is an excellent thing to do. I just really think it makes a person feel that it is very holistic and it is a person, not just a heart, and that people aren't just looking at the plumbing of you; it is looking at actually how it relates to you. As long as the stroke risk is managed, having AF is more about how it affects your quality of life, really, isn't it, and whether you decide to have an ablation or not, really, is if it will improve your quality of life, which can get so difficult that you can't cope* (IPA 040).

The relevance of specific items to AF were also highlighted and supported the face and content validity of AF PROM. One PwAF (IPA 040) reported '*I think it was really good that things like longer journeys [are included], because that can be quite concerning about how you are going to cope; what if you are unwell at an airport or when you are away or when you are travelling? So, I thought that was good as well*'.

6.7.2.2 Results: Study Five: Theme 2: Suggestions or areas for further consideration for AF PROM

Two main areas for further consideration were noted during this stage concerning the items included in AF PROM and additionally focusing on the impact of AF on domains of HRQoL. Some PwAF made suggestions regarding aspects of AF PROM; these considered the wording of items, stems, the number of response categories and the non-inclusion of some domains. PwAF highlighted how some items may be '*not applicable*' (IPA 040) to some individuals and considered the addition of open questions which allowed PwAF to comment on current and proposed treatments, ability, concerns and other symptoms.

Although most PwAF (n=7) did not consider any items to be rude or off-putting, one participant's (IPA 038) feedback indicated the removal of item 28 ('o*ver the past 4 weeks, have the following been negatively affected: Sexual relationships*?') reporting that '*I just think most people have got AF, if they're older, they wouldn't want to be asked questions about their sex life*' (IPA 038). However, another participant highlighted the need for this item in AF PROM, reporting that '*if people are affected by beta-blockers and it impairs their sex life, then it is important to put that in, I think, because otherwise there is a part of your life that is not included [but acknowledges that] … people could take offence at it, perhaps'* (IPA 040).

Although most PwAF (n=8) reported that the items in AF PROM were clear and easy to understand, one PwAF reported difficulty understanding the item stem (for items 1–17, which asks '*Over the past 4 weeks, how much have you been bothered by the following*?'). This PwAF reported:

> *I found it quite difficult with the word 'bothered', because I wasn't sure whether that meant, when I had an episode of AF, was I bothered, or whether it was used in* '*how often are you bothered by the AF?' So, I found that quite ambiguous. So, I found that a little bit difficult to decide.* [She then suggests an alternative stem could be] '*... If you have been in AF over the past four weeks, how much have you been bothered by the following?*' *... because that would clarify that the bothering is when you are in AF, rather than saying,* '*How many episodes are you having in four weeks?*' (IPA 040).

One PwAF reported that AF PROM had not covered an important domain of HRQoL (spiritual aspects) which may impact the PwAF's ability to cope with AF, but acknowledged the inclusion of such an item might be inappropriate for some individuals:

[AF PROM] '*didn't* [include] *anything about the spiritual aspects for people …*' [reporting that] '*some people might be offended by that …*' [suggesting that a question such as] '*What coping mechanisms do you have to help manage it?*' *which could be spiritual or, as I say, meditation, mindfulness, something like that*' [would overcome potential offence]. (IPA 040)

The relevance of item 21 ('Over the past 4 weeks, how much have the following activities been negatively affected by your AF**:** doing my usual study or work?') to all PwAF was questioned, and one PwAF highlighted that this item may not be applicable if someone is retired:

> [referring to item] *21, about, if you are retired, you are not generally studying or working, although you might have put leisure. That is leisure activities there, isn't it, above? But that is not applicable to everybody.*

Participant IPA 040 suggested the inclusion of an open item which allowed PwAF to note '*other symptoms that you found* [which] *were intrusive*' and experienced, not accounted for in AF PROM. This is supported by the PwAF quote below:

> *No, I thought they were good that they covered most of the areas that have your symptoms. I suppose I wondered if, perhaps, there might be a place where you could add other symptoms that you found were intrusive. That might have been something that sometimes you have other things.*

> Interviewer: *Like an open question?*
> *Yes, 'Is there anything else that you would like* [to mention]*?*' *I find it hard to think clearly when I am having an episode. Some of the time I can't think very clearly. It is almost as if there's not enough blood to go into your brain. And there could be other people who have other things. Sometimes you get an ache in your throat and jaw, and things like that. I just find that that might be a good idea to have a section like that.*

Participant IPA 040 further suggested making two amendments to two items which could improve the data collected from AF PROM. The first involved amending item 12 ('*Over the past 4 weeks, how much have you been bothered by the following?: Feeling anxious or worried about my treatments')* to also measure the impact of feeling anxious or worried about '*current and proposed treatments*' (IPA 040). The other suggestion involved amending item 19 ('*Over the past 4 weeks, how much have the following activities been affected? Taking care of my household chores, such as cooking and cleaning, shopping*') to additionally ask, '*do you need assistance*' (IPA 040), which would provide an additional perspective that may be valued by members of the multidisciplinary team.

Two PwAF (IPA 069 and IAS 099) highlighted not '*know*[ing] *whether …* [symptoms are] *due to AF* [or something else such as] … *being overweight or lack of exercise or lack of sleep. So, it's difficult as a PwAF, perhaps, to be specific, because I just don't know if it's due to AF. I can only describe how things are*' (IAS 099). This PwAF further suggested removal of '"*is due to AF*" [as] *unless one knows for definite whether it's due to AF, perhaps it needs to be a more general* "*feeling unwell generally" or "feeling tired or fatigued" rather than saying "due to AF*"'. This participant further described how 's*omebody looking at this might think* "*this person, he sleeps well, he doesn't seem to have any problem" but, actually, I've only ticked "not at all" because of the fact that I don't know if it's due to AF or not.*' Upon rereading the item stem, this PwAF is reminded that AF PROM is investigating the impact of AF on their HRQoL and acknowledged that changing this '*might defeat the purpose of what you want … but otherwise I think* [referring to AF PROM] *it's fine*' (IAS 099).

One PwAF highlighted the benefit of including a statement that asked PwAF to indicate if they have '*been diagnosed with paroxysmal, persistent or permanent AF … If paroxysmal, how often would it generally affect you?*' (IPA 040).

> *I think I have written down, I wonder if it needs to say whether you are in permanent or paroxysmal, and, if you are paroxysmal, how often?* (IPA 040)
> Interviewer: *How do you think we should phrase that? What way would you think it would be helpful?*

> *At the top, before you start it,* '*Have you been diagnosed with paroxysmal, persistent or permanent AF? If paroxysmal, how often would it generally affect you?*' *because I think that makes quite a lot of difference to your outcome questions, because, if it is only once a month, it can be more bearable, or once every three months, and then suddenly it gets closer and closer, and it is more difficult. So, I think you get different answers from somebody who is in permanent AF that is symptomatic, because not everyone is symptomatic, are they?*' (IPA 040).

Another PwAF (IPA 041) highlighted that AF PROM '*seem*[ed to] *... be about ongoing, constant AF*' rather than someone with paroxysmal AF which is '*sporadic*'; further suggesting the inclusion of an item reflecting the '*unpredictability*' (IPA 041) of AF such as, '*If your AF is infrequent and unpredictable, a section there, so you could say, "yes" or "no" at the start. If it is "yes" and then some questions based around that, things like ... "I feel like I can't do things on my own unless somebody is with me*"' (IPA 041).

6.7.3 Results: Study Five: Analysis: Relatives' perceptions

All the participating relatives (n=3) indicated that the AF PROM appeared clear and relevant and focused on aspects important to PwAF. It was reported as being '*the sort of life questions that, generally, medics don't ask about*' (IRoC 051). This relative (IRoC 051) also highlighted how the symptoms of AF at night can lead to sleep interruptions which can additionally lead to changes in mood.

> *It is quite stressful in its own right to be awake in the night with a racing heart, not just losing sleep and resting enough, but also how it affects your mood the next day* (IRoC 051).

Although all these participants reported that items were '*not rude*' (IRoC 055) or off-putting, one relative noted that item 28 (sexual relationships) '*made me pause for a while*' (IRoC 055).

One relative described how items regarding negative feelings related to AF '*were all relevant*' to them (IRoC 042), which suggests that AF may also impact relatives as well as PwAF. This statement is supported by the quote below:

> 'Were *you worried?*' '*Were you anxious?*' '*Had it impacted your life?*' *Yes, those were all relevant to me* (IRoC 042).

Another participant (IRoC 051) reported a similar viewpoint and suggests that PwAF with long-term conditions such as AF may be unaware of how AF may also be affecting others. This relative suggests that this may be captured by '*expanding on these* [referring to item 27 and item 28] *a little bit – relationships with family and friends, sexual relationships*'. These statements are supported by the quote below.

> *I think often people close to someone who* [is] *ill, whatever their illness, they are not asked how they manage it or how it affects the relationships or family life … maybe … expanding on these a little bit – relationships with family and friends, sexual relationships. Maybe about 'Do you feel your illness impacts on your close relatives or your partner or your children?' or something like that. Personally, I think it would be interesting to know about, but also I think it might just trigger some people to thinking, 'It does affect everybody, not just me,' because it is very easy, when you are wrapped up in an illness, to be self-absorbed with that illness. That is right because they need to get well and they are thinking about that, but also how you are not alone with this; it is affecting everybody around you, including work colleagues* (IRoC 051).

6.7.4 Discussion: Study Five

The purpose of Study Five was to further assess the face and content validity of AF PROM, allowing the identification of unambiguous items and for the quality of such items to be improved if needed. Participant feedback was generally positive and supported the validity of AF PROM allowing objective 4.6 to be achieved.

Although the phrasing of items was considered by researchers to be appropriate, and most PwAF did not voice concern, a small number of PwAF (n=2), relatives (n=1) and healthcare professionals (n=1) highlighted throughout development that the inclusion of the 'Relationship' domain or item (28) could be viewed as inappropriate or offensive. In order to address this issue it could be useful to insert an additional response category which would allow PwAF to respond, '*prefer not to answer*' which may be perceived as being more sensitive to PwAF's privacy. In addition to this, amending the first response category (not at all) to include 'not at all or not applicable (NA)' is preferred. Such amendments would need to be assessed, and due to time limitations this could not be accommodated at this stage. Therefore, researchers recommend making these amendments and assessing the face validity in a think-aloud study following the preliminary validation stage.

Some PwAF (IPA 069 and IAS 099) expressed difficulty in ascertaining for '*definite whether* [the symptoms or the impact on HRQoL is] *due to AF (IAS 099)* [or something else such as] *… being*

overweight or lack of exercise or lack of sleep'. Although the removal of '*due to my AF*' in some items was considered, such an amendment changes the focus of AF PROM. This difficulty in ascertaining which condition or disease is causing symptoms in this population is widely documented (Zoni-Berisso et al, 2014), and this issue has implications for future research and indicates the importance of clear, unambiguous instructions which provide guidance for instrument completion.

Although it is acknowledged that spiritual or religious beliefs may be an important aspect of HRQoL to some PwAF, which is supported by the concepts being captured in various HRQoL questionnaires (Pilger et al, 2016; Nordblom et al, 2016), this area was not noted by any other participants in the interviews, nor was it apparent in the analyses of the focus-group content. Therefore, after discussion and consideration, this was not added.

It is acknowledged that comorbidities were a sub theme identified from the focus groups; however, the purpose of this questionnaire is to understand the effect of AF on HRQoL. To overcome this issue, it could be suggested that this questionnaire be used in collaboration with another generic HRQoL questionnaire.

6.8 Conclusion

The development of the 28 items of AF PROM in version eleven were based upon five domains that were noted as being affected or had an impact on HRQoL (Physical or Symptom-Related Effects, Your Feelings, Your Activities, Relationships, Treatments) that were identified from focus groups with PwAF, relatives of those with AF and healthcare professionals. This chapter has reported the item selection and content validation stages for AF PROM which involved an iterative process of seeking and responding to feedback for several versions of AF PROM; with this feedback enabling improvements to the content and structure of the measure. These interlinked studies conducted to assess and develop the measure lead to the conclusion that AF PROM is suitable for a preliminary validation stage to allow the identification of the underlying factors of the measure. This next stage will also allow researchers to potentially reduce the number of items and reorganise items on the basis of the pattern of responses.

Chapter 7: Studies Six and Seven: Preliminary Validation and Psychometric Testing of AF PROM

Preceding chapters have outlined the clinical and public health importance of AF, and the need to accurately measure the effects of this condition on patients' quality of life. Although several AF specific measures are available, as Chapter Three describes, these measures have typically been developed with little input from patients with the condition. This appears a key limitation of some of the measures. Patient involvement is essential to the development of a PROM for patients with AF. The inclusion of patients with the condition has been shown to improve the content validity of measures, allowing a more accurate reflection of the impact of the condition from the patients' perspective (Wiering et al., 2017). The literature review in Chapter Three identified the development and validation of the measures and highlighted some of the inadequacies of the existing tools. This is further supported by a very recent literature review (Kotecha et al., 2016) which has further examined the psychometric properties of these measures, noting that further development and psychometric testing in all measures are essential.

In this thesis I have argued that PROM developed with patient input will demonstrate greater validity and reliability. This principle was applied to the development of a new HRQoL measure for patients with AF. Chapters Five and Six described the process of item generation and selection resulting in a 28-item PROM for patients with AF. The item generation phase involved the thematic analysis of data from eight focus groups with patients with AF (n=21), relatives (n=3) and healthcare professionals (n=7). The item selection stage involved experts and patients with AF (n=8) who reviewed initial domains and items. To allow content validity to be assessed, 18 individual interviews with participants with asymptomatic (n=5), paroxysmal (n=5) and persistent AF (n=5) and healthy volunteers (n=3) took place. This chapter reports the preliminary psychometric testing of this tool by examining the factor structure, internal consistency and validity of AF PROM.

7.1 Introduction

Having produced a prototype AF PROM questionnaire, preliminary psychometric testing is essential prior to use in larger population samples (FDA, 2009). Guidance promotes the inclusion of patients with the condition at this stage as well as the inclusion of healthy participants (FDA, 2009). The current chapter will present the results of Study Six and Study Seven which is the final stage of this thesis. This study uses principle component analysis (PCA) to examine the underlying factor structure (dimensions) of the measure. PCA can guide item reduction by identifying items which do not fit well in the underlying structure or items that are functionally redundant. In a second stage of exploration,

the chapter will examine the convergent and discriminant validity of AF PROM by comparing its performance against other measures of established validity and reliability. These stages of development in this thesis are shown in Figure 7.1.

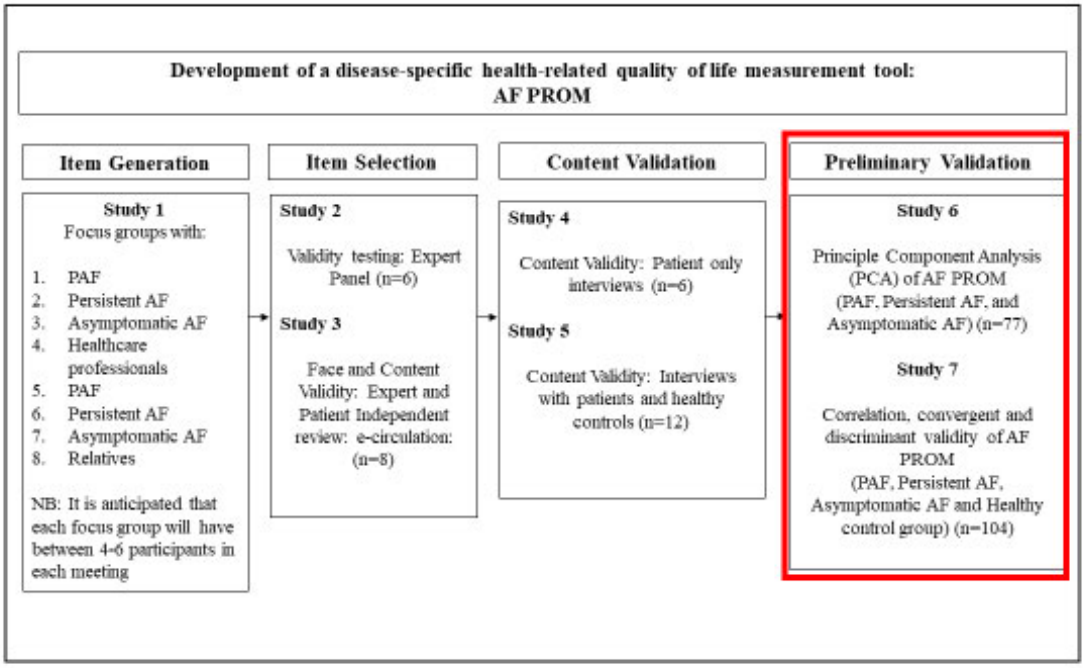


Figure 7.1: AF PROM study overview.

7.1.1 Aims and Objectives

The aim of this chapter is to describe the preliminary psychometrics of a newly developed 28-item measure of HRQoL for patients with AF.

7.1.1.1 Objectives: Study Six

The specific objectives of Study Six are to:

- Identify the underlying factor structure (dimensions) of AF PROM questionnaire and suggest appropriate titles which conceptually reflect the items that load onto each factor.
- Identify items in AF PROM which do not fit into the underlying factor structure or are functionally redundant and remove items so as to reduce the total number of items.

7.1.1.2 Objectives: Study Seven

The specific objectives of Study Seven are to:

- Investigate the convergent and discriminant validity of AF PROM by comparing participants' scores with scores of the WHOQOL-BREF and AFSymp questionnaire.
- Carry out a preliminary examination of the known group validity of AF PROM, i.e. determine whether the scores from patients with AF are different from those of the healthy control group.

7.2 Methods

Participants recruited (n=104) into stage six of this study were recruited between July 2016 and April 2017 from Barts Health NHS Trust and from an advertisement placed on an AF-specific patient website. Participants either had AF (paroxysmal: n=46; persistent: n=22; asymptomatic: n=9) or were healthy controls (n=29) who were either relatives or friends of those with AF. Once AF PROM is validated, it will be used in patients receiving treatment or therapy for AF. Patients with permanent AF are not likely to receive treatment for their AF and therefore were excluded from this stage of the study.

As part of this study, participants were asked to complete a battery of questionnaires (Appendix F 7.1):

- A demographic information section
- AF PROM (v11) (newly developed, disease-specific HRQoL measure)
- WHOQOL-BREF (generic QoL questionnaire).
- AFSympt questionnaire

All participants were given at least two options of where to complete the questionnaires. Participants who were recruited at Barts Health NHS Trust were asked to complete the questionnaires in an outpatient setting, either in the presence of the researcher (SH) or, if requested, alone in the outpatient setting. The researcher (SH) was available to answer any questions regarding any uncertainties or questions during completion. Completion in the outpatient setting was the preferred method, however some patients requested that the questionnaires be completed at home due to other commitments. Therefore, to reduce burden, patients were given a stamped, addressed envelope and were asked to send back the questionnaire within two weeks. Participants who contacted the research department from the advertisement online or in outpatient and ward settings were offered an appointment to meet with the researcher (SH) to discuss the study; additionally, they were given the opportunity to have several telephone conversations with the researcher (SH). Those who preferred to complete the questionnaires in a home setting were also given the contact details of the researcher (SH) to contact

by telephone and additionally offered the opportunity to have an appointment at a suitable time with the researcher to complete the questionnaire. Twelve participants who consented to take part in Study Six and Study Seven also consented to take part in a short individual interview to allow face and content validity of AF PROM to be assessed as part of Study Five. These interviews were voice recorded and the methods and results of this study are discussed in Chapter Six. Participation in this study was complete once questionnaires were completed and returned.

7.2.1 WHOQOL-BREF: Psychometric Properties and Rationale for Use

The inclusion of a generic QoL questionnaire allows the construct validity of AF PROM to be assessed and furthermore permits score comparison between patients with AF and the general population, allowing the known groups validity to be assessed. While many generic QoL and health scales exist (for example, the SF-36 and EuroQoL), most have been developed based upon clinicians' input. Skevington et al. (2012) argue that the WHOQOL-BREF takes a more patient-centred approach to measuring QoL as it was developed based on the qualitative data from interviews and focus groups, adhering to the FDA guidance (2009) which has been promoted throughout this thesis.

The WHOQOL-BREF is a 26-item, self-reported generic QoL measure using a five-point Likert scale. It is a shorter version of the 100-item questionnaire developed by the World Health Organisation (WHO) (Skevington et al., 2004). This questionnaire focuses on four areas of QoL: physical health, psychological health, social relationships and environment; it also asks respondents to self-rate their overall QoL and overall health. The WHOQOL-BREF questionnaire was considered appropriate for this study because its development in various cultures (23 countries, including the United Kingdom; n=11,830 participants) led to the neutral language being more suitable for a multicultural population such as London (Skevington et al., 2004). The shorter length of the questionnaire was considered advantageous at reducing respondent burden and improving completion rates, with Skevington et al. (2012) reporting that completion in well patients takes less than five minutes (Skevington et al., 2004). On the basis of the results of the literature review, it was anticipated that certain domains such as physical symptoms, psychological implications and relationships may be more relevant in the AF population, and it was noted that these are captured by domains in WHOQOL-BREF.

The psychometrics of WHOQOL-BREF have been presented in several different papers which report the validity and the reliability scores ranging from good to excellent (Skevington et al., 2004). This questionnaire has been used in the general population (Skevington et al., 2012) in various conditions and in different cultures (Areias et al., 2014; Lee et al., 2016; Oliveira et al., 2016; Sreedevi et al., 2016).

Reliability: The initial internal consistency of the total scores of WHOQOL-BREF was reported by Skevington et al. (2004) as being good (>0.7). The internal consistency (reported as Cronbach's alpha) of the four domains were reported as follows: Cronbach's alpha 0.82 (physical health domain), Cronbach's alpha 0.80 (environment domain), Cronbach's alpha 0.81(psychological domain) and Cronbach's alpha 0.68 (social relationship domain).

Validity: Skevington et al. (2004) reported good discriminant validity (significant in most countries) for each domain for both sick and well participants; t-test mean scores for the physical domain were reported as 13.1 for sick participants (15.4 for well participants). The mean score for sick participants in the psychological domain were 13.7 (14.8 for well participants); the mean score for sick participants in the social domain was 14.0 (14.8 for well participants); the mean score for sick participants in the environment domain was 13.8 (14.1 for well participants) (Skevington et al., 2014).

7.2.2 AFSympt: Psychometric Properties and Rationale for Use

Including an AF-specific symptom questionnaire in the validation stage allows the construct validity of AF PROM to be assessed. Although there are a few other AF-specific symptom questionnaires, including the Arrhythmia Symptom Checklist, Frequency and Severity scale (SCL) and the University of Toronto Atrial Fibrillation Severity Scale (AFSS), the AFSympt questionnaire was included in this study based on several strengths of this measure. The AFSympt questionnaire is an 11-item, self-reported measure. Seven of the eleven items allow the formation of a global scale. Two items are recommended to only be used for descriptive purposes as they do not demonstrate adequate factor loadings, which is a potential limitation of the use of this questionnaire. Although only recently developed and validated, its development has followed FDA guidance (2009) focusing on including patients and relevant clinicians from five different countries and cultures, which is a major strength of this questionnaire. A further practical reason for inclusion was the availability of the measure, which has no costs associated with its use in academic studies. Although this measure has been developed cross-culturally (including in the UK), the validation of this measure took place in a mainly Caucasian population in the USA, which may be a limitation.

The validation and the psychometric properties of the AFSympt are presented by Medin et al. (2014). Validation involved an AF (paroxysmal, persistent and permanent) population (n=313) in the USA.

Reliability: The internal consistency (Cronbach's alpha) was strong, being reported as 0.91 for the subscale tiredness, 0.82 for the subscale heart symptoms, 0.79 for the subscale chest discomfort and 0.87 for the single global score (Medin et al., 2014). The test-retest reliability of this measure was described as being acceptable (>0.7), with an intraclass correlation of 0.77 for the tiredness domain, 0.76 for the chest discomfort domain, 0.74 for the heart symptom domain and 0.78 for the seven-item measure.

Validity: Construct validity (convergent and discriminant validity) was assessed by comparing the results of a disease-specific measure (AFEQT) and a generic measure (SF-36). The results were significant (all $p<0.0001$), correlating as the author expected (Pearson's r range = -0.38 to 0.72) (Medin et al., 2014). Strong reproducibility was demonstrated in the subscale scores, with an intraclass correlation (ICC) of 0.76 for the chest discomfort domain, 0.77 for the tiredness domain and 0.74 for the heart symptom domain, and with an ICC coefficient of 0.78 for the seven-item global score (Medin et al., 2014).

7.2.3 Inclusion and Exclusion Criteria

As part of the referral system from primary to tertiary care, HCP at Barts Health NHS Trust receive a referral letter from the primary care setting which outline the patient's diagnosis and past medical history. Therefore, HCP are (in most cases) aware of the patient's past medical history prior to their clinic appointment. Researchers were informed of patients who have a diagnosis of AF and were potentially suitable for this study from relevant HCPs. Those who were recruited from the website and who self-reported AF were requested to provide medical details regarding diagnosis. Participants enrolled were screened according to the inclusion and exclusion criteria set out below.

Inclusion Criteria:

Age: >18 years old

Clinical criteria: application of diagnostic criteria for AF (according to NICE guidelines)

(i) asymptomatic AF

(ii) paroxysmal AF

(iii) persistent AF

(iv) control group: individuals who self-reported that they did not have a diagnosis of AF or any other heart arrhythmia. Those who were approached were relatives or carers of those with AF identified in the outpatient setting or who had contacted the research department directly. This allowed preliminary testing of the discriminant validity of AF PROM to be measured.

Exclusion Criteria:

(i) Cognitive impairment. Presence of cognitive impairment was assessed based on past medical history and assessment by their cardiac consultant. For example, patients whose medical history reported a previous stroke which resulted in impairment to their memory or understanding were excluded. **Rationale:** to ensure that patients were able to provide informed consent according to Good Clinical Practice (GCP) guidelines through Barts Health NHS Trust.

(ii) Patients who have one (or more) severe comorbid medical condition (as noted in their medical history) which is self-reported as significantly impairing or effecting their function or HRQoL. For example, a patient who has severe shortness of breath due to a comorbid condition such as chronic obstructive pulmonary disease (COPD) may be unable to distinguish which condition (e.g. AF or COPD) is having a negative impact on their HRQoL. **Rationale:** This was to reduce confusion about which condition is impacting HRQoL.

7.2.4 Recruitment

All participants were approached by the researcher (SH) following either (a) a referral from a cardiac consultant or healthcare professional (HCP) or (b) contacting the researcher after seeing the advertisement which was posted on an AF patient website and in outpatient departments throughout the hospital. To aid recruitment, HCPs were also reminded of recruitment via weekly email newsletters sent to HCP associated with the Electrophysiology Research Department (recipients included consultants, specialist nurses and pharmacists) and at the three-monthly audit days at Barts Health NHS Trust. Recruitment for Study Six and Study Seven occurred between July 2016 and April 2017.

As shown in Figure 7.2, the initial eligibility of patients from a specialist centre were screened (n=2,047). The eligibility of patients was determined initially by relevant health care professionals reviewing the reason for referral and or reviewing case notes in line with GCP guidance. Of the total sample of referrals and clinic attenders (n=2047), a substantial majority did not have AF as their current diagnosis or reason for referral (n=1851). Of the remaining 196, 72 either declined involvement or were deemed unsuitable (n=12) as indicted in Figure 7.2 resulting in a final sample of 112.

As stated in the provided patient information sheet, all participation in this study was voluntary, and therefore all participants were reminded of their right to withdraw from the study at any time. All patients had sufficient time to read and process the information contained in the patient information sheet and discuss the study with the researcher. Upon approach by the clinician and researcher, all participants stated they were happy to take part in this stage of the study; however, a small number of these (n=8) later contacted the research department to state they no longer wished to take part and would like to withdraw, and their decision to withdraw was respected and documented. Reasons for withdrawing included no longer being interested in the research study. Others mentioned they would prefer not to state a reason for withdrawal.

Due to time limitations and the importance of writing up the results of this PhD study, the recruitment for Study Six and Study Seven was paused, resulting in n=104 participants for preliminary analysis.

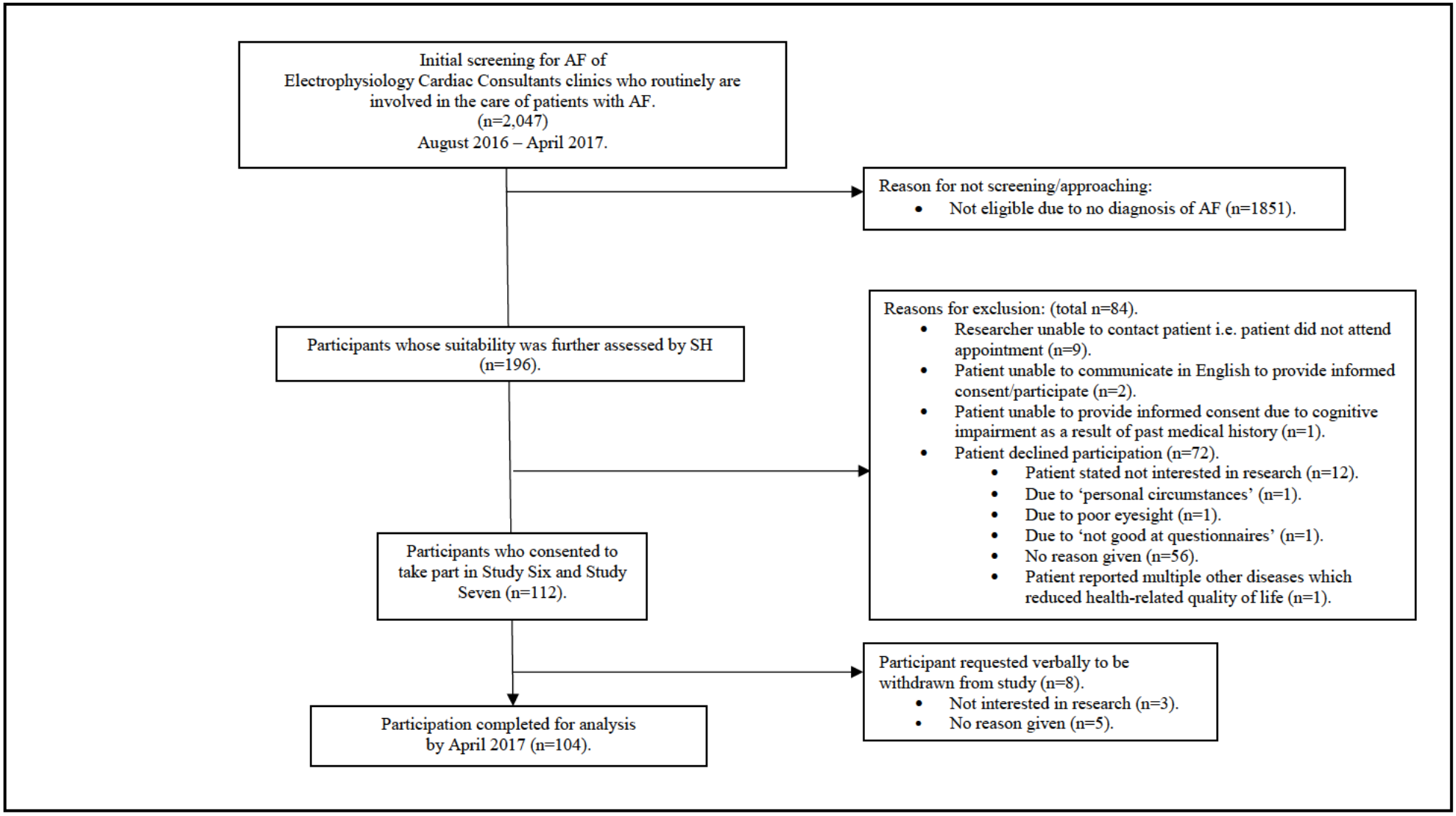
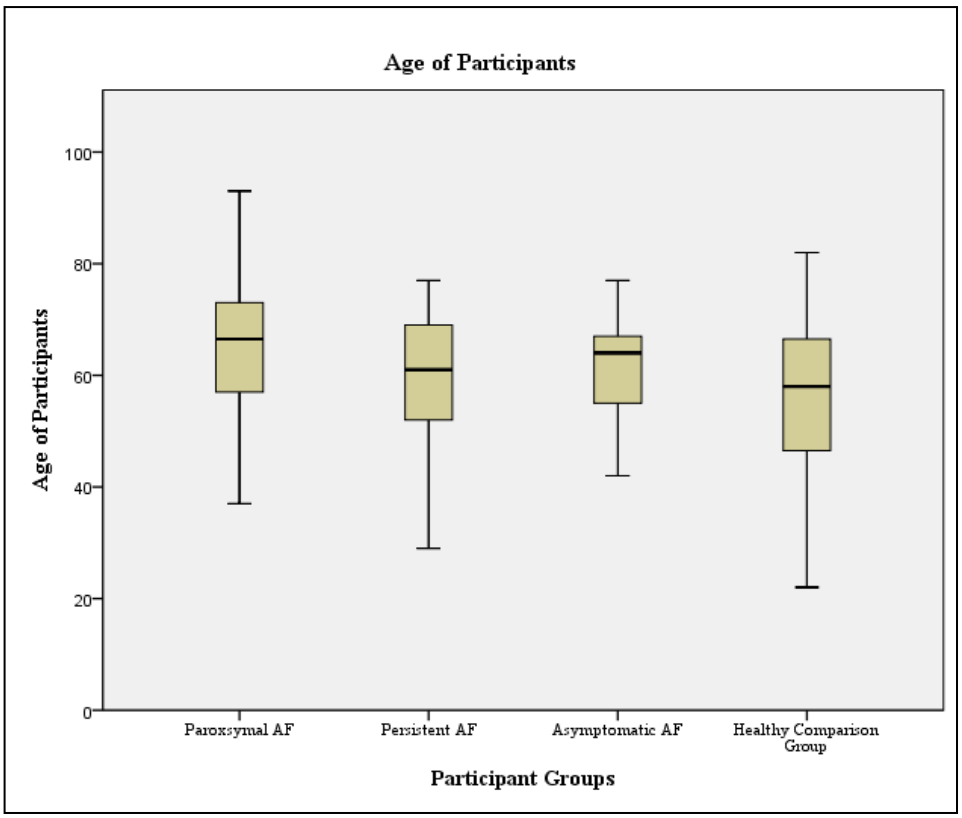


Figure 7.2 Recruitment process

7.2.5 Sample Characteristics

For clarity and consistency, the characteristics of each of the subgroups will be considered separately. The participants' characteristics can be reviewed in Figure 7.3 and Table 7.1. Ages of participants ranged from 22 to 93 years old, with a mean age of 61.6 years (SD 13.64) for all participants. The mean ages were similar, with a difference of 8.63 years between the oldest and youngest groups. The group with the highest mean was that of the patients with PAF and the group with the lowest mean age was that of the healthy controls.



Paroxysmal AF	Total (n)	46
	Mean	65.33
	Min-Max	37-93
Persistent AF	Total (n)	22
	Mean	59.82
	Min-Max	29-77
Asymptomatic AF	Total (n)	9
	Mean	61.56
	Min-Max	42-77
Healthy Comparison Group	Total (n)	27
	Mean	56.70
	Min-Max	22-82

Figure 7.3 Sample characteristics: Age

The largest patient group was comprised of those with PAF (n=46). This group was almost equally split between males (n=22) and females (n=24). Most were White British, Irish or White Other (n=43). A small number reported as having a Black (n=2) or Asian Pakistani (n=1) ethnic background. Most of those in this patient group had received a tertiary (n=23) or secondary education (n=20) and were either currently employed (n=19) or retired (n=25). Most were married (n=26) or had been married and were now separated (n=2), divorced (n=5) or widowed (n=4). Although none had received a catheter ablation for AF, most in this group were receiving a treatment or therapy for their AF, with a large number currently being on a rate-controlling medication (n=29) or rhythm-controlling medication (n=15) or both (n=8). Most of those in this group were on a non-vitamin K antagonist oral anticoagulant (NOAC) (n=22). A smaller number were on a Vitamin K antagonist such as warfarin (n=6).

Many patients enrolled with persistent AF (n=22) were male (n=16). There was a smaller number of female patients (n=6). Most of this group were White British or Irish (n=20). Most were married (n=12) or had been married and were now separated (n=1), divorced (n=1) or widowed (n=1). Most had received a secondary school education (n=14) or tertiary education (n=8). Most were employed (n=11) or retired (n=9). Only one patient in this group had received a catheter ablation for persistent AF in the past. All patients were on a heart rate (n=21) or rhythm (n=3) controlling medication, with a small number being on both types of medications (n=2).

Patients with asymptomatic AF (n=9) were mostly male (n=8), with only one female patient in this group. All patients were White British or Irish (n=9). Most were married (n=7) or separated (n=2). All were either employed (n=7) or retired (n=2). Most were on a rate controlling medication only (n=7), with two patients taking no medications for their AF. Most of these patients were on a Vitamin K antagonist (n=4) or a NOAC (n=2).

Most of the participants enrolled into the healthy control group (total n=27) were female (n=22). Most participants were married (n=20) or living as married (n=2). Many participants in this group were White British or Irish (n=21). A smaller number of participants reported having an Asian ethnicity (n=2 Asian Pakistani; n=2 other Asian) or Black African ethnicity (n=1) or reported having a mixed Black and White ethnicity (n=1). Most of this group reported that the highest level of education they had received was secondary (n=13) or tertiary (n=14). Most were currently employed (n=12) or retired (n=11).

Table 7.1 Study Six and Study Seven: Sample Characteristics						
Sample Characteristics	**PA**	**PE**	**AS**	**HC**	**Total (n=104)**	**Percentage (%)**
Participant group						
PAF	46	0	0	0	46	44
Persistent AF	0	22	0	0	22	21
Asymptomatic AF	0	0	9	0	9	9
Healthy Control	0	0	0	27	27	26
Sex						
Female	22	6	1	22	51	49
Male	24	16	8	5	53	51
Relationship status						
Single	6	3	0	5	14	13.5
Married	26	12	7	20	65	62.5
Living as married	2	4	0	2	8	7.7
Separated	2	1	2	0	5	4.8
Divorced	5	1	0	0	6	5.8
Widowed	4	1	0	0	5	4.8
Missing data	1	0	0	0	1	1
Ethnic background						
White British/Irish	37	20	9	21	87	83.7
Other White background	6	0	0	0	6	5.8
Mixed: White and Black African	0	0	0	1	1	1
Asian: Indian	0	0	0	1	1	1
Asian: Pakistani	1	0	0	0	1	1
Other Asian background	0	1	0	2	3	2.9
African	2	0	0	2	4	3.8
Other Black/African/Caribbean background	0	1	0	0	1	1
Highest education						
Primary school	1	0	0	0	1	1
Secondary school	20	14	6	13	53	51
Tertiary	23	8	3	14	48	46.2
Missing data	2	0	0	0	2	1.9
Employment status						
Employed	19	11	7	12	49	47
Unemployed	2	2	0	4	8	8
Retired	25	9	2	11	47	45
Treatment for AF (NB: only includes participants with diagnosis of AF) (n=77)						
Previous catheter ablation treatment for atrial fibrillation	0	1	0	NA	1	1
Currently on heart rate controlling medication(s)	29	21	7	NA	57	74
Currently on heart rhythm controlling medication(s)	15	3	0	NA	18	23
On both a heart rate and rhythm controlling medication	8	2	0	NA	10	12
No current treatment for AF	4	0	2	NA	6	7
AF-related stroke preventive medications (NB: only includes participants with diagnosis of AF)						
Currently taking VKA	6	3	4	NA	13	16
Currently taking NOAC	22	14	2	NA	38	49

7.3 Study Six: Statistical Analysis: Principle Component Analysis (PCA)

The use of factor analysis allows item reduction by identifying items which are either strongly correlated (being too strongly correlated may indicate these items are essentially the same) or poorly correlated (as they are measuring a different construct) to the underlying factors of the questionnaires, allowing the removal of functionally redundant items (Field, 2009; Pallant, 2010; Fayers, 2016). This technique provides insight into the underlying factor structure which can lead to the development of the titles of factors.

Factor analysis is considered an umbrella term which encompasses three main approaches: Principle Component Analysis (PCA), Exploratory Factor Analysis (EFA) and Confirmatory Factor Analysis (CFA) (Field, 2009; Pallant, 2010). Although EFA, CFA and PCA are valid and reliable for data reduction and are similar in technique, the intent of each approach varies. PCA and EFA are typically used to generate an initial understanding of the underlying factors while CFA is often used at a later stage, often on a different sample, to confirm or support the description of the factor structure (Field, 2009; Pallant 2010; Fayers, 2016). Although some authors have argued that EFA and PCA are essentially the same technique as both aim to reduce the number of combinations of linear data (thereby reducing the data and making it easier to understand) and may even provide similar results, there are key differences between these techniques (Pallant, 2010). EFA involves a more complex mathematical technique that analyses only the shared variances between variables, allowing the estimation of the underlying factors; this is most appropriately used when there is a theoretical model which is to be tested (Pallant, 2010). PCA reconstructs the variables into combinations which are fewer in number (Pallant, 2010). PCA considers all variance leading to a more empirical approach to the dataset, which is an advantage of this method (Stevens 1996; Pallant, 2010). Some researchers report preference using PCA because the mathematical analysis is less complex, leading to fewer problems than the EFA technique (Stevens, 1996). Although both techniques can be used for descriptive analytic purposes in questionnaire development, PCA is commonly used in social science and some researchers consider it to be the best technique (Coste et al., 2004). Therefore, as part of the preliminary analysis, PCA was considered most suitable for this stage of the study to identify underlying factors and unrelated items.

7.4 Analysis

An initial frequencies analysis was completed for each item for all the participants. The results of this are shown in percentage form in Appendix 7.5. The items with the most missing data were item ten (7%), which refers to side effects of medications; item five (5%), which refers to feeling unwell due to AF; and item fifteen (4%), which refers to not feeling like oneself due to AF. All other items had less than 3% missing data. In this project, cases were excluded during analysis if they did not have complete datasets. Although this led to variability between the number of participants and limited sample size, it ensured analysis was carried out only on complete datasets. Upon reflection, the exclusion of cases pairwise may have been more appropriate.

Principle Component Analysis (PCA) will be used to analyse the data in Study Six. For clarity this will be presented in three steps (as suggested by Pallant, 2010):

1. Suitability of PCA for AF PROM
2. Initial Factor Extraction
3. Final Analysis and Interpretation

7.4.1 Suitability of PCA for AF PROM

The results of the preliminary analysis are presented in this section. Responses to the 28 items of AF PROM from patients with AF (n=77) were analysed using IBM SPSS Statistics v23. The results from the healthy control group were excluded from the PCA analysis. A preliminary PCA allowed the suitability of the data to be assessed prior to a final analysis. As part of this process the correlations (linear relationship) between items were considered to identify items that are significantly poorly correlated (i.e. Pearson's r <0.3) or items that are too highly correlated with other items (i.e. Pearson's r >0.9). If items are too highly correlated, this means some items are redundant because they are generating essentially identical responses from participants and this may cause problems associated with multicollinearity. Of the items that were highly correlated with each other in this study (> 0.9), all but one were removed. In the initial analysis, all coefficients were less than 0.9, which meant all items were included for the PCA. Fifteen items were noted as being significantly poorly correlated (<0.3 as recommended by established consensus; Tabachnick and Fidell, 2007; Pallant, 2010) with at least one other item (see correlation matrix, Appendix F 7.2). This suggests that such items are measuring something different compared to the other items. These items have been examined and poor correlation is reported amongst items which appear to be theoretically unrelated concepts, although it is acknowledged that the inclusion of items which are poorly correlated to a number of

items may distort the loading of other items. Bartlett's test of sphericity can indicate if overall there are enough significant correlations between variables and thereby indicate whether PCA is appropriate for the data. Furthermore, the determinant of the correlation matrix is greater than 0.00001, indicating there is enough correlation between variables (Field, 2009); this and all other preliminary results indicated that this data was suitable for analysis (Field, 2009).

Another method of assessing the suitability of data for PCA is to examine the Kaiser-Meyer-Olkin (KMO) measure and Bartlett's test of sphericity. The KMO values range from zero to one; a value closer to zero indicates that PCA is not appropriate and a value close to one indicates that PCA is a suitable method of analysis and reliable factors or components should be identified from the dataset. Kasier (1970, 1974) more specifically outlines that when the KMO value is below 0.5, this suggests that PCA is not appropriate for this data set and that either items should be removed or a larger sample size should be sought (Field, 2009). For PCA to be appropriate, in addition to the KMO value being above 0.5, Bartlett's test of sphericity should be significant ($p<0.5$). In regard to this study, Bartlett's test of sphericity was statistically significant ($p<0.001$), indicating that PCA was appropriate. The Kaiser-Meyer-Olkin measure also confirmed there was a credible sample for analysis. The KMO value = 0.787, which Kaiser (1974) describes as 'middling' but Field (2009) describes as 'good'. All values for individual items were >0.576, which is above the acceptable limit of 0.5 (Field, 2009).

7.4.2 Factor Extraction

The decision regarding the number of factors which should be retained (or extracted) can be assisted by considering the eigenvalue rule (Kaiser's criterion). This is the most commonly used rule which outlines that factors are only retained if they have an eigenvalue of 1 or more (Pallant, 2010). The aim of this analysis is to keep the smallest number of factors which account for the greatest amount of variance. This eigenvalue is a figure which reports the amount of variance which is explained by each factor (Pallant, 2010).

Another approach to deciding the number of factors to be retained is by using Catell's scree test (Cattell, 1966), this diagram indicates which factors account for most of the variance. Although it may be subjective, this assessment allows a visual representation of the eigenvalues for each factor. As shown in Figure 7.4, all factors which are on the left side of the point of inflection (the point at which the slope changes direction) should be retained. An initial PCA obtained the eigenvalues for each component for the 28-item AF PROM.

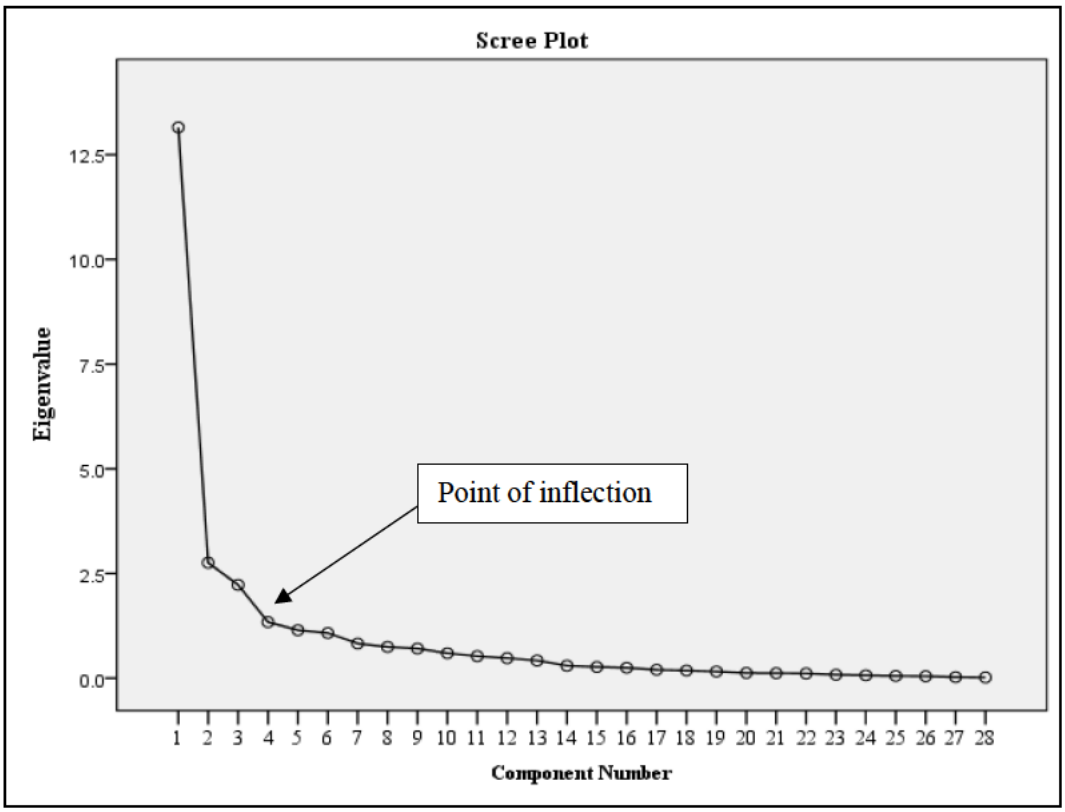


Figure 7.4 Principle Component Analysis: Scree plot (unrestricted PCA total n=77, list wise n=58).

In this study, six components (factors) had eigenvalues over Kaiser's criterion of 1 and in combination these explained 77.49% of the variance (46.97%, 9.84%, 9.84%, 4.78%, 4.09% and 3.84% respectively). However, when considering the scree plot (Figure 7.4), the specific number of underlying components is not clearly defined, with possible 3, 4, 5, or 6-component models apparent.

The result shown in the communalities table (Appendix F 7.3) for each analysis were examined as part of the interpretation of the factor solution. The communalities table reports how much variance is accounted for in relation to each item for each factor solution. When a value of less than 0.3 is presented in the results, this suggests that less than 30% of the variance of this item is explained by this factor solution. This is considered low by Pallant (2010) and would suggest that this item may not be suitable in this component and should be removed from further analysis (Pallant, 2010). The magnitude of communalities can be impacted by sample size. The results of one study suggested that if communalities are greater than 0.6 (indicating that 60% or more of the variance of this item is explained by this factor solution), then sample sizes below 100 are adequate (Field, 2009). In the unconstrained PCA solution, the communalities were reported as being above 0.6, indicating that the sample size was sufficient (Field, 2009).

Rotating the factor structure can enable a better interpretation of the results from the PCA. There are two main rotation methods: orthogonal rotation and oblique rotation. Orthogonal rotation is mainly used when the variables are considered to be unrelated. Oblique rotation is more complex but allows the variables to be related to one another (Field, 2009) and is most commonly used within psychology and human sciences. When using an oblique rotation, two tables are of interest to assist in the interpretation of the data: the pattern matrix and the component matrix. The factor loadings presented in the pattern matrix represent the regression coefficient, whereas the structure matrix considers the variable and factor and presents the correlation coefficient as the loading factor (Field, 2009). Although researchers advise considering the pattern and structure matrix together, the pattern matrix provides a simpler presentation of the data and is suitable for the purposes of this exploratory stage. Although factors are referred to as components in PCA, for clarity and consistency each component in this study will be referred to as a factor. As oblique rotation was used in the principle component analysis, the pattern matrix was considered appropriate to allow initial analysis. The results of the pattern matrix and structure matrix are presented in Appendix F (7.3). Inconsistencies between the pattern and structure matrix may be due to the low recruitment numbers. Differences between the results of the pattern matrix and structure matrix are highlighted in Appendix F (7.3). It should be noted, however, that these results are not final and may fluctuate with larger numbers.

Some authors suggest that for a factor to be appropriate, at least three items (variables) must load onto one factor, and ideally each item should load clearly onto one factor (Field, 2009). However, for the purposes of this study, any variables which loaded onto more than one factor were retained on the factor on which they loaded highest. This provided an initial understanding of these factors and their content. In addition to the factor structure, the communalities of each factor solution were considered in the hope of gaining a factor solution in which the content was structured in a way that made sense and the communalities were as high as possible. As the results of the scree plot were unclear, it was decided to explore all factor options (2-6) and evaluate the interpretability of the results in an exploratory approach which is supported by many authors (Tabachnick and Fidell, 2007; Pallant, 2010). The process led to the conclusion that a five fixed factor solution provided the clearest initial results. This allowed more than three items to load onto each factor (with a loading factor >0.4), and when the content was examined the items which loaded onto each factor were considered conceptually to be measuring a similar concept. There were differences between the concept being measured in each factor. Although there were some items which loaded almost equally onto more than one factor, overall, this solution provided an understanding of potential underlying concepts with most items loading heavier onto one factor compared to the others, which is consistent with the interpretability criteria suggested by O'Rourke and Hatcher (2013).

7.4.3 Preliminary PCA: Final Analysis

In this section the five-factor solution is reported in full. Bartlett's test of sphericity was statistically signification ($p<0.001$), indicating that PCA was appropriate. With a KMO value of 0.787, which Kaiser (1974) describes as 'middling' but Field (2009) describes as 'good', the sample was confirmed as credible for analysis. All values for individual items were >0.576, which is above the acceptable limit of 0.5 (Field, 2009). An initial PCA obtained the eigenvalues for each component of the 28-item AF PROM. Six components (factors) had eigenvalues over Kaiser's criterion of 1, and in combination these explained 77.49% of the variance (46.97%, 9.84%, 9.84%, 4.78%, 4.09% and 3.84% respectively).

A fixed, five-factor solution accounted for 73.64% of the variance (46.97%, 9.84%, 9.84%, 4.78%, 4.09%) An oblique rotation of the data was performed as it was expected that the theoretical concepts were related. With an oblique rotation of the data, both the pattern and structure matrix were considered in addition to the communalities. When a fixed, five-factor solution was examined, four items (1, 7, 9 and 10) had a communality of less than 0.6 (the lowest being 0.476), indicating that less than 60% of the variance of this item was explained by this factor solution. Although the full results of this fixed factor solution can be reviewed in Appendix F 7.3, a simpler version can be reviewed in this chapter, which allows transparency and outlines the factor loadings into each of the five domains.

Table 7.2 AF PROM: Preliminary PCA: Fixed Five-Factor Solution: Factor Loadings

Item number	Item content (condensed items)	Component 1 My physical ability to carry out activities	Component 2 My physical symptoms	Component 3: My treatment and psychological concerns	Component 4: Impact on my social relationships	Component 5: Ability and future concerns	Communalities
20	Doing my usual leisure activities	**.719**					.863
26	My normal social activities	**.689**					.855
25	Going on longer journeys (holidays)	**.659**					.783
16	Not being able to do things I used to (hobbies)	**.652**		.470			.814
21	Doing my usual study or work	.561			-.444		.746
24	Day-to-day travel (shops)	.440					.748
4	Irregular heart beat		**.888**				.758
5	Feeling unwell due to my AF		**.836**				.846
2	Palpitations (being aware of my heart beating)		**.776**				.738
3	My heart rate (fast or slow)		**.725**				.729
1	Chest pain		**.703**				.573
7	Feeling lightheaded or dizzy		**.690**				.569
8	Shortness of breath		**.686**				.696
6	Feeling tired or fatigued due to my AF		**.666**				.732
14	Feeling that 'I can't cope' because of my AF			**.874**			811
10	Side effects of my other medications for AF			**.718**			.573
13	Feeling down or depressed because of my AF			**.621**			.748
9	Side effects of anticoagulants (blood thinners)			.598			.476
17	Not being able to eat/drink the things I used to			.586			.690
15	Not feeling like myself anymore			.570			.790
28	Sexual relationships				**-.849**		.704
27	Relationships with friends and family				**-.696**		.774
19	Taking care of my household chores	.400			**-.692**		.825
22	Sleep and rest				-.539		.710
18	Taking care of my personal needs					.569	.758
23	Getting about indoors		.465			.487	.663
11	Feeling anxious/worried about AF progress		.404			-.444	.816
12	Feeling anxious/worried about AF treatments			.420		-.435	.833
(PCA; oblique rotation n=58)							

Table 7.3 AF PROM: Preliminary PCA: Fixed Five-Factor Solution: Component Labels

Component 1: My physical ability to carry out activities	Component 2: My physical symptoms	Component 3: My treatment and psychological concerns	Component 4: Impact on my social relationships	Component 5: Ability and future concerns
16. Over the past 4 weeks, how much have you been bothered by: Not being able to do things I used to (such as sports or hobbies)	1. Over the past 4 weeks, how much have you been bothered by: Chest pain	9. Over the past 4 weeks, how much have you been bothered by: Side effects of anticoagulants (blood thinners)	19. Over the past 4 weeks, how much have the following activities been negatively affected by your AF: Taking care of my household chores (such as cooking and cleaning, shopping)	11. Over the past 4 weeks, how much have you been bothered by: Feeling anxious or worried about how my AF will progress in the future
20. Over the past 4 weeks, how much have the following activities been negatively affected by your AF: Doing my usual leisure activities (such as gardening, sports)	2. Over the past 4 weeks, how much have you been bothered by: Palpitations (being aware of my heart beating)	10. Over the past 4 weeks, how much have you been bothered by: Side effects of my other medications for AF	22. Over the past 4 weeks, how much have the following activities been negatively affected by your AF: Sleep and rest	12. Over the past 4 weeks, how much have you been bothered by: Feeling anxious or worried about my AF treatments
21. Over the past 4 weeks, how much have the following activities been negatively affected by your AF: Doing my usual study or work	3. Over the past 4 weeks, how much have you been bothered by: My heart rate (fast or slow)	13. Over the past 4 weeks, how much have you been bothered by: Feeling down or depressed because of my AF	27. Over the past 4 weeks, how much have the following been negatively affected by your AF: Relationships with friends and family	18. Over the past 4 weeks, how much have the following activities been negatively affected by your AF: Taking care of my personal needs (such as washing and dressing)
24. Over the past 4 weeks, how much have the following activities been negatively affected by your AF: Day-to-day travel (such as going to the shops)	4. Over the past 4 weeks, how much have you been bothered by: Irregular heart beat (skipping, chaotic or missed beats)	14. Over the past 4 weeks, how much have you been bothered by: Feeling that 'I can't cope' because of my AF	28. Over the past 4 weeks, how much have the following been negatively affected by your AF: Sexual relationships	23. Over the past 4 weeks, how much have the following activities been negatively affected by your AF: Getting about indoors
25. Over the past 4 weeks, how much have the following activities been negatively affected by your AF: Going on longer journeys (such as holidays)	5. Over the past 4 weeks, how much have you been bothered by: Feeling unwell due to my AF	15. Over the past 4 weeks, how much have you been bothered by: Not feeling like myself anymore		
26. Over the past 4 weeks, how much have the following activities been negatively affected by your AF: My normal social activities	6. Over the past 4 weeks, how much have you been bothered by: Feeling tired or fatigued due to my AF	17. Over the past 4 weeks, how much have you been bothered by: Not being able to eat or drink the things I used to (such as coffee, alcohol, particular foods)		
	7. Over the past 4 weeks, how much have you been bothered by: Feeling lightheaded or dizzy			
	8. Over the past 4 weeks, how much have you been bothered by: Shortness of breath			

As seen in Table 7.2, all 28 items had greater than 0.4 loading into at least one factor of the fixed, five-factor solution. Six items loaded into two separate factors. The factor loading results on the pattern matrix were reviewed and the factors were given initial labels to reflect the content. These provisional factor labels were: Factor 1: 'my physical ability to carry out activities'; Factor 2: 'my physical symptoms'; Factor 3: 'my treatment and psychological concerns'; Factor 4: 'impact on my social relationships'; and Factor 5: 'ability and future concerns'. Items included in these factors are shown in Table 7.3 (above).

Although there is a consensus that a factor loading greater than 0.3 or 0.4 is significant, some authors suggest that the size of the sample can impact the magnitude of the factor loading and its reliability. One author suggested that if a sample size is less than or equal to n=100 then a factor loading should only be considered significant at 0.72 or above. If this is applied to the results in the fixed, five-factor solution (AF PROM), then only five variables (items) would be considered reliable in three of the five domains (these results are highlighted in bold in Table 7.2.). Another argument presented in the literature is that the factor loading should be considered reliable if it is greater than 0.6 and the factor has four or more variables loaded heavily on to it. If this is applied to the fixed, five-factor solution, then the factor loadings for only two full factors (physical limitations and physical symptoms) would be considered reliable regardless of the sample size. This is highlighted in bold in Table 7.2.

Although the sample size is smaller than anticipated, the PCA five fixed factor solution has provided a theoretically plausible and parsimonious model. It is noted that these are preliminary results and findings may change when these stages are completed in a larger sample. The relationship between items in each component are summarised below. The relationships between items in components 3, 4 and 5 are noted to be unclear.

Component 1: My physical ability to carry out activities. Six items (16, 20, 21, 24, 25, 26) loaded into Component 1. These items were related to the impact of AF symptoms on ability to complete activities associated with daily life.

Component 2: My physical symptoms. Eight items (1, 2, 3, 4, 5, 6, 7, 8) loaded into Component 2. All these items were symptoms described by PwAF in Chapter Five.

Component 3: My treatment and psychological concerns. Six items (9, 10, 13, 14, 15, 17) were noted to be included in Component 3. The relationship between the items included is not entirely clear, although the theoretical relationship may be split into two sections. Three items (9, 10, 17) appear to be focused on treatments and three items (13, 14, 15) appear to be focused on the negative psychological implications of living with AF, such as feeling down or not feeling like oneself and reduced ability to cope. The complex relationship between these negative psychological feelings and the exact cause of such feelings, was unclear. Chapter Five highlighted that some treatments may

affect aspects of some individuals' lives, for example, by impacting their diet, including their consumption of alcohol. The interaction between AF symptoms and the side effects of medications (such as tiredness) may also lead to avoidance of social activities, which could impact negative feelings. Side effects of medications for AF may increase tiredness, impact sleep and impact ability to cope, leading to further negative feelings.

Component 4: Impact on my Social Relationships. Four items (19, 22, 27, 28) have been included in Component 4 following a fixed, five-factor solution. The theoretical relationship between these items may be highlighted upon reviewing the results presented in Chapter Five. Symptoms and side effects limited some individuals' ability to perform daily tasks such as cooking. Furthermore, some individuals expressed that they self-limited activities due to fears or concerns surrounding the uncertainty of symptoms or concern that their limitations would limit the experience of others. Some individuals expressed this was leading to a sense of isolation and reduction in social interaction negatively affected some relationships.

Component 5: Ability and future concerns. In the preliminary PCA results of a fixed, five-factor solution, Component 5 was noted to have four items (11, 12, 18, 23). There is some uncertainty about how such items would be theoretically related. Upon reviewing the results of Chapter Five, it could be suggested that the limited ability (potentially caused by AF symptoms or side effects of treatments) may lead to negative feelings such as concern or worry about the future progression of AF or the implications of necessary future treatments. The negative impact on ability that symptoms or side effects had on some PwAF, such as feeling *'washed out'* (RE031) after completing indoor tasks such as personal washing and dressing (PE006), was presented in Chapter Five. Limitations due to AF, whether currently or previously experienced, may lead to concerns or uncertainty regarding how AF may progress in the future. There may also be concerns about whether future treatments and their side effects may be more severe, leading to further reduction in ability and negatively affecting HRQoL.

To ensure reliability and follow consensus guidelines, this initial PCA will be repeated on a larger sample size to examine whether a fixed, five-factor solution is suitable.

7.4.4 Theoretical Underpinning of Items Which Load Onto More Than One Component

As seen in the Pattern Matrix in Table 7.2, six items loaded into two components. Although the preliminary results suggest that the sample size was large enough for this type of analysis, it is accepted by most researchers that in factor analysis, larger sample sizes provide more credible results. This was an initial analysis, and at this early stage of measure validation it was judged inappropriate to exclude those scale items for which there was cross-loading; further analysis using larger samples will be a crucial part of the process of instrument validation. Therefore, no items were considered redundant and all items were retained to evaluation in future analysis. Each item which loaded onto more than factor was examined. Although all items made conceptual sense to load into more than one

factor (see qualitative data presented in Chapter Five), in the interest of achieving conceptual clarity in this early validation stage, if items loaded into more than one factor, they would be retained only in the factor for which they showed strongest loading. All items and domains which were affected were reviewed. Removing items from the domain with the weaker loading did not appear to undermine the overall interpretability or conceptual integrity of the domain.

For example, item 19, 'Taking care of my household chores (such as cooking and cleaning, shopping)' and item 21, 'Doing my usual study or work)', both loaded into Components 1 ('My physical ability to carry out activities') and 4 ('Impact on my social relationships'). Item 19 loaded more strongly in Component 4, 'Impact on my social relationships' (-0.692), than in Component 1, 'My physical ability to carry out activities' (0.400), therefore this item was retained in Component 4. It is accepted that on face value, the loading of this item seems strange; however, when re-reflecting upon the qualitative data presented in Chapter Five, one patient with AF expressed that she previously would have dinner parties for many friends but due to the symptoms of AF she is unable to complete the tasks associated with this activity, and this had reduced this degree of socialisation, as the following quote reveals:

> *But social interaction, like what we are doing now, in the evening it is like, 'I can't do this, I am just too tired.' But, again, I try and adapt by having a rest before we go. I don't do big meals anymore. We used to have five or six people round for dinner, but I have stopped doing all that, because, by the time I have cooked it all, I am like, 'Can I go to bed now, please?' So, it definitely affects me in that respect, but that is basically evenings, I guess.* (PE025)

Another potential reason may be because the patient with AF may consider that their role within a relationship has changed, leading to the participant's partner/spouse having to take on the burden of household chores, which may have an impact on the relationship.

Item 21, 'Doing my usual study or work', loaded more heavily into Component 1 (0.561) ('My physical ability to carry out activities') than Component 4 (-0.444) ('Impact on my social relationships'). Therefore, this item was retained into Component 1. As stated, the qualitative data was reviewed as part of this process and it was noted that items which loaded into more than factor made theoretical sense to do so. This suggest that some items are not independent of one another, further suggesting that there may be some relationship between these items and components. For example, one participant described how the symptoms of AF impacted her ability to do activities such as shopping and working and also impacted on her relationships with others:

> *For me, when friends or family say, 'Shall we go out and just shop or look around?' I just say, 'No, thank you' ... I don't want them to see how vulnerable I am, with gasping and so ... had a full-time volunteering job ... I gave up the [job] ... because just going out I'm afraid that I will feel breathless, I have to stop and people look at you and you are embarrassed.* (PE010)

Justification for the other four items can be reviewed in Appendix F 7.4.

7.4.5 Internal Consistency of the Five Sub-Scales

Assessment of reliability often requires smaller sample sizes, but the assessment of validation requires larger sample sizes. Reliability considers the questionnaire's ability to provide consistent results. Methods of assessing reliability include testing the internal consistency (measured by Cronbach's alpha) of a measure and examining its ability to measure the intended concept over two-time points (test-retest). The preliminary reliability of AF PROM is presented in Table 7.4. Although it was intended to measure the test-retest of AF PROM, unfortunately due to time restrictions an adequate sample size was not attained to present results. The aim is to perform this in future psychometric testing.

The reliability of the initial 28-item AF PROM was assessed using Cronbach's alpha with the sample of all participants (those with paroxysmal, persistent and asymptomatic AF and healthy controls). Items in AF PROM were negatively phrased, therefore a high score indicated less HRQoL. To allow the reliability of this measure to be assessed, the AF PROM scores were reversed (i.e. they became positively phrased for scoring purposes) using SPSS v23, with a higher score indicating a higher HRQoL, as this can impact the internal reliability when assessed using Cronbach's alpha. The results are presented in Table 7.4.

Table 7.4 AF PROM: Internal Consistency: PCA: Fixed, Five-Factor Solution					
Overall AF PROM 28 items Cronbach's alpha (whole sample) (n=82)	Domain Name	Domain: Cronbach's alpha	Items number in domain (whole sample)	Corrected item – total correlation (whole sample)	Cronbach's alpha if item is deleted (whole sample)
.965	1: My physical ability to carry out activities (n=6) (sample size: n=100)	.942	**16**	.840	.930
			20	.909	.920
			21	.699	.945
			24	.814	.933
			25	.847	.929
			26	.863	.927
	2: My physical symptoms (n=8) (sample size: n=97)	.934	**1**	.569	.938
			2	.770	.925
			3	.862	.918
			4	.840	.919
			5	.863	.918
			6	.800	.923
			7	.711	.929
			8	.751	.926
	3: My treatment and psychological concerns (n=6) (sample size n=94)	.868	**9**	.530	.869
			10	.648	.852
			13	.774	.826
			14	.762	.836
			15	.758	.829
			17	.605	.858
	4: Impact on my social relationships (n=4) (sample size n= 98)	.823	**19**	.723	.747
			22	.706	.752
			27	.633	.796
			28	.592	.810
	5: Ability and future concerns (n=4) (sample size n=101)	.779	**11**	.789	.602
			12	.769	.613
			18	.478	.792
			23	.440	.790

As seen in Table 7.4, the overall reliability score of AF PROM is α = 0.956, which suggests excellent internal consistency, indicating that this measure and the individual domains are reliable ('My physical ability to carry out activities' α = 0.942; 'My physical symptoms' α = 0.934; 'My treatment and psychological concerns' α = 0.868; 'Impact on my social relationships' α = 0.823; 'Ability and future concerns' α = 0.779).

For 26 of the 28 items, the findings presented in Table 7.4 suggest an increase in the Cronbach's α if that item is deleted. Only two items (11 and 12) resulted in a decrease in the Cronbach's α if the item is deleted. This could support the importance of these items, which consider anxiety and worry regarding the progression of AF and further treatment.

The results suggest that the removal of six items (items 1, 9, 17, 18, 21, 23) would increase the reliability of domains 1, 2, 3 and 5. One of these items (21) loaded onto more than one factor. The items are outlined in Table 7.3. However, some authors (Streiner and Norman, 2008) suggest that a Cronbach's α greater than 0.9 is too high, which can indicate that some items are measuring the same item and are redundant. Due to the small sample size, this should be repeated in a larger sample size to confirm the reliability. For the purposes of this study, the fixed, five-factor analysis was repeated with four items removed, however this did not provide results which were interpretable. Therefore, it is considered the sample size may be too small and the PCA should be repeated.

7.5 Study Seven: Validity

This chapter presents the initial results of preliminary psychometric properties of the newly developed AF PROM measure in an AF population. The validation and reliability of questionnaires is important to assess, especially prior to use in the intended population.

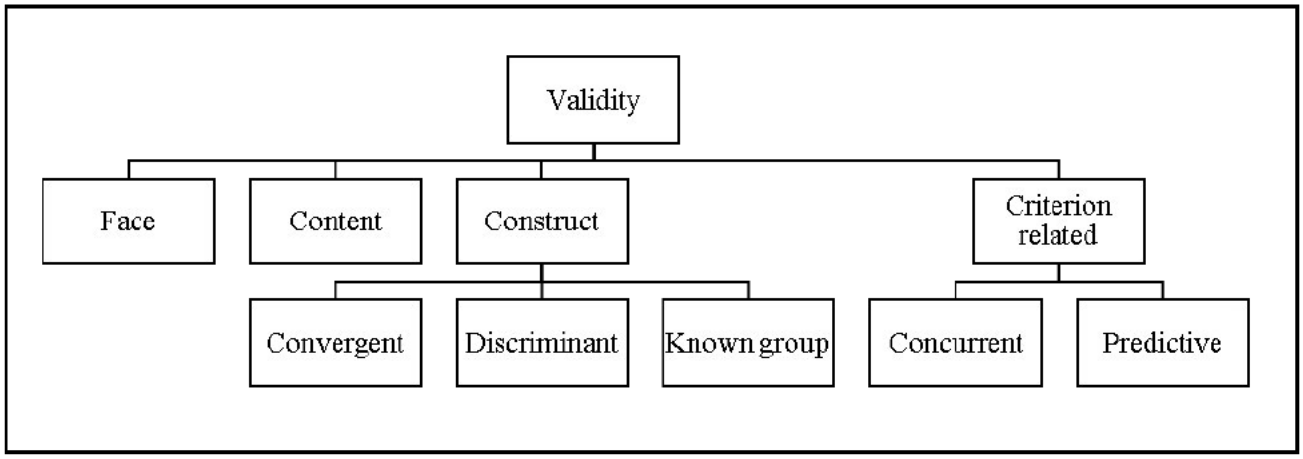


Figure 7.5: Validity diagram.

Validity is focused on assessing the questionnaires' ability to measure the construct intended (in this case HRQoL in the AF population). Validity can be assessed in different ways, including face, content, construct and criterion-related validity, as highlighted in Figure 7.5 above (based upon aspects of validity described by Bowling, 2005). The studies so far have focused on the assessment of face and content validity, which is a systematic assessment of the comprehensiveness of the measure and is often completed by a panel of experts (either patients with the condition or HCP) as was presented in Study Two and Study Three in relation to the expert and patient panel.

Although considered superficial, face validity can also provide an initial understanding of whether the intended construct is being measured. This was presented in Study Five, which sought to assess the content and face validity of AF PROM through patient interviews. Internal construct validity can be assessed using factor analysis (FA) or exploratory factor analysis (EPA). Such assessments examine the relationship between the items in the measure and the construct under consideration, indicating the consistency of the structure. External construct validity of measures can be assessed by testing hypotheses about the relationships to other existing validated measures. This can be assessed measuring the correlations between the scores of the new measure and the scores of other questionnaires which measure similar (convergent) or different (divergent) concepts.

To assess the construct validity of AF PROM, the AF PROM questionnaire was compared to a validated generic measure of QoL (WHOQOL-BREF) (Skevington, 2004) and a validated measure of AF symptoms (AFSymp) (Medin, 2014). Construct validity (convergent and discriminant validity) can be assessed using the Pearson correlation coefficient, which tests the hypotheses about the relationship between concepts; these hypotheses are outlined in Section 7.5.2 (Abma et al., 2016). Known group validity is the ability to distinguish between groups based on the scores of the separate groups using this measure (DeVellis, 2016). For example, based on data from the literature presented

in Chapter Three, it is anticipated that the HRQoL scores of the control (or healthy) group should be higher than those with AF.

7.5.1 Convergent Validity

To demonstrate convergent validity, there should be evidence of relationships between questionnaires that measure the same or closely related constructs (e.g. physical functioning). To demonstrate discriminant validity, there should be evidence of negative or inverse relationships between questionnaires that measure different constructs (Fayers and Machin, 2007; Mokkink et al., 2010; Reeve et al., 2013; Streiner et al., 2015). The strength and direction of correlation between questionnaires are dependent on the similarity of the concepts being measured. Although the classification of values for correlations is vague throughout the literature (Abma et al., 2016), it is accepted that a higher correlation between questionnaires is suggestive that both questionnaires are measuring similar concepts and a lower correlation is suggestive that different concepts are being measured (Smith, 2005; Reeve et al., 2013). For current purposes a correlation of 0.0-0.19 would be classed as very weak (this is highlighted in grey in the correlation matrix, Appendix F 7.2); 0.2-0.39 is classed as weak (highlighted in blue); 0.40-0.59 is classed as a moderate correlation (highlighted in orange); 0.60-.079 is considered a strong correlation (highlighted in yellow); and 0.8 or greater is considered very strong (Evans., 1996).

7.5.2 Hypothesis: Convergent Validity and Discriminant Validity of AF PROM

As all the items of AF PROM were originally negatively phrased questions (e.g. 'Over the past 4 weeks, how much have you been bothered by: Feeling that I can't cope because of my AF?'), the scores have been reversed and are now considered as being positively phrased for scoring purposes, with a high score indicating a high HRQoL. The items of WHOQOL-BREF are positively phrased when calculating domain scores, with a higher score indicating a higher QoL. AFSymp employs negatively phrased items to measure the symptoms of AF. At this early exploratory stage, it was expected that the AF PROM total and subscales would correlate positively with the WHOQOL-BREF score, indicating that a high score indicates a high QoL (Table 7.5). It was expected that AF PROM would negatively correlate with the AFSympt questionnaire (Table 7.6). Domains which are thought to be measuring differing concepts will allow discriminant validity to be examined. It was expected that domains such as the environment (WHOQOL-BREF) and physical symptoms (AF PROM) would show a weaker correlation, indicating they are measuring theoretically unrelated concepts.

Table 7.5 Hypothesised Convergent and Discriminant Validity of WHOQOL-BREF and AF PROM

WHOQOL -BREF domains	**WHOQOL - BREF items in domains**	**AF PROM domains**	**AF PROM items in domains**	**Hypothesised relationship between domains of AF PROM and WHOQOL-BREF (direction and strength)**
Physical domain	Q3 Q4 Q10 Q15 Q16 Q17 Q18	Components 1 and 2	Items 1-8, 16, 20, 21, 24- 26	Positive correlation (weak to moderate correlation = >0.2 <0.4)
Psychological domain	Q5 Q6 Q7 Q11 Q19 Q26	Components 3 and 5	Items 9-15,17,18, 23	Positive correlation (weak to moderate correlation = >0.2 <0.4)
Social relationships domain	Q20 Q21 Q22	Component 4	Items 19, 22, 27, 28	Positive correlation (weak to moderate correlation = >0.2 <0.4)
Environment domain	Q8 Q9 Q12 Q13 Q14 Q23 Q24 Q25	Components 1 and 2	Items 1-8, 16, 20, 21, 24 - 26	Positive but lower correlation indicating divergent validity (weak correlation <0.3)

Table 7.6 Hypothesised Convergent and Discriminant Validity of AFSymp and AF PROM				
AFSymp domains	**AFSymp items in domains**	**AF PROM domains**	**AF PROM items in domains**	**Hypothesised relationship between domains of AF PROM and AFSymp (direction and strength)**
Heart symptoms	Q1 Q3 Q7 Q8	Component 2	Q 1-8	Stronger negative correlation than WHOQOL-BREF (moderate correlation = >0.2 <0.7)
Tiredness	Q4 Q5 Q9	Component 2	Q 1-8	Stronger negative correlation than WHOQOL-BREF (moderate correlation = >0.2 <0.7)
Chest discomfort	Q2 Q10	Component 2	Q 1-8	Negative correlation but treated cautiously

7.5.3 Findings: Validity of AF PROM

Tables 7.7-7.9 provide a summary of the relationships between the total score and the domain scores of the three completed questionnaires (AF PROM, AF symptom questionnaire (i.e. AFSymp) and WHOQOL-BREF). The full correlation matrix can be seen in Appendix F 7.6.

Table 7.7 Hypothesised Convergent and Discriminant Validity of WHOQOL-BREF and AF PROM				
		AF PROM Total Score	**Summary score of AF symptom questionnaire i.e. AFSymp**	**WHOQOL-BREF Overall QoL**
AF PROM Total Score	Pearson correlation	1	-.734**	.624**
	Sig. (2-tailed)		<.001	<.001
Summary score of AF symptom questionnaire i.e. AFSymp	Pearson correlation	-.734**	1	-.576**
	Sig. (2-tailed)	<.001		<.001
WHOQOL-BREF: Overall QoL	Pearson correlation	.624**	-.576**	1
	Sig. (2-tailed)	<.001	<.001	
** Correlation is significant at the 0.01 level (2-tailed). Listwise n=100 Relationship strength (as suggested by Evans, 1996): 0.0-0.19 = very weak (grey); 0.20-0.39 = weak (blue); 0.40-0.59 = moderate (orange); 0.60-0.79 = strong (yellow); 0.80-1.0 = very strong (red)				

Table 7.8 Hypothesised Convergent and Discriminant Validity of WHOQOL-BREF and AF PROM

WHOQOL-BREF domains	AF PROM domains	Hypothesised correlation AF PROM and WHOQOL-BREF	Findings	Hypothesis confirmed? (direction, strength)
Physical domain	**Component 2**	Positive correlation (weak to moderate correlation = >0.2 <0.4)	AF PROM Component 2 0.665** p < 0.01	**Direction:** Yes **Strength:** Slightly stronger than anticipated
Psychological domain	**Components 3 and 5**	Positive correlation (weak to moderate correlation = >0.2 <0.4)	AF PROM Component 3 0.476** p < 0.01	**Direction:** Yes **Strength:** Slightly stronger than anticipated
			AF PROM Component 5 0.375** p < 0.01	**Direction:** Yes **Strength:** Weaker relationship than anticipated
Social relationships domain	**Component 4**	Positive correlation (weak to moderate correlation = >0.2 <0.4)	AF PROM Component 4 0.361** p < 0.01	**Direction:** Yes, **Strength:** Weaker relationship than anticipated
Environment domain	**Component 2**	Positive correlation but lower correlation to indicate divergent validity (weak correlation = <0.3)	AF PROM Component 2 0.313** p < 0.01	**Direction:** Yes **Strength:** Slightly stronger than anticipated Supports discriminant validity

Relationship Strength (as suggested by Evans, 1996): 0.0-0.19 = Very weak (grey); 0.2-0.39= weak (blue); 0.40-0.59 = moderate (orange); 0.60-0.79 = strong (yellow); 0.80-1.0 = very strong (red)

Table 7.9 Hypothesised Convergent and Discriminant Validity of AFSymp and AF PROM				
AFSymp domains	**AF PROM Domains**	**Hypothesised correlation between domains of AF PROM and AFSymp**	**Findings**	**Hypothesis confirmed? (direction, strength)**
Heart symptoms	**Component 2**	Stronger negative correlation than WHOQOL-BREF (moderate correlation = >0.2 <0.7)	AF PROM Component 2: -0.649** $p < 0.01$	**Direction:** Yes **Strength:** Yes
Tiredness	**Component 2**	Stronger negative correlation than WHOQOL-BREF (moderate correlation = >0.2 <0.7)	AF PROM Component 2; -0.645** $p < 0.01$	**Direction:** Yes **Strength:** Yes
Chest discomfort	**Component 2**	Negative correlation but treated cautiously as suggested by authors	AF PROM Component 2: -0.526** $p < 0.01$	**Direction:** Yes **Strength:** Yes
Relationship strength (as suggested by Evans, 1996): 0.0-0.19 = very weak (grey); 0.2-0.39= weak (blue); 0.40-0.59 = moderate (orange); 0.60-0.79 = strong (yellow); 0.8-1.0 = very strong (red)				

7.5.4 Relationship between AF PROM and WHOQOL-BREF

For this section of the thesis, the domains of AF PROM and WHOQOL-BREF will be referred to respectively as follows: AFP: Ability; AFP: Symptoms; AFP: Treatment; AFP: Relationships; AFP: Concerns; WQB: Physical; WQB: Psychological; WQB: Relationship; WQB: Environment. The scores of AF PROM have been reversed so that a higher score of AF PROM indicates a higher HRQoL.

The relationship between the impact of AF on HRQoL (as measured with AF PROM) and QoL (as measured by the self-reported summary score of the WHOQOL-BREF) was examined using the Pearson correlation coefficient. There was a strong positive relationship between these two variables ($r=0.624$; $n=100$, $p<0.00$), meaning that high scores of AF PROM were associated with high self-reported QoL scores as indicated by the WHOQOL-BREF.

The relationship between the physical domains of the two questionnaires was examined using the Pearson correlation coefficient. It was expected that at least two domains of AF PROM (AFP: Ability and AFP: Symptoms) would examine the physical impact of AF on HRQoL. The relationship between AFP: Ability and WQB: Physical was examined using the Pearson correlation coefficient. The results showed a strong positive relationship between these domains ($r=0.688$, $n=100$, $p<0.01$). When the relationship between AFP: Symptoms and WQB: Physical was examined using Pearson's correlation coefficient, the results again suggested a strong positive relationship ($r=0.665$, $n=100$, $p<0.01$). This is highlighted in yellow and bold in Table 7.5. These results suggest that high scores on the physical symptom or physical ability domains in AF PROM were also associated with high scores in the physical domain of QoL (as measured by the WQB).

It was expected that at least two domains of AF PROM (AFP: Treatment and AFP: Concerns) would examine the psychological impact of AF on HRQoL to some degree. The relationship between the domains AFP: Treatment and WQB2: Psychological was examined using the Pearson correlation coefficient. The results showed a moderately positive relationship between these variables ($r=0.476$, $n=100$, $p<0.01$). The relationship between the domain AFP: Concern and WQB2: Psychological was also examined using the Pearson correlation coefficient. This showed a weaker positive relationship ($r=0.375$, $n=100$, $p<0.01$) than expected according to the criteria used. These scores suggest that high scores in both of these domains on AF PROM (AFP: Treatment and AFP: Concerns) are associated with high scores in the WQB2: Psychological domain.

The relationship between AFP: Relationship and WQB: Social was examined using the Pearson correlation coefficient. There was a weaker positive relationship between these two variables ($r=0.361$, $n=100$, $p<0.01$) than expected according to the criteria, with high scores in the AFP: Relationship domain being moderately associated with high scores in the WQB: Relationship domain. Overall, these results support the direction of the relationship in the hypothesis, although they had been expected to show a stronger relationship between these variables. This may indicate that the domain AFP: Relationship may require further consideration and more items may need to be included to more comprehensively measure this concept.

The relationship between AFP Component Two (Physical domain) and WHOQOL-BREF Environment was expected to show a weak positive correlation. As expected, there was weak positive relationship between these variables (r=0.313, n=100, p=0.002). This supports the discriminant validity of this measure.

7.5.5 Relationship between AF PROM and AFSymp

For this section of the thesis, the domains of AF PROM and AFS will be referred to respectively as follows: AFP: Ability; AFP: Symptoms; AFP: Treatment; AFP: Relationships; AFP: Concerns; AFS: Heart Symptoms; AFS Tiredness; AFS: Chest Discomfort. As previously stated, the items of AF PROM were reversed to be positively phrased so that a high score indicates a higher HRQoL. The items in AFSymp are negatively phrased, so a high score indicates a high symptom burden. The relationship between the impact of AF on HRQoL (AF PROM) and the symptoms of AF (as indicated by the total summary score of the AFS) was investigated using the Pearson correlation coefficient. There was a strong negative relationship between these two variables (r= -0.734; n=100, p<0.00) (see Appendix 7.6).

The relationship between AFP: Symptoms and AFS: Heart Symptoms was investigated using the Pearson correlation coefficient. There was a strong negative relationship between these two variables (r= -0.649, n=100, p< 0.001). The results suggest that a lower score in the AFP: Symptoms domain was associated with a higher score on the AFSym questionnaire. The relationship between the two domains AFP: Symptoms and AFS: Tiredness was examined using the Pearson correlation coefficient. There was a strong negative relationship between these two variables (r= -0.645, n=100, p< 0.001). These results suggest that a higher score in the AFP: Symptoms domain was associated with a lower score on the AFSym questionnaire. The relationship between the domains AFP: Symptoms and AFS: Chest Discomfort was examined using the Pearson correlation coefficient. There was a strong negative relationship between these two variables (r= -0.526, n=100, p<0.001). These results suggest that a higher score in the AFP: Symptoms domain was associated with a lower score in the AFS: Chest Discomfort domain.

The relationships between AF PROM and WHOQOL-BREF and additionally AFSymp questionnaire presented by these results are in the same direction as hypothesised prior to analysis. Although preliminary, these initial results support the convergent validity of AF PROM.

7.6 Score Differences between Sample Subgroups

This section examines the mean total and mean domain score of each of the subgroups. As the score of AF PROM has been reversed to indicate a positive score, a higher score indicates a higher HRQoL. It was hypothesised that there should be differences between each subgroup. It was anticipated that those in the healthy control group should have the highest mean HRQoL scores whereas those who are more impacted by their AF will have a lower mean score, indicating a lower HRQoL. The mean scores for each domain and total score are presented in Table 7.10.

Table 7.10 Mean Total and Subscale Scores of AF PROM

	Healthy Control Group	**Asymptomatic AF**	**Paroxysmal AF**	**Persistent AF**
Component 1: My physical ability to carry out activities	Mean **23.07**	Mean **22.22**	Mean **16.65**	Mean **15.63**
	(n=27)	(n=9)	(n= 46)	(n=22)
Component 2: My physical symptoms	Mean **31.37**	Mean **25.55**	Mean **20.58**	Mean **21.31**
	(n=27)	(n=9)	(n=46)	(n=22)
Component 3: My treatment and psychological concerns	Mean **23.55**	Mean **21.44**	Mean **18.51**	Mean **17.95**
	(n=27)	(n=9)	(n=45)	(n=22)
Component 4: Impact on my social relationships	Mean **15.00**	Mean **15.11**	Mean **12.69**	Mean **12.63**
	(n=27)	(n=9)	(n=46)	(n=22)
Component 5: Ability and future concerns	Mean **15.70**	Mean **14.77**	Mean **12.28**	Mean **11.77**
	(n=27)	(n=9)	(n=46)	(n=22)
AFPROM Total Score	Mean **108.70**	Mean **99.11**	Mean **80.32**	Mean **79.31**
	(n=27)	(n=9)	(n=46)	(n=22)

As hypothesised and as shown in Table 7.6, there are differences between the mean total scores in each subgroup. Those who were included in the healthy control group had the highest mean score (indicating the highest HRQoL), while those with persistent AF have the lowest overall AF PROM mean scores (indicating a lower HRQoL).

To assess the known group validity of AF PROM, the mean summary scores of each domain and the overall summary score were compared against each group. The results can be reviewed in Appendix F 7.7. As hypothesised, the results indicated there was a significant difference ($p<0.001$) between the overall summary scores of those who had had AF (PAF and Persistent) and those who were in the healthy control group. There was also significant difference ($p<0.05$) between the overall summary scores of those who had had symptomatic AF (PAF and Persistent) and those who were asymptomatic of AF. As expected, there was significant differences ($p<0.001$) noted between groups who were symptomatic with AF (PAF and Persistent) and those who were the healthy control group in domain 2 (*My physical symptoms*). These results may suggest that AF PROM is able to provide distinguish between scores of those who are symptomatic and those without AF. Significant differences between the groups with symptomatic AF (PAF, Persistent) and the healthy control group were noted in most domains except for domain four (*impact on my social life*).

A significant difference ($p<0.05$) was noted between the score of the group with persistent AF and the group with asymptomatic AF for domain five (ability and future concerns), this may suggest those with persistent AF had increased concerns regarding their future compared to those who were asymptomatic. Although current literature indicates that HRQoL may be reduced in individuals who are asymptomatic (Savelieva et al., 2001), the results in this stage do not appear to indicate significantly lower HRQOL in those who had asymptomatic AF and those in the healthy control group. However, it is difficult to draw definitive conclusions due to the small sample size and ($n=104$) and inconsistency of the number of participants in each subgroup (PAF, persistent and asymptomatic and healthy controls), which is a limitation. It is recommended that known group validity requires a minimum of $n=50$ per group; given the variability between group sizes ($n=9$; $n=22$; $n=27$; $n=46$) it is anticipated that this will be repeated once the size of the sample is increased to a satisfactory size (de Vet et al., 2011). One limitation of this stage was that an ECG was not captured at the time of completion, whether a person was currently experiencing AF may have impacted their perception of AF.

7.7 Discussion

The purpose of this chapter is to identify the underlying factor structure (dimensions) of AF PROM allowing the identification of items which do not fit into the underlying factor structure or are functionally redundant. This chapter also aims to examine aspects of validity and reliability of AF PROM.

This chapter has presented the findings of the preliminary validation stages of AF PROM. The preliminary results of Study Six indicate that AF PROM has five main underlying factors. The five main factors were given the following provisional names: 'My physical ability to carry out activities' (six items), 'My physical symptoms' (eight items), 'My treatment and psychological concerns' (six items), 'Impact on my social relationships' (four items) and 'Ability and future concerns' (four items). Those items (n=6) which loaded on more than one factor were forced into a single factor based on the highest loading score on the pattern matrix for this preliminary stage. The inclusion of these items appeared initially to make conceptual sense when referring to the qualitative data. The reliability (as measured by Cronbach's alpha) was high, suggesting good internal consistency of each of the domains. However, upon closer inspection, the data suggested the removal of six individual items which would improve the Cronbach's alpha in four separate domains. This may suggest that these four items are redundant. These items were removed and the PCA repeated but the result indicated a three-factor solution. Although the results of a fixed, three-factor solution were reviewed, they did not make as much conceptual sense as the fixed, five-factor solution. This provides a strong rationale for further evaluation of the 28-item AF PROM with a larger sample, which is planned in the future.

Chapter Three evaluated existing measures against an adapted version of Smith et al. (2005) and Fitzpatrick et al. (1998, 2006) and the minimum standards for PROM developed by ISQOL (Reeve et al., 2013).
Although this evaluation is at an early stage, it is important to seek to rigorously address the various elements and stages of psychometric assessment and validation. This development and testing in relation to the criteria outlined in Chapter Three is presented in Table 7.11 below.

Table 7.11 Appraisal Criteria Applied to AF-specific HRQoL Measures Applied to AF PROM								
		Validity		**Reliability**		**Responsiveness**	**Practical properties**	
PROM	**Conceptual and measurement model**	**Content**	**Construct**	**Test-retest reliability**	**Internal consistency**	**Responsiveness**	**Acceptability**	**Feasibility Translation Patient Burden**
AF PROM	++	+++	++	0	+++	0	+	++
Supporting evidence	Relationship between items and concepts described in Chapters 5, 6 and 7.	Quantification of expert ratings of themes and items presented in Chapter 6 (+).	**Internal:** EFA indicates internal consistency of structure. All individual items >0.4(+). ICC: not assessed (-). **External:** Convergent and discriminant validity consistent with most hypotheses when compared to WHOQOL-BREF; AFSympt (+). **Known group:** was assessed but had low recruitment numbers (?).	**Test-retest** reliability not performed due to low recruitment numbers (n=6) (-).	See Table 7.4. Cronbach's alpha group correlation 0.965 (+), which is above the acceptability of >0.70.	Not completed. To be assessed at next validation stage (-).	Response Rate: Not reported (-). Missing data: Percentage of missing data reported in Appendix F 7.6. Handling of missing data in analysis reported in Section 7.4	Assessment of compressibility of items (see Study Four and Study Five) (+). Chapter Six: No concerns regarding patient burden raised by expert or patient group (+). Currently no licence cost (+). Current method of administration is paper. Online edition is available (+). Average completion time not recorded (-). No training required (+).
0 = No evidence/Not reported/Not available in English; + limited evidence; ++ some evidence but some aspects not reported; +++ acceptable (+) supporting evidence; (?) unclear; (-) limited evidence								
Criteria adapted from Smith et al. (2005) and Fitzpatrick et al. (1998; 2006) and the minimum standards for PROM developed by ISQOL (Reeve et al., 2013).								

Table 7.11 presents the initial results of the preliminary psychometric testing of AF PROM against the appraisal criteria presented in Chapter Three. Although preliminary psychometric testing is planned to continue, early results indicate that AF PROM displays key aspects of validity and reliability in measuring HRQoL in the AF population. As shown in Table 7.10, previous stages of the research study support the face and content validity of AF PROM. This chapter has considered the construct validity of AF PROM, particularly the convergent validity in relation to the WHOQOL-BREF and discriminant validity in relation to the AFSymp questionnaire. The preliminary results are consistent with hypotheses made prior to analysis, which support the convergent and discriminant validity of AF PROM. The relationship between the self-rated QoL scores as measured by WHOQOL-BREF and AF PROM scores was moderately to strongly positive (as outlined by Abma et al., 2016). Reverse scoring of AF PROM meant that those who scored highly in the domains of AF PROM would also have scored highly in the domains of QoL as measured by WHOQOL-BREF, indicating a high overall QoL.

These preliminary results suggest that AF PROM is a valid questionnaire, comprised of items and domains that have high internal consistency (as measured by Cronbach's alpha) which could be used in the AF population. However, as the sample sizes were smaller than anticipated, these results are preliminary and no definite claims regarding the validity or reliability of AF PROM can be made at this stage. Although the internal reliability could be improved by removing four items, the internal reliability for each domain is above 0.7 for group comparison, which is above the level of acceptability outlined by most literature (Pallant, 2010). At this stage all items have been retained to allow further analysis in a larger sample size, which would remove the main limitation of this study.

7.7.1 Strengths and Limitations of Study

A major strength of this study is the involvement of participants with paroxysmal, persistent and asymptomatic AF throughout all stages of development and initial preliminary psychometric testing. This stage of the study was carried out in a multicultural population with participants having different educational backgrounds across different age groups (as shown in Table 7.1).

A limitation of this study is that the difference between the mean age of the oldest and youngest subgroup was only 8.6 years. This may impact the HRQoL scores. Some studies have suggested that age may influence the burden of AF symptom and HRQoL scores (Aliot et al., 2014). For example, some suggest that those who are younger may be more affected by the symptoms of AF, leading to higher symptoms scores and perhaps a greater negative impact on their HRQoL. However, those who are older may be more impacted by comorbid conditions than by AF, which are more likely in an older population (Reynolds et al., 2006). Another limitation of this study which could be further

investigated is the influence of AF comorbid conditions as a compounding factor in AF. This influence has been well investigated in the literature and this may have an impact on scores and is therefore an area for future research.

For Study Six, based on the subject-to-variable ratio method and the anticipation that AF PROM might include approximately 28 items, I expected to recruit 300 participants for the PCA study (i.e. 10 participants per item). However, I was only able to recruit 77 patients with AF. Sample size may influence the number of factors when using PCA (Coste et al., 2004; Field, 2009; Pallant 2010). There is some disagreement concerning the best sample size for factor analysis, and unfortunately, there is limited evidence on which to base an approach (Osborne and Costello, 2004). Two main approaches to sample size are considered in the literature: total sample size and subject-to-variable ratio (SVT). However, some researchers suggest that sample size may be more dependent on other factors such as the study design, the consideration of communalities and the KMO, which may be more relevant to determining whether a sample is of adequate size (Field, 2009).

The total sample size approach suggests that an overall sample of 50 or less would be considered poor, a sample of 300 would be considered fair and a sample of 1000 or more would be considered excellent (Comfrey and Lee, 1992). Although this approach, which favours larger sample sizes, could lead to more stable loadings and reduced likelihood of errors, suggesting more generalisable results (Osborne and Costello, 2004), a major limitation is that it fails to consider the number of items in the questionnaire in relation to the total sample size. The alternate subject-to-variable ratio approach stipulates a minimum of 100 observations and further recommends sample sizes of between 5-10 per variable. Although this approach considers the number of items in the question, it appears to be based on limited evidence (Field, 2009; Pallant, 2010).

If using the subject to-variable ratio for the preliminary validation of a 28-item PROM, the sample size ideally should be between 140 and 280. For this study, I aimed to recruit a sample of n=300, which would have been satisfactory in relation to both approaches. However, because of time constraints and recruitment problems, I was unable to secure the sample size originally anticipated. Although the sample recruited for this initial psychometric evaluation is smaller than planned and indicated by the approaches outlined, some researchers (e.g. MacCallum et al., 1999) argue that for these types of analysis sample size is more dependent on measure and data characteristics and suggest that samples of less than 100 may be adequate. MacCallum et al. (1999) suggest that communalities of the data can give an indication of whether the sample size is sufficient, suggesting that a larger sample size is more important when communalities are lower (i.e. less than 0.5). The authors suggest that if all communalities of all the data are above 0.6 then a smaller sample size is appropriate for PCA (Field, 2009). All communalities in the initial PCA were above 0.6, which provides an indication

that the sample size could be sufficient for this analysis. Another approach may be through sampling adequacy, whereby KMO may indicate whether PCA is an appropriate method of analysis (Kaiser, 1970). Kaiser suggests that scores greater than 0.49 are 'unacceptable' and should lead to the collection of more data; scores between 0.70 and 0.79 are 'middling' (which Field (2009) suggests means 'good') and scores between 0.90 and 1.00 are 'marvellous' (Hutcheson and Sofroniou, 1999; Field, 2009). The preliminary KMO results for this study were 0.787, which is considered good for this stage. However, it is acknowledged that the current sample size is smaller than those suggested by other approaches.

7.7.1.1 Method

The choice of analysitical method was considered. Either Exploratory Factor Analysis or Principle Component Analysis is an appropriate technique for the initial exploration of the factor structure of a newly developed questionnaire (Field, 2009). As discussed, it is anticipated that this stage of preliminary analysis will resume to reach the anticipated sample size (n=300). Although, the preliminary sampling adequacy results suggest that PCA appears to be suitable for this sample size, I would suggest that this should be repeated in a larger sample size before statements regarding reliability and validity are assured. A larger sample would also allow the test-retest reliability to be further examined. Although it was intended that this would be investigated at this study stage, time and logistics did not allow sufficient recruitment numbers to report.

A larger sample size would further allow different statistical analyses, for example item response theory (IRT) or CRT as suggested by some PROM guidance (FDA, 2009; Nguyen et al., 2014), to be used to further assess the validity of the PROM. Although both statistical analyses have been shown to be beneficial in the development of PROM, some studies report that IRT is able to provide further details regarding necessary improvements to PROM (Petrillo et al., 2015). Although this method has many benefits and is promoted for use by large pharmaceutical companies, there are many practical considerations of using IRT analysis. For example, a larger sample size and specific statistical software are required together with additional training and expertise which are all less readily available (Petrillo et al., 2015). This method therefore is not viable for this stage of this study.

7.7.1.2 Logistics

Although ethical approval was gained to allow participants the option of completing AF PROM on an online platform, one limitation of providing an electronic version was that some participants expressed difficulty and confusion about gaining access as they did not have internet access. To overcome this, the use of a tablet device was considered. However, as there was insufficient funding and currently no online platform approved by ICT at Barts Health NHS Trust, it was decided to complete the preliminary psychometric testing in paper format for all questionnaires at the current time. This also resulted in participants completing all documents in paper formats. The use of paper format for WHOQOL-BREF and AFSymp (as stated in the licence agreements) in addition to an electronic version of AF PROM may have been viewed as more burdensome for participants.

Completing an electronic version of AF PROM may overcome some limitations noted when using the paper version, allowing adjustments to the size of font and perhaps making it easier to complete. For example, some participants who had arthritis in their hands were offered support from the researcher when completing the questionnaires; participants may have found completion easier if available in an electronic format. It is also noted that one participant did not wish to take part due to 'poor eyesight'. If using an electronic format suitable for a tablet device, this may have reduced missing data in AF PROM (see Appendix F 7.5). It is possible that if participants had the option to complete the questionnaire electronically, the response rate may have been greater. This was investigated, and several discussions occurred between SH and an AF patient charity website to investigate the viability of sending a generic email to all individuals with AF who are listed on the patient website to highlight the study with a link to the electronic version. However, due to funding issues, this was not viable at this stage and would require further ethical approval.

This chapter has allowed the preliminary psychometrics of AF PROM to be examined in greater detail. This has allowed the construct of AF PROM to be examined and preliminary underlying factors identified and named. Furthermore, this chapter has allowed preliminary psychometrics of AF PROM to be examined. Although further work is essential to ensure the validity and reliability of AF PROM, initial results support that AF PROM is a valid and reliable measure for patients with AF.

7.8 Conclusions

The aims of this study included identifying the underlying factor structure (dimensions) of the AF PROM questionnaire and developing appropriate titles which conceptually reflected the items that loaded onto each factor, removing any redundant items and investigating the construct validity of AF PROM. This chapter has presented the preliminary psychometric evaluation of this new 28-item PROM for individuals with AF. The results suggest that there are five underlying components: 'My physical ability to carry out activities' (Component 1); 'My physical symptoms' (Component 2); 'My treatment and psychological concerns' (Component 3); 'Impact on my Social Relationships' (Component 4); and 'Ability and future concerns' (Component 5). All the questionnaire items were retained on the basis of their relevance to measured concepts and factor loading on the pattern matrix; cross-loadings and inconsistencies in component loadings that were evident in this first testing will need to be re-examined in a further study using a larger sample. The convergent and discriminant validity of AF PROM were assessed in this part of the study and reported in this chapter. The hypothesised relationships between instrument findings were largely supported by the analysis, suggesting that this tool is measuring concepts similar to those of the WHOQOL-BREF and AFSymp questionnaire. Assessment of known group validity was performed as part of the preliminary analysis, but the sample size was less than that recommended for statistical analysis (n=50). The scores of participants with AF (paroxysmal, persistent) were significantly lower than those of healthy participants, which could suggest that scores from this measure could differentiate between subgroups. However, this statement should be treated cautiously, and further research is needed with a larger sample to confirm these provisional results using statistical analysis. The initial test-retest reliability of AF PROM was investigated; however, findings are not presented due to the small sample size. In the next chapter, the study and its findings will be and anticipated future research will be noted.

Chapter 8: Overall Discussion and Conclusions: AF PROM

Chapters Five and Six described the process of the item generation for a 28-item PROM for patients with AF. The item generation phase involved the thematic analysis of eight focus groups with participants with AF (n=21), relatives (n=3) and healthcare professionals (n=7). The item selection stage involved experts and patients with AF (n=8) reviewing the initial domains and items. To allow content validity to be assessed, 18 individual interviews with participants with AF (asymptomatic: n=5; paroxysmal AF: n=5; persistent AF: n=5) and healthy volunteers (n=3) took place. Chapter Seven presented the preliminary psychometric testing of this tool (AF- PROM). This stage identified five main underlying components of this measure and the preliminary results support the reliability and validity of this PROM. Each results chapter included a discussion section or discussion throughout to address key issues for context. Chapter Eight discusses the findings overall and presents the novel contributions of this study to the literature and recommendations for future clinical practice and future research. The overall strengths and limitations of this study are also presented.

8.1 Study Overview

Throughout this study, the complexities of AF and measuring HRQoL have been highlighted to the reader. It is hoped that this thesis will provide an insight into the patient's experience of living a life with AF and that the development of AF PROM may directly improve the care provided to patients in clinical practice. The potential journey of a life with AF and its management were initially presented in Chapter One of this thesis. The data presented in Chapter Five has built upon this knowledge base with the personal accounts of patients with AF who participated in the focus groups for this study. Patients describing the impact of AF on their HRQoL in their consultations with healthcare professionals led to the identification of a need for a measure through which to record the impact of AF and associated treatments and therapies suitable for patients with AF in a London population. To improve care, this measure needed to be suitable for research and clinical practice by accurately recording the impact of AF and capturing aspects of HRQoL which are important to patients and by being developed with methods consistent with the relevant guidance.

Development of AF PROM has involved mixed methods, the results of which were presented in Chapters Five, Six and Seven. The use of mixed methods has allowed this study to promote the involvement of patients throughout, resulting in a newly developed measure which is focused on capturing the perspective of people with AF. The development of a 28-item PROM is grounded upon the results from the thematic analysis of data collected from focus groups with patients with AF (n=21) and additional focus groups with relatives (n=3) and healthcare professionals (n=7) presented

in Chapter Five. This process has allowed the impact of AF on HRQoL to be further examined and highlighted five main domains of HRQoL which were affected: (i) physical or symptom-related effects, (ii) your feelings, (iii) your activities, (iv) relationships and (v) the impact of AF treatments or associated therapies.

8.2 Novel Contributions to the Literature

This PhD research study has developed a new HRQoL measure suitable for patients with AF with extensive involvement of participants with AF throughout. This study has also demonstrated how repeated use of qualitative methods can shape a questionnaire over several iterations.

8.2.1 Physical or Symptom-Related Effects

Much research and guidance has already identified the physical symptoms of AF (Thrall et al., 2006; NICE, 2014). Chapter Five of this research study presents these symptoms as described by patients, relatives and healthcare professionals in a specialist centre in a London population. A benefit of the publication of this work will be the impact on increasing knowledge and understanding of AF. Chapter Five highlighted the complexity of AF and its implications for various aspects of HRQoL, emphasising how each domain of HRQoL is not independent but rather is related to the others. For example, this study has reported that negative psychological feelings such as fear and anxiety were associated with the symptoms of AF, a finding which supports other quantitative and qualitative research (e.g. McCabe et al., 2015). Some of these negative feelings were expressed as being related to the uncertainty of symptoms, either because of the unexpectedness of those symptoms, especially in the paroxysmal AF participants, or anxiety about the length of symptoms and consequential necessary treatments, especially in the participants with persistent AF.

The results reported in Chapter Five led to the inclusion of items in a physical symptom domain in the new measure (AF PROM). The results reported in Chapter Six supported the inclusion of this physical symptom domain and associated items in AF PROM by assessing the content and face validity through expert and patient feedback. The preliminary psychometric testing of AF PROM (presented in Chapter Seven) further supports the inclusion of this domain, identifying that all items related to physical symptoms loaded most heavily onto Component 2 when using PCA with a fixed, five-factor solution'. As part of development, the scores of AF PROM were reversed and when compared to the scores of a validated symptom questionnaire. The items in this domain were strongly negatively correlated, suggesting that those who scored highly in this domain (in AF PROM) scored lower on the symptom questionnaire (indicating fewer symptoms), supporting the validity of this domain.

Although these results are treated cautiously due to the smaller than anticipated sample size, the preliminary mean scores in the physical domain were lower for the persistent AF group compared to the healthy control group, indicating a lower HRQoL score as hypothesised. However, due to the small known group sample sizes, the known group validity could not be statistically assessed and must be completed in a future stage.

8.2.2 Inclusion of the Psychological Domain

The importance of the inclusion of the psychological domain in AF PROM (presented in Chapter Five), referred to as 'My feelings' in Chapter Six, is highlighted by research which has considered the impact of AF on HRQoL. Many research studies have noted a decrease in HRQoL and an increase in depression and anxiety in participants with AF when compared to the general population. For example, Perret-Guillaume et al. (2010) note significant differences in scores in psychological domains (anxiety and depression levels and mental function) in patients with AF compared to a healthy comparison group but did not note significant differences in physical domains when comparing these groups using generic questionnaires. Other examples of such studies include research by Thrall et al. (2007) and Dabrowski et al. (2010).

The results reported in Chapter Five suggest that the psychological domain of HRQoL is complex and related to many aspects of HRQoL. Some participants in Study One reported accessing additional support or advice to better cope with a diagnosis of AF. Lane et al. (2009) reported that perception of the impact of AF at baseline is significantly positively related to mental health improvements over a twelve-month period; in other words, those participants who expressed more concerns regarding the impact of AF on their health, relationships and finances at baseline demonstrated greater improvement. This may be due to patients perceiving a diagnosis of AF (and the need for associated treatment) as being a stressful event and therefore seeking additional education and support (either from healthcare professionals or from relatives and friends) in order to cope. The effect of adequate knowledge and support on reducing the long-term psychological impact of AF is noted by McCabe et al. (2011), whose study, although focused exclusively on a symptomatic population, found that negative emotions were reduced when patients had a good understanding of their AF.

NICE guidance (2014) acknowledges the impact of AF on the psychological wellbeing of patients, and both quantitative and qualitative research has explored the impact of the psychological effects of AF. The qualitative data presented in Chapter Five complements such research by adding more data specific to a London population. This study also presents the perspectives of relatives and healthcare professionals from a specialist centre. Negative feelings associated with AF were noted to have led some participants to adapt their behaviour in order to reduce symptoms or to cope better with AF. It

was noted that the psychological implications of AF were a common theme across various domains. This study has provided a wealth of data relating to this theme, providing a unique insight into the experiences of some individuals living with AF and additionally presenting the psychological implications of good and poor clinical practice.

A sense of awareness of living a life with AF was noted by participants in all subgroups (paroxysmal, persistent and asymptomatic). This was related to symptoms, risk of stroke, taking medications and attending hospital appointments for AF. It was noted that healthcare professionals expressed awareness of the psychological implications of living with AF but highlighted that much emphasis is placed on treating the physical symptoms; due to lack of time, occasionally there is less emphasis placed on the psychological concerns of patients unless clearly voiced. However, one healthcare professional (HP011) acknowledged how some patients appeared to contact healthcare professionals to discuss physical symptoms but instead expressed psychological concerns and required further support. This highlights the importance of knowledgeable healthcare professionals with good communication skills.

The results presented in Chapters Six and Seven have supported the inclusion of the psychological domain. However, they have also highlighted that this domain is related to many other aspects of HRQoL and is not independent. Results from the PCA in relation to the fixed, five-factor solution (presented in Chapter Seven) indicate that psychological items may be related to Components 3 and 5 ('My treatment and psychological concerns' and 'Ability and future concerns'). This could suggest a relationship between the psychological concerns regarding treatments and ability and its impact on daily life.

On initial inspection, there may appear to be discrepancies between the PCA results (Chapter Seven) and the domains presented in Chapter Five. This may be due to the low sample size; alternatively, Chapter Five may provide a deeper insight into the complicated and interlinking relationships between domains, and the PCA results may support this. For example, a patient may have previously experienced or may currently be experiencing limited ability due to AF, as described in the following quote.

> *By the time I have got up and had a bath, got my breakfast, maybe done a little bit of washing up, which is not much – a cup, saucer and plate – I've got to sit down.* (PE024)

This experience may impact the patient's perspective and lead to worry about the future progression of AF or required treatments. For example, patients expressed concerns about

having an AF-related stroke and the potential impact this may have on their ability. This is supported by the following quote.

> *That's what frightens me more … I don't want to be suddenly disabled to the point where you're talking care homes and having family having to look after you … That, for me, is one of the biggest worries.* (PA005)

This may explain in part why these items loaded most highly (in the pattern matrix) into Component 5.

Taking medications such as anticoagulants and their accompanying side effects were described by some PwAF as a reminder of having an increased risk of stroke. Some patients also described having to alter their diet as a result of taking medications. These implications of living with AF may lead to associated negative feelings. Such qualitative experiences presented in Chapter Five may account for the complex relationship between these domains; furthermore, they may account for the factor loading of such items onto Component 3.

As discussed briefly in Chapter Three, much research suggests that there is a correlation between psychological comorbidities such as depression and anxiety and cardiovascular disease particularly in AF (Patel et al., 2013; Emdin et al., 2016). Research studies which focus on the relationships between psychological comorbidities and AF potentially may further highlight the importance of the inclusion of this domain ('My emotions') when assessing HRQoL. Furthermore, such research highlights the complexity of caring for patients with AF, requiring the treating clinician to have a detailed understanding of such conditions and the ability to perform comprehensive clinical assessments to correctly identify patients' needs and consequently provide the correct support and care (Thompson et al., 2014).

Some studies suggest that those patients with AF and psychological comorbidities used more healthcare resources than those who did not have psychological comorbidities, due to the transfer of psychological distress leading to the sensation of increased symptoms (Gehi et al., 2012). Therefore, it could be argued that as well as providing more patient-centred care, such comprehensive assessments may have financial consequences that lead to fewer healthcare resources being used longer term. Although the investigation of the psychological comorbidities and implications of AF was not the focus of this study, it is felt that this study has acknowledged the complexity of this and the importance of capturing this domain. However, the complexity of the psychological comorbidities of AF may not be captured solely by the items included in two domains of AF PROM. For a

comprehensive assessment of the psychological domain in this population, the use of other questionnaires specifically developed for such populations should be used.

8.2.3 Implications of AF on Daily Life

Chapter Five presented the implications of living with AF on daily life, which further highlighted the difficulties in maintaining these domains as separate concepts. For example, participants described how the symptoms of AF and associated negative psychological concerns led to behaviour adaptations which affected their ability to perform daily activities. Relatives of patients with AF were aware of these behaviour adaptations to improve coping with AF. Negative implications of AF on various aspects of daily activities were expressed as also negatively affecting friends, family and work relationships. Some participants also voiced concerns or increased anxiety and sadness when their ability to perform expected tasks was restricted due to AF or psychological concerns. Further to this, the implications of taking regular medications and associated side effects were also noted as affecting their daily life, even in those who were asymptomatic of AF. Although the implications for daily life are recorded by other research studies (Deaton et al., 2003; Tsuneda et al., 2006; Altiok et al., 2015), this study has led to the inclusion of items in AF PROM which are specific to a UK population and therefore may be more valid than other disease-specific questionnaires for this population. Existing measures included items which measure aspects of the impact on daily life (see Chapter Three). However, there was a notable inconsistency between the activities measured and the number of items measuring such concepts in current questionnaires (see Chapter Six). Study Five may have provided novel contributions to this literature, highlighting the aspects of activities of daily living which are voiced by patients as being important but are not currently included in current measures, such as washing and dressing and the impact of AF on sleep and work.

The results presented in Chapter Five have highlighted that healthcare professionals in one specialist centre were aware of some of the implications of living with AF such as the side effects of anticoagulants, the financial implications of travelling and fear and concern regarding the proximity to healthcare facilities. In addition to this, these healthcare professionals reported negative psychological feelings associated with loss of ability to perform previous activities either because of symptoms or because of the implications of treatments or therapies such as anticoagulants. However, it could be suggested that this sample was comprised of experts in the field and the perspective of these participants may be different than those from other facilities. One implication which healthcare professionals did not note was the impact of symptoms and side effects of medications on daily activities such as cooking, which some participants described as having a major impact on their HRQoL and was therefore included as an item in AF PROM (item 19 version 11). The inclusion of

PwAF who were asymptomatic was also viewed as beneficial, allowing the addition of views of this population, which is lacking in the current literature (Altiok et al., 2015).

One potential limitation of the final outcome of AF PROM was that it did not include an item which captures the impact of the unpredictability of AF on the activities of daily life, such as individuals having to cancel plans due to the symptoms of AF. Such concerns were raised in Study One and this stage highlighted that plans may have to be altered due to the unpredictability of symptoms. This aspect of the measure received criticism during the content review (Study Five), in which one individual suggested that this measure is more suited for someone who has persistent AF than for someone who has paroxysmal AF and experienced unpredictable episodes. This is one limitation of this current measure and upon reflection, due to its importance, should have been included. It is anticipated that such an amendment will be facilitated in the next stages of the development and validation of the measure.

8.2.4 Impact of AF on Relationships

The qualitative data also identified that AF had an impact on relationships with others. This was expressed as being caused by several factors including a lack of understanding from others regarding AF and its impact on daily life. This also appeared to be strongly related to psychological concerns such as a sense of increased vulnerability and a change in the expected role of the patient within relationships, which led to some expressing that they had become less independent and more reliant on others. Some participants expressed that concerns regarding AF which were raised by family members led to increased concern; however, others suggested this was reassuring. It is also important to consider that although some participants described not currently experiencing an impact on relationships, they had fears about being a burden on others if suffering from an AF-related stroke and suffering from the associated implications such as communication difficulties. A change in the relationship dynamics noted in Chapter Five is supported by a systematic review by Dalteg et al. (2011), which presents the impact on relationships of AF along with other cardiac diseases. As well as the impact that AF can have on the relationship, other research suggests that relatives or carers of PwAF may have reduced or negatively affected wellbeing whilst supporting or caring for PwAF (Ekblad et al., 2014). Such literature may support the idea that the fears expressed by patients (such as being more dependent on others) are not unfounded.

The psychological implications caused by changes in relationships, in addition to the implications of symptoms, also led to changes in some participants' social lives, leading to some feeling vulnerable and isolated. It is important to consider that the degree of impact varied between participants, with some expressing it as significant while others expressed that AF had no impact on their relationships.

Increased dependence on others and concerns regarding the impact on others' daily lives due to associated inconveniences (such as attendance at hospital appointments) which was presented in Study One is highlighted throughout the literature (Altiok et al., 2015).

Chapter Six and Chapter Seven further suggest that this domain is not an independent concept. For example, some items loaded more heavily into domains one and four ('My physical ability to carry out activities' and 'Impact on my social relationships'), suggesting an association between ability and relationships.

8.2.5 Impact of AF Treatments or Associated Therapies

Although it is accepted that treatment and therapies associated with AF is not a specific domain of HRQoL, it was a noted theme which impacted HRQoL in those participants with AF. The data presented in Chapter Five described patients voicing concern regarding stroke risk and the implications of taking regular anticoagulants such as VKAs and NOACs. Some research has explored the perception and attitude of patients and healthcare professionals toward anticoagulants and emphasis has been placed on involving patients and relatives in care decisions in regard to anticoagulants, which may influence the number of patients on these medications (Ferguson and Hendriks, 2017; Mas Dalmau et al., 2017). Attitudes were noted to differ between clinicians in specialist centres and those working as general practitioners. Such research has recommended further qualitative studies exploring attitudes towards and perception of anticoagulants, especially NOACs (Mas Dalmau et al., 2017). Researchers in this study consider that the qualitative data presented in Chapter Five complement this finding and provide further support for future research into perception of and attitude toward anticoagulants from a patient's perspective and how this may change with increased patient education. Some research has highlighted the influence of different cultures on perspectives of living and coping with AF, such as the influence of religious or spiritual means (St-Louis and Robichaud-Ekstrand, 2003; Silverman et al., 2009; Altiok et al., 2015). Although the focus groups did not discuss such concepts, one patient interview in the content validation stage highlighted the non-inclusion of such an item in AF PROM.

Participants also expressed the implications of symptom management such as the implications of taking regular medications, the side effects of such medications and concerns regarding future treatments and AF progression. The implications of attending regular hospital appointments and the inconvenience of last-minute adjustments to such appointments impact daily activities such as work and were described as also leading to negative psychological feelings. It was also noted that while some asymptomatic patients felt overall that their AF had no impact on their HRQoL, attendance at such appointments led to negative feelings such as anxiety. This is one of the few qualitative studies which have recorded the perspective of those participants who are asymptomatic with AF. Other available measures have either not included or have included few participants who are asymptomatic.

Recent publications have focused on stroke risk assessment and prevention in the AF population, with experts in the field calling for the government to make improvements (Begg et al., 2012). Such publications have anticipated and welcomed the publication of updated NICE guidance (2014) for AF management, which places much emphasis on stroke risk assessment using CHA2DS2-VASc scores, initiating appropriate anticoagulation and assessing bleeding risk when on anticoagulants using HAS-BLED scores. Although care improvements such as audit tools (GRASP AF) have been introduced for

patients with AF in the community, the provision of such improvements varies throughout the UK, with areas such as Scotland and Northern Ireland having no such provision (Begg et al., 2012; NHS, 2016), which may suggest patient experience may be different in other parts of the UK.

There has been recent emphasis by patient charities and research centres on the early detection of AF, which can lead to the assessment of the risk of stroke. Although not mandatory, charities and some healthcare facilities have promoted opportunistic screening in clinical settings, for example, pulse checks at flu clinics or the recent promotion of the use of mobile devices to screen for AF in some research studies (Lewis et al., 2011; Rhys et al., 2013; Lowres et al., 2015; Chan et al., 2016). In addition to the increased promotion of screening, attention has been placed on improving patient education and the standard of information sheets and highlighting the need to make information easy to understand (Begg et al., 2012). The qualitative data in this study (reported in Chapter Five) has also highlighted this need and suggests a need for greater emphasis on what to expect when living with AF, including common psychological concerns and advice about how to find available support.

8.2.6 Development of AF PROM

Apart from reducing the risk of stroke, the management of AF is focused on reducing symptoms to improve HRQoL. This management can involve medications or invasive treatments such as catheter ablation. Although many studies have investigated which treatment options provide greatest improvement in HRQoL as measured by generic and disease-specific measures, there is currently no clear best treatment (Thrall et al., 2006). The benefits and limitations of generic and disease-specific measures have been considered and although the use of generic measures has much benefit, disease-specific measures appear to allow a deeper understanding of the impact of AF on HRQoL (Aliot et al., 2014). After examination of the available measures, it was highlighted that development of these tools has been based largely upon clinicians' perspectives with limited patient input in developmental stages. The need of an AF-specific PROM with significant patient input throughout development but particularly in the initial stages has been highlighted throughout this thesis. AF PROM is considered to be an AF-specific measure which may better capture changes in HRQoL in a London population.

Although comparison against other measures is difficult until the process of development and validation is complete, the content of this measure (AF PROM) is based on the qualitative data from eight focus groups with patients with AF, relatives and healthcare professionals presented in Chapter Five. The content and face validity have been assessed with patients and healthcare professionals and overall has been found to be appropriate for this population. The researchers involved in this study have accepted that that the inclusion of patient input and feedback throughout development has improved the content and overall format of this measure. One example of such improvements is the

addition of the phrase, ‘my AF’, which is suggested as making this questionnaire more patient-focused and was supported by some of the statements from individual patient interviews. The process of development has welcomed constructive feedback, and improvements to the content and format have been made throughout. In addition to the changes described in the results chapters, further changes occurred based on the verbal feedback from some participants who completed AF PROM but were not taking part in an interview stage. For example, one participant stated to the researcher whilst completing AF PROM that it would be beneficial to include the date of completion on the questionnaire. This omission was an oversight by the researcher and therefore a welcome improvement. Although the sample sizes were smaller than anticipated, initial psychometric results suggest that AF PROM is a valid and reliable measure suitable for an AF population.

The accounts presented in Chapter Five described how AF and associated treatments and therapies impacted various aspects of patients’ lives and in some cases, have had a significant impact on HRQoL. Although their experiences were unique, similarities were noted throughout. Aspects of the development of AF PROM required detailed consideration, as AF is associated with other medical conditions which can lead to some participants being unable to clearly identify if the impact on HRQoL was caused by symptoms of AF or other factors such as reduced fitness, age or other medical conditions. Throughout development it was noted this would be a limitation of developing such a measure. It is unclear how this limitation can be completely overcome in future practice, but the researchers included the term ‘due to my AF’ to remind the patient that this was the researchers’ main area of consideration. However, the interviews in the content validation stage suggested that this also led to some difficulties for a small number of participants who were unsure how to best answer the question, not knowing whether their symptoms were caused by AF.

Another aspect which was considered was the length of the recall period, which needed to be short enough time period for participants to recall but long enough to capture the experiences of those with paroxysmal AF. This is not accounted for by some generic measures such as the EQ-5D discussed in Chapter Three. Other areas of consideration included the wording of the stem items and the wording and number of categories of answers. The aim was to ensure these were easy to understand and the number of options were not so large as to be burdensome for patients and healthcare professionals, increasing the feasibility of the measure.

8.3 Recommendations for Clinical Practice and Future Research

This study presented the patient’s perspective on living a life with AF and its impact on HRQoL. It has additionally presented the perspective of relatives of those with AF and healthcare professionals

from an AF specialist centre. Areas of HRQoL which were voiced as being impacted were recorded and were used as the basis of a disease-specific HRQoL measurement tool. In addition to the main aim of developing this measure, the qualitative results have highlighted some examples of good and poor care in clinical practice which have impacted patients' experience and HRQoL. These results have highlighted the importance of the promotion of patient-centred care. It is important to highlight how patients may have concerns and increased anxiety regarding their condition and available treatments when in an unfamiliar environment such as a hospital (Gluyas, 2015). To allow this to be carried out, it is crucial that healthcare professionals have a good understanding of the patient's perspective. This has been also highlighted by the recommendations of the SAFE report (Begg et al., 2012).

It was important to the researchers that the perspective of relatives and healthcare professionals was also sought, as some studies have highlighted the discrepancies between treatment perception of medical staff and patients with AF (especially regarding anticoagulants for AF-related stroke prevention) and in other specialities (Lee et al., 2010; Dalmau et al., 2017). Although it is acknowledged that there are some factors which can act as barriers to providing patient-centred care including patients, healthcare professionals or healthcare structural factors (Gluyas, 2015), one way to overcome some of these barriers is to increase the understanding of healthcare professionals of the perspective of the patient. Healthcare facilities should provide training which can improve skills such as communication skills (Begg et al., 2012; Kitson et al., 2013; Gluyas, 2015). The qualitative data from this study has complemented such research by highlighting the importance of clear communication and its consequential impact on HRQoL. For example, some participants explained how lack of knowledge and poor communication by healthcare professionals led some participants to have a poor understanding of their condition and resulted in negative psychological feelings following a diagnosis of AF. The qualitative data also highlighted that due to time constraints and low staffing levels, some healthcare professionals felt that there was insufficient time to focus on educational needs and psychological support, placing greater priority on managing the physical symptoms. The use of AF PROM (once validated) may be able to help patients voice what factors have the greatest impact on their HRQoL and which they feel require more of the healthcare professionals' attention.

The recent focus on health promotion by AF patient charities as well as the promotion of the patient and family contribution to care by the NHS may have resulted in fewer patients accepting a paternalistic healthcare model and welcoming a more patient-centred approach to care. There is much benefit in utilising such an approach, which allows patients to be treated as individuals, increases patients' and relatives' satisfaction and improves patient outcomes, leading to decreased healthcare costs (Charmel and Framptom, 2008; Mazurenki et al., 2015). The provision of patient-care can also

provide healthcare professionals with a sense of pride in and satisfaction with the care they are providing (Charmel and Framptom, 2008; Gluyas, 2015).

8.3.1 Anticipated Next Stages of AF PROM Development and Validation

The next stages of AF PROM will involve the continuation of recruitment for the preliminary validation. Upon completion of this stage, it is anticipated that a larger validation stage will occur. Current ethical approval allows three major steps which assess various aspects of AF PROM validity, such as responsiveness, test-retest reliability and construct validity.

The anticipated assessment of the ability of AF PROM to respond to change will involve the recruitment of 300 participants who will complete several other disease-specific and generic measures (SF-36, WHOQOL-BREF and Canadian Cardiovascular Society (CCS) Severity of AF (SAF) Scale) as well as AF PROM on two occasions, at baseline before treatment and three months after receiving a catheter ablation for their AF.

Further test-retest reliability will be assessed by recruiting 100 participants with AF who have not been involved in development of the measure. Participants will be asked to complete AF PROM on two occasions: two weeks prior to their clinical appointment and again at their clinical appointment. The second PROM will include an additional question asking if anything which may have impacted their HRQoL has happened in the past two weeks, which may impact the results. The inclusion of such a statement in the preliminary validation was a noted oversight and limitation and therefore this data will be collected in future stages.

As part of the process to further assess the construct validity of this newly developed measure, 280 patients listed for a catheter ablation for AF will be asked to complete AF PROM at two time points, baseline and three months after their ablation. The results of the scores of AF PROM will be used to test two hypotheses: first, that those who have had a successful catheter ablation of their AF will have higher scores compared to their previous score; and second, that patients whose ablation has been unsuccessful will have less or no noted change between scores. In addition, AF reoccurrence will be recorded on a holter monitor and correlations between reoccurrence of AF and patient scores will be noted.

8.4 Overall Strengths and Limitations of the Study

It is considered that the qualitative and quantitative research methods used were appropriate for the development of this tool. The accounts of patients heard in clinical practice before this study commenced highlighted the depth and value of data collected by qualitative means. The limitations of these methods and alternative methods to overcome limitations were discussed in the context of the

results presented in each chapter. For example, while having focus groups was considered a beneficial methodology for allowing the generation of ideas, an alternative methodology may have been to have in-depth individual interviews and base the main themes upon this data.

It would have been preferable to have made use of technological advances especially in the preliminary validation stages, which may have increased participant numbers; however, as previously noted, due to insufficient funding this could not be accommodated. Additionally, it would have been preferable to involve participants in the London area whose first language is not English in order to improve the generalisability of the measure, although this was not performed at this stage, the researchers would recommend the investigation of AF PROM content and face validity in other populations whose first language is not English. This could be performed by the use of a think aloud study to ensure that all relevant domains are included.

A major strength of this study is the inclusion of patients throughout all stages in its development. In addition to this, the perspectives of healthcare professionals and relatives of those with AF were also captured. Having numerous stages of development has allowed the involvement of various PwAF. Although some stages have been highlighted as having a lower number of participants than anticipated (e.g. Study Three, which included only one PwAF to review the initial draft measure), having several iterations of the measure has allowed amendments to be made and reviewed by different individuals and is thought to have improved the relevance and clarity of the measure, further ensuring that aspects of HRQoL which are important to the PwAF are included.

For future research developing similar tools, the researchers would recommend further patient involvement. Upon reflection the inclusion of patient involvement in the development of the study documents (such as the topic guides) may have been of benefit. In addition to this, the development of such a tool by a patient group which could have been supported by the researchers may have been beneficial and could be an area for future research in other conditions. Although there has been much research and various improvements which have been made in recent years, such as the focus on screening AF, pulse checks, health promotion and stroke risk assessment and reduction, there is still more to be done. This study has highlighted some areas for future research and improvements to clinical care.

8.5 Final Thought

This thesis has made several novel contributions to the literature, the main one being the development of an AF-specific HRQoL PROM. To the author's knowledge, this is the first study to develop such a

measure which has included input from patients, relatives and healthcare professionals from the beginning of development in a London population. Although it is acknowledged that further work is needed to support the validity and reliability of AF PROM, mixed methods have increased our understanding of the impact of AF and associated therapies on HRQoL in a UK, healthcare setting and have added to the available qualitative literature.

This study may have several implications for future clinical practice. In addition to the qualitative data generated by this study, the development of this tool may lead to an increase in the level of understanding among healthcare professionals in specialist and non-specialist centres of the impact of AF on HRQoL, leading to more patient-focused care in a UK healthcare context. As poor communication in some clinical practice settings was an expressed concern voiced by some participants in this study (presented in Chapter Five), the use of this tool, once validated, may improve communication between patients and healthcare professionals, making it simpler for patients to express concerns and articulate needs. As one participant explained, AF PROM may be used to improve the identification of the current need and allow patients access to available support, which could lead to *'their experience[and] their journey [with AF] … [being] better'* (PA021). The recording of this data over several time points may allow any improvements or deterioration in HRQoL due to interventions or therapies to be recorded for each individual patient. This can provide clinicians and current governing bodies with a more detailed understanding of the impact of the condition and treatments, which may influence policies and funding nationwide.

Chapter 9 Appendices

Appendix A Chapter Two

Appendix A 2.1 Search list and Database list

Search completed: September 2018.

Completed by: SH.

Search Terms: (qualitative or quantitative or interview or questionnaire or focus group or disease specific or generic) and (treatment or management or comparison or catheter ablation or medication) and (AF or Atrial Fibrillation) and (health-related quality of life or HRQoL or quality of life or QoL) not (treatment not INR or warfarin or anticoagulant or NOAC or DOAC or DIrect oral anticoagulant Novel oral anticoagulant).

Databases searched using Ovid:

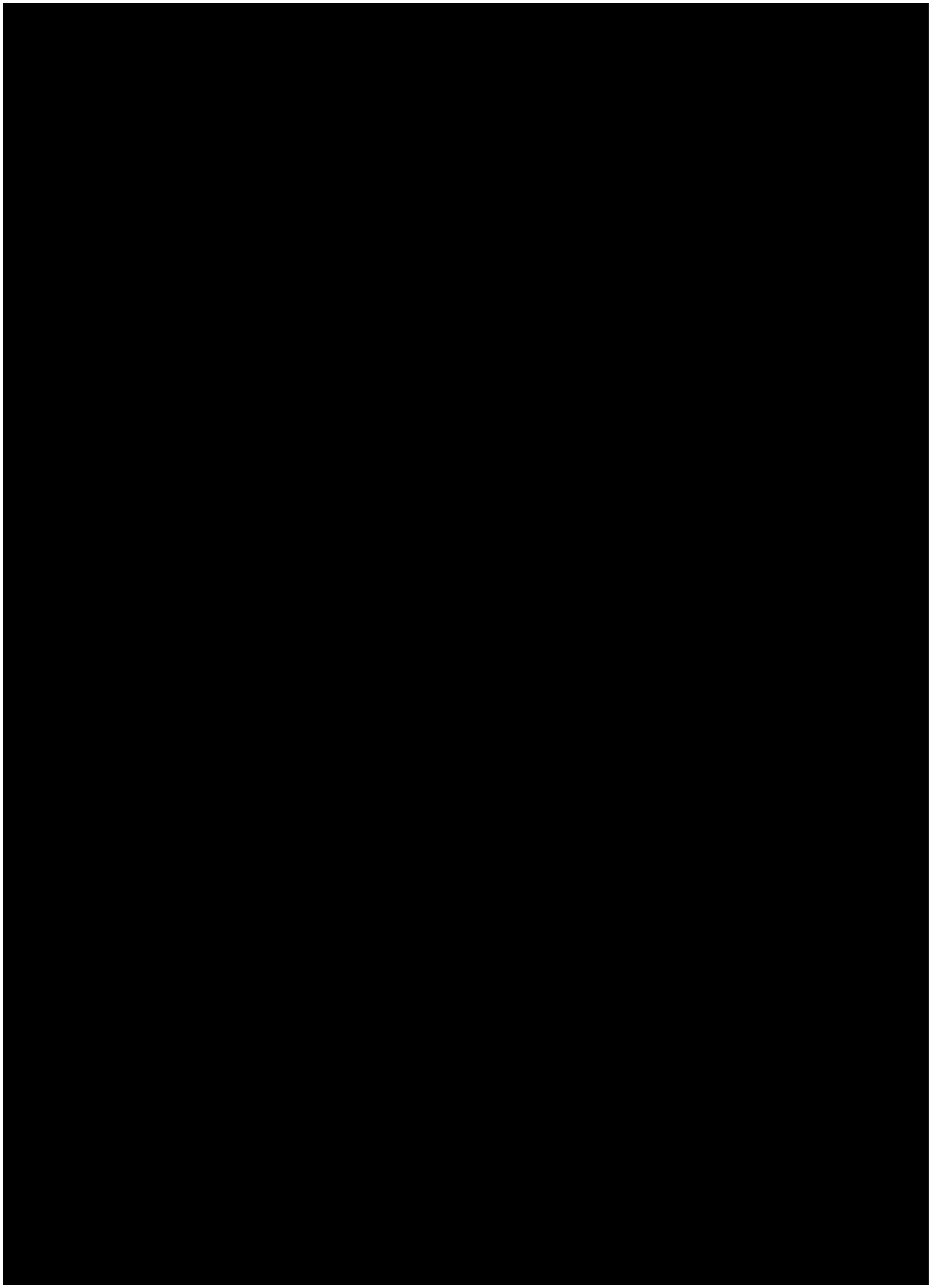
- Database: AMED (Allied and Complementary Medicine) (1985 to September 2018)
- EBM Reviews - Cochrane Database of Systematic Reviews (2005 to September 12, 2018)
- EBM Reviews - ACP Journal Club (1991 to August 2018)
- EBM Reviews - Database of Abstracts of Reviews of Effects (1st Quarter 2016)
- EBM Reviews - Cochrane Clinical Answers (August 2018)
  EBM Reviews - Cochrane Central Register of Controlled Trials (August 2018)
- EBM Reviews - Cochrane Methodology Register (3rd Quarter 2012)
- EBM Reviews - Health Technology Assessment (4th Quarter 2016)
- EBM Reviews - NHS Economic Evaluation Database (1st Quarter 2016)
- Embase (1974 to 2018 Week 38)
- Global Health (1973 to 2018 Week 36)
- Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (1946 to September 17, 2018)
- Social Policy and Practice (201807)
- Ovid Nursing Database (1946 to September Week 1 2018)

Appendix B Chapter Three

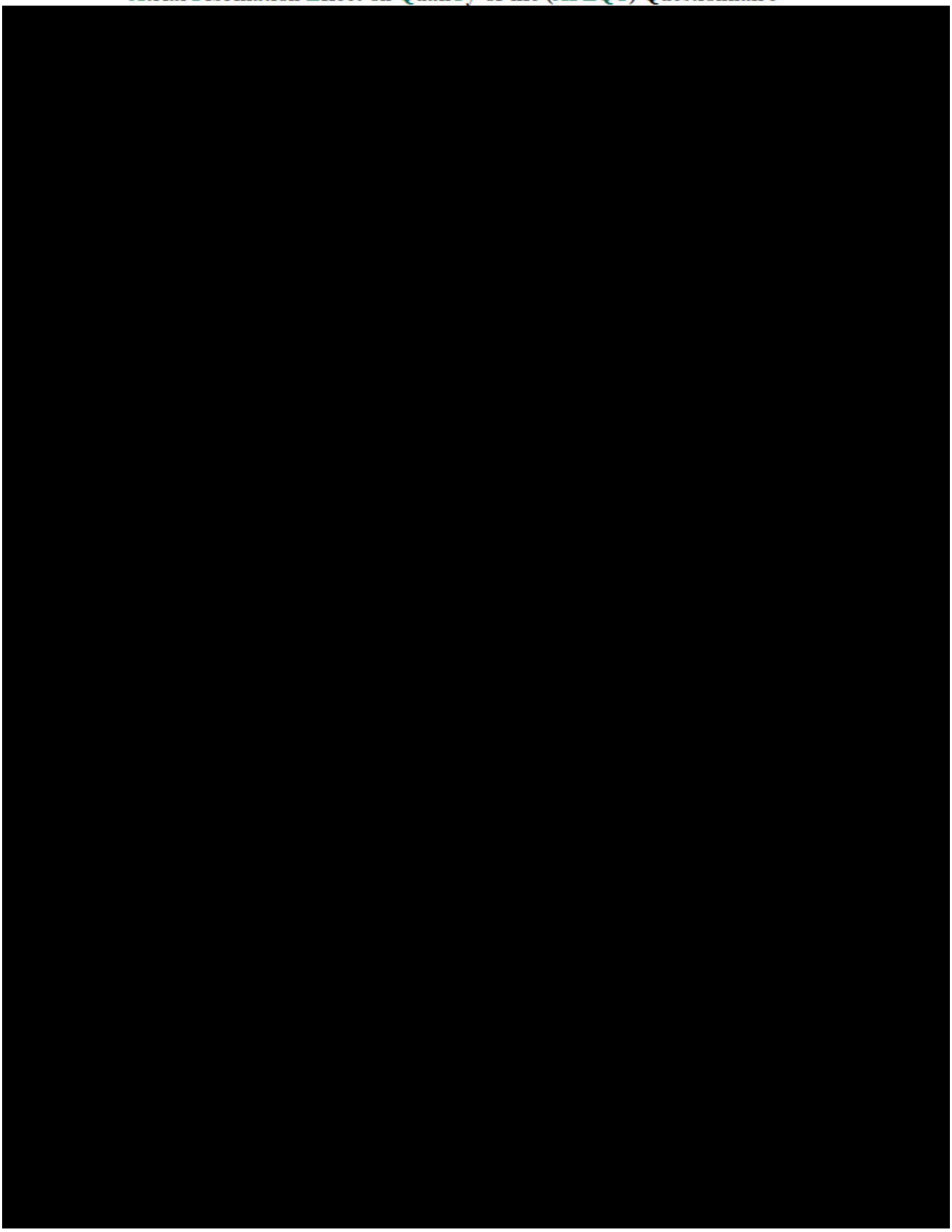
Appendix B 3.1 Literature Review Search List of Databases

Your University Journals@Ovid,
Journals from Ovid,
Embase
AMED (Allied and Complementary Medicine)
EBM Reviews - ACP Journal Club
EBM Reviews - Cochrane Central Register of Controlled Trials
EBM Reviews - Cochrane Database of Systematic Reviews
EBM Reviews - Cochrane Methodology Register
EBM Reviews - Database of Abstracts of Reviews of Effects
EBM Reviews - Health Technology Assessment
EBM Reviews - NHS Economic Evaluation Database
Global Health
HMIC Health Management Information Consortium
Maternity and Infant Care
Ovid MEDLINE(R)
Ovid MEDLINE(R) Daily Update
Ovid OLDMEDLINE(R)
Ovid Nursing Full Text Plus, Social Policy and Practice

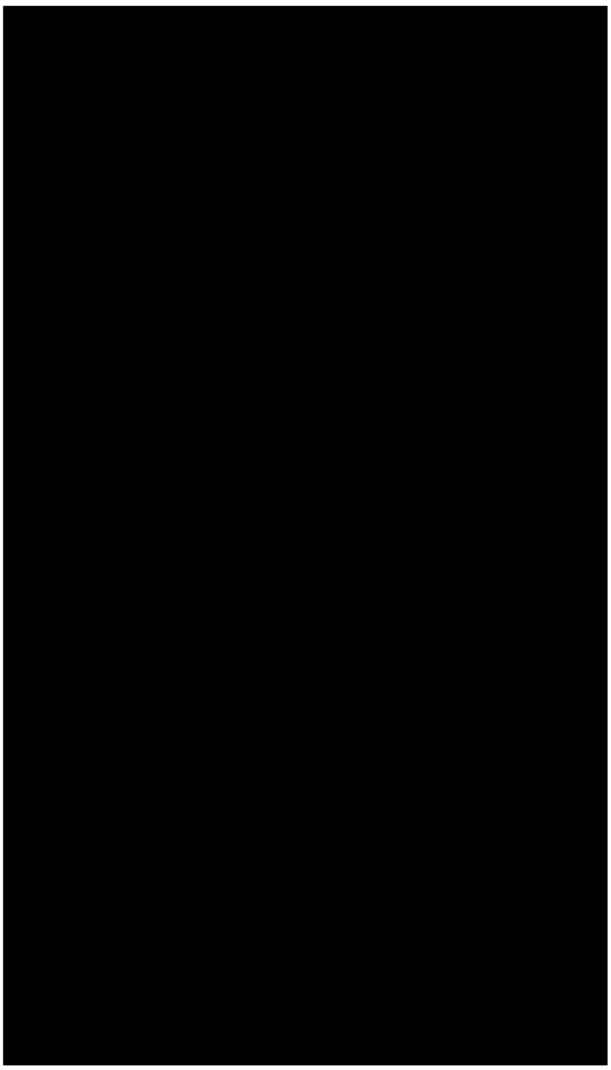
Appendix B 3.2 AFEQT Questionnaire



Atrial Fibrillation Effect on QualiTy-of-life (AFEQT) Questionnaire

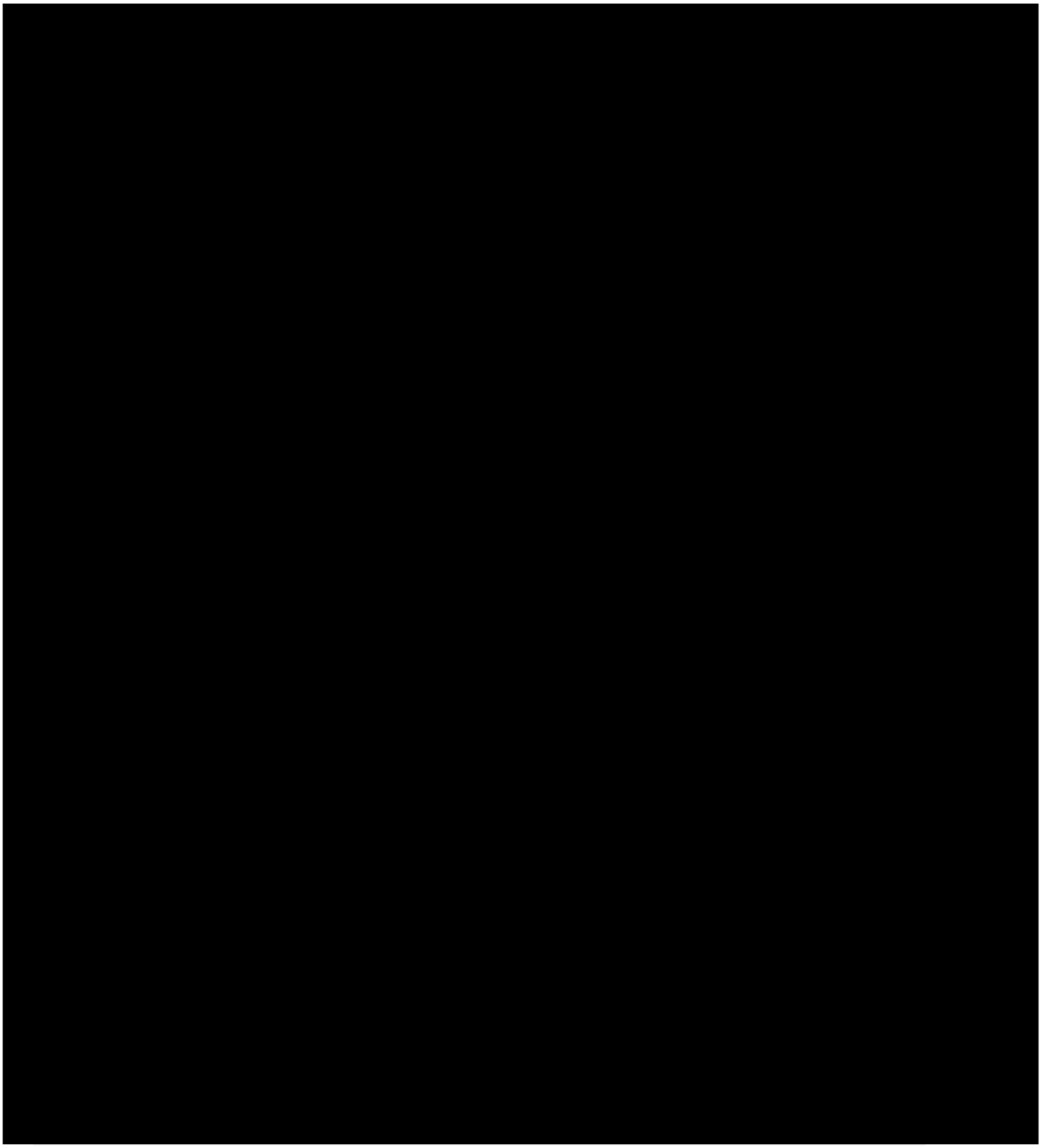


Appendix B 3.3 AFQOL Questionnaire

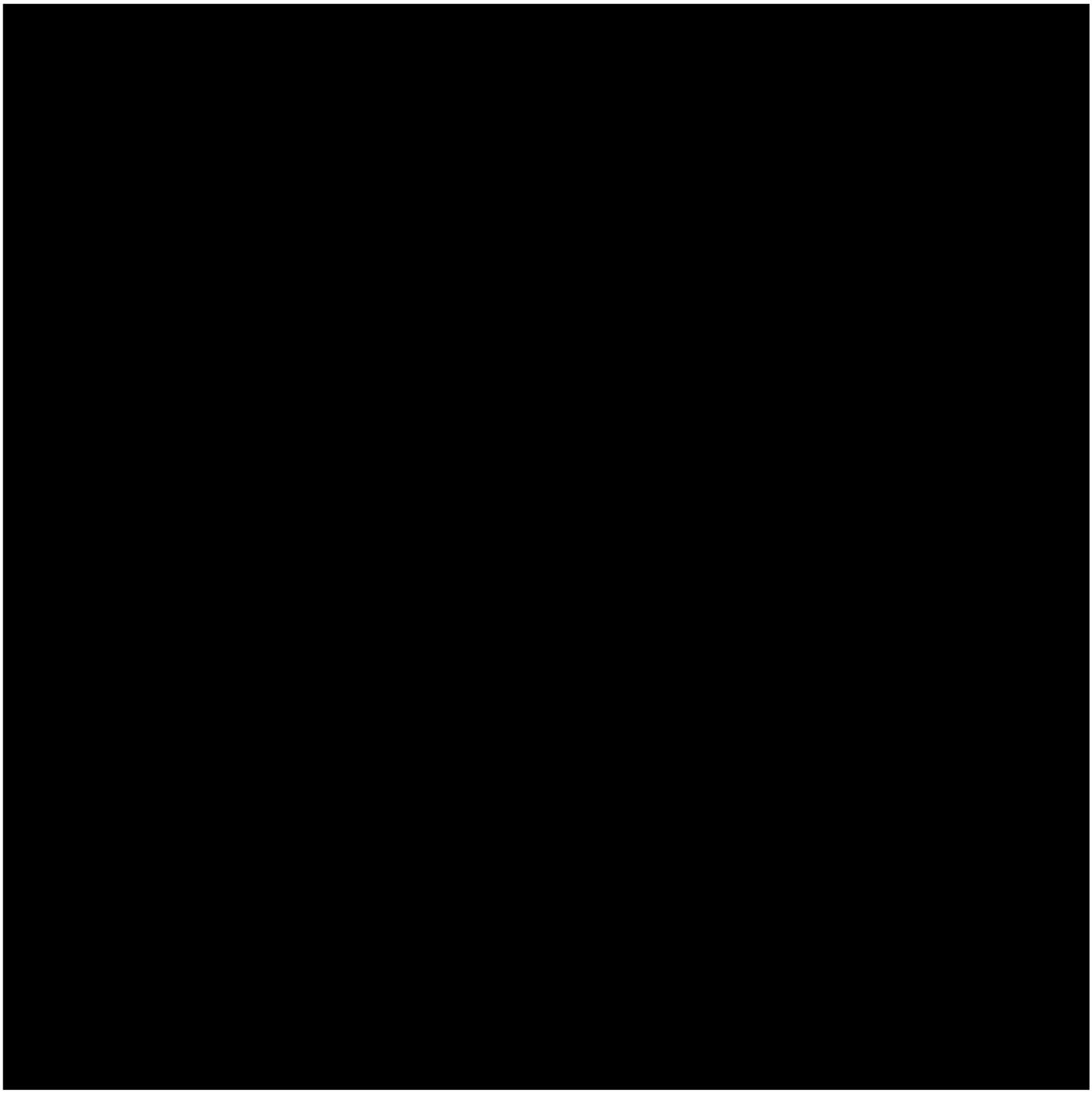


Accessed from Arribas, F., Ormaetxe, J.M., Peinado, R., Perulero, N., Ramírez, P. and Badia, X., 2010. Validation of the AF-QoL, a disease-specific quality of life questionnaire for patients with atrial fibrillation. *Europace*, *12*(3), pp.364-370. Accessed: 07/07/16: by permission of Oxford University Press

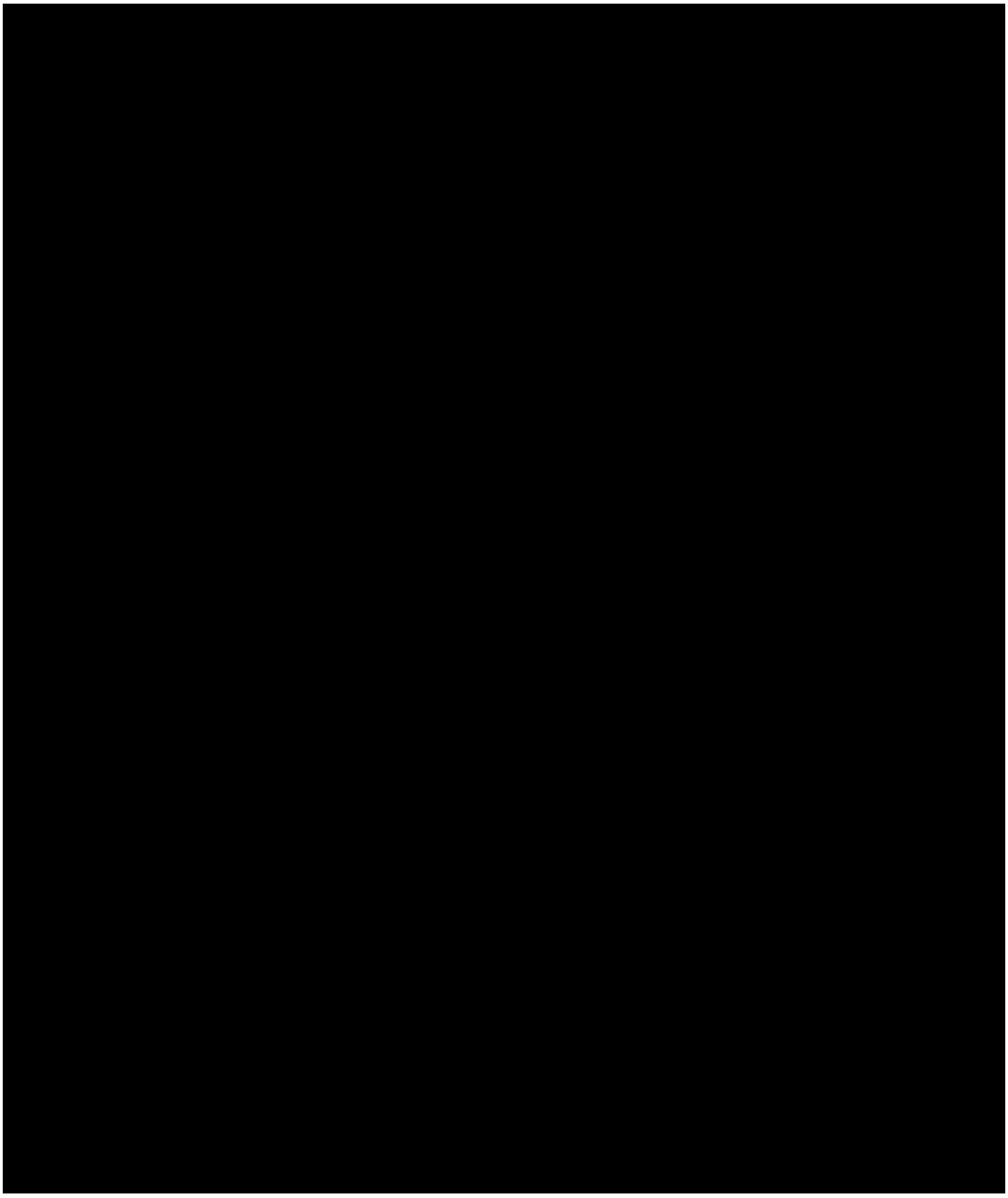
Appendix B 3.4 AFQLQ Questionnaire: Japanese and English version



Yamashita T, Kumagi K, Koretsune Y, Mitamura H, Okumura K, Ogawa S, et al. A new method for evaluating quality of life specific to patients with atrial fibrillation: Atrial fibrillation quality of life questionnaire (AFQLQ). Jpn J Electrocardiology. 2003; 23:332–43. 16. Translated and included with permission of the author and publisher October 2017.

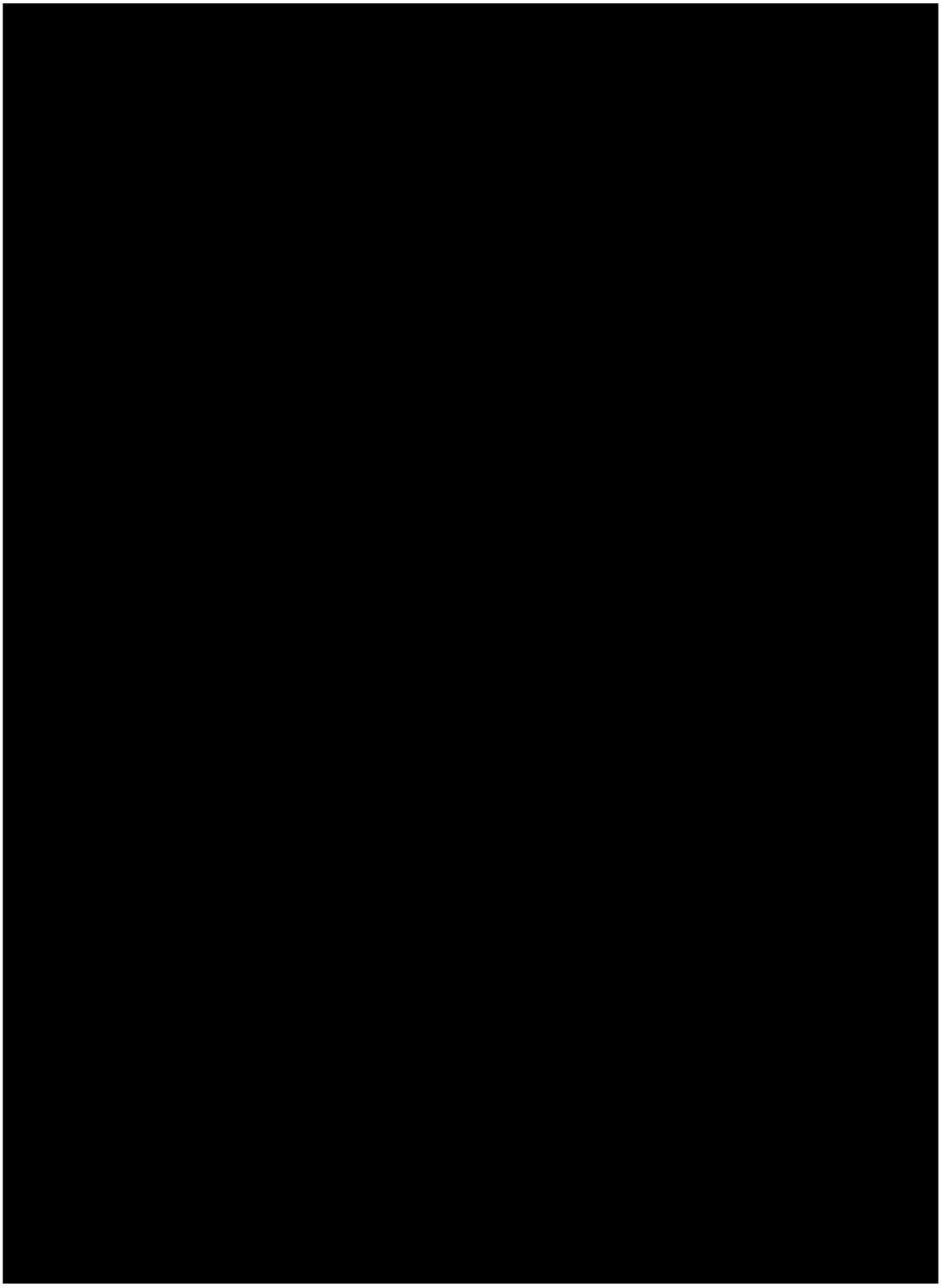


Yamashita T, Kumagi K, Koretsune Y, Mitamura H, Okumura K, Ogawa S, et al. A new method for evaluating quality of life specific to patients with atrial fibrillation: Atrial fibrillation quality of life questionnaire (AFQLQ). Jpn J Electrocardiology. 2003; 23:332–43. 16. Translated and included with permission of the author and publisher October 2017.



AFQLQ Translated from Japanese to English via Google Translate. Checked 08/06/16 08/06/16. V3

Yamashita T, Kumagi K, Koretsune Y, Mitamura H, Okumura K, Ogawa S, et al. A new method for evaluating quality of life specific to patients with atrial fibrillation: Atrial fibrillation quality of life questionnaire (AFQLQ). Jpn J Electrocardiology. 2003; 23:332–43. 16. Translated and included with permission of the author and publisher October 2017.



AFQLQ Translated from Japanese to English via Google Translate. Checked 08/06/16. V3

Yamashita T, Kumagi K, Koretsune Y, Mitamura H, Okumura K, Ogawa S, et al. A new method for evaluating quality of life specific to patients with atrial fibrillation: Atrial fibrillation quality of life questionnaire (AFQLQ). Jpn J Electrocardiology. 2003; 23:332–43. 16. Translated and included with permission of the author and publisher October 2017.

Appendix B 3.5 QLAF Questionnaire: (version 1 and version 2)

- QLAF version 1
- QLAF version 2 now referred to as AFQLQ

Braganca, É.O.V., Filho, B.L., Maria, V.H., Levy, D. & de Paola, A.A.V. 2010, "Validating a new quality of life questionnaire for atrial fibrillation patients", *International journal of cardiology,* vol. 143, no. 3, pp. 391398.Accessed 07/07/16: used with permission from Elsevier

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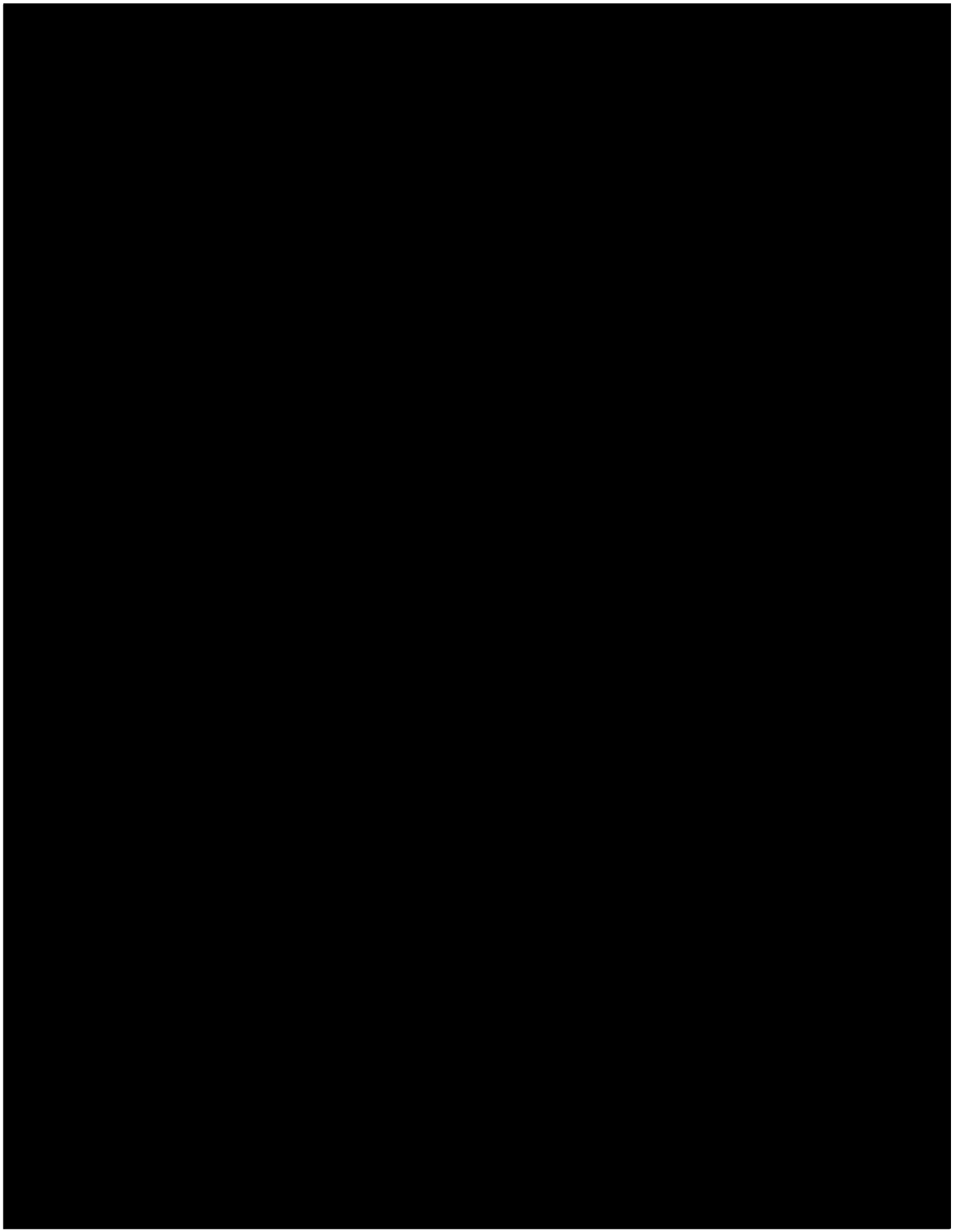
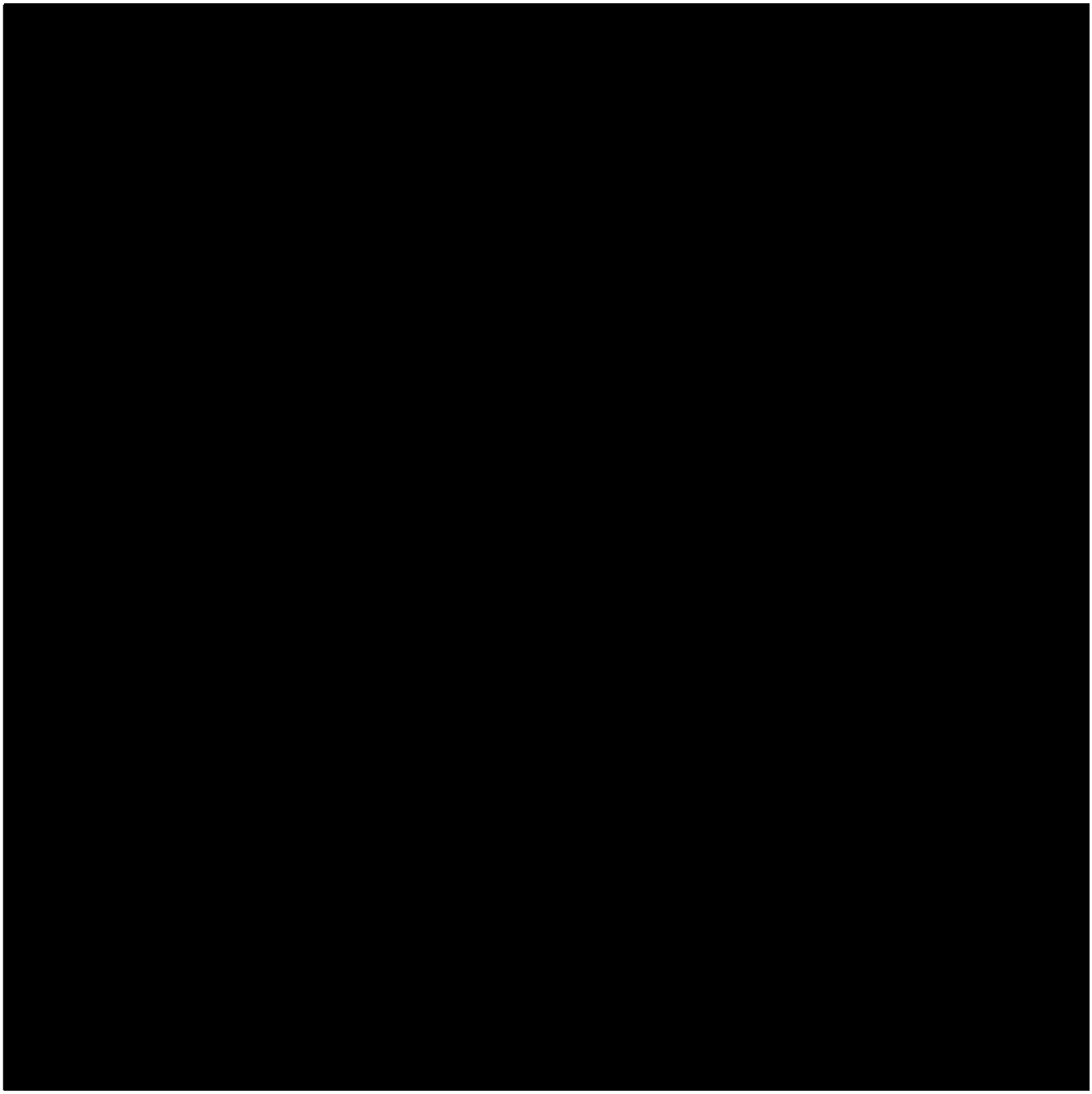




Appendix B 3.6 PubMed search results

Table 3.4 PubMed Results: AFEQT (repeated search results October 2017 and September 2018)					
Author (s), Location	**Population**	**Study Type**	**Questionnaires used**	**Results**	**Summary critique**
Allen et al. (2015) USA	PAF and persistent AF (with or without heart failure)	Observational study investigating the outcome of digoxin use	European Heart Rhythm Association (EHRA) score AFEQT (baseline, 12 and 24 months)	Outcome of focus was death. Symptoms and HRQoL were additionally measured but not the focus. HRQoL was reported as lower in patients on digoxin at baseline and at 12 months as measured by AFEQT (p=0.0002).	Might not be generalisable to all patients outside of USA (-).
Angaran et al. (2015) Canada	Diagnosis of atrial fibrillation or atrial flutter (n=128)	Observational: Pilot study: to investigate the impact of a protocol care for patients admitted to emergency room into community care	AFEQT (baseline and 3 months)	Significant improvement in HRQoL as measured with AFEQT from 56.4±25.5 at baseline to 76.4 ±20.0 at 3 months (p<0.0001).	Single centre (-). Observational nature (-) Not randomised (-). Unknown generalisability (-). Short follow up (-).
Bai et al. (2015) China	AF: RFA group (n=44), non-RFA group (n=61).	RFA versus non-RFA catheter ablation (year 2011- 2013)	AFEQT	Full paper only available in Chinese. Abstract available in English. Mean score changes from baseline to 6-month follow up all p<0.05. No significant difference in the change from baseline to 6-month follow up between the two groups (all p>0.05).	Full text not available in English; unable to critique (-).
Bai et al. (2015) China	PAF (n=133) non PAF (n=89)	Radiofrequency ablation (RFA)	AFEQT	Baseline scores were compared to 6-month follow up. Global scores in both groups showed significant improvements (p<0.001). Significant improvements noted in all domains (p<0.001) apart from non RFA group in the treatment satisfaction domain (p=0.10). No significant difference between groups apart from treatment satisfaction domain (p=0.007).	Potential selection bias as study design is observational study (-). Potential placebo effect of catheter ablation which may have increased treatment satisfaction scores (-). Short follow up (-).
Bostrom et al. (2017) USA	Symptomatic AF (n=218)	Observational study	Montreal Cognitive Assessment Battery (MoCA); Patient Health Questionnaire (PHQ-9); Generalized Anxiety Disorder-7 scale; AFEQT	Higher burden of psychosocial/cognitive impairment was associated with lower HRQoL scores as measured with AFEQT.	Only symptomatic patients included, so not generalisable to asymptomatic population (-). Mostly PAF patients (-).

Cherian et al. (2017) USA	10,135 AF (PAF, persistent, permanent)	Registry: Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF)	AFEQT	HRQoL results split between 2 groups: those without heart failure (no HF) and those with heart failure (HF).The median overall score in the no HF group was 83.3 (IQR 68.5-93.5) and the median score in the HF group was 76.9 (IQR 61.1-90.7) (p=<0.0001). The median results for the daily activities subscale was 81.0 (IQR 58.3-95.8) in the no HF group; the median score was 66.7 (IQR 41.7-87.5) for the HF group (p=<0.0001). Other subscale results showed no significant difference between groups: Symptoms subscale (p=0.96); treatment concern (p= 0.36); and treatment subscale (p=0.92).	Observational methodology leads to potential enrolment bias.
Du et al. (2017) China	PAF and Persistent AF (n=151 ablation arm; 318 AAD arm)	Prospective, non-randomized, single-centre	AFEQT; SF-36 (baseline, 3, 6 and 9 months)	Ablation arm had significantly better HRQoL scores as measured with SF-36 and AFEQT. AFEQT: PAF: Baseline score: 54.4; 9-month follow up: 79.19 ($p < 0.001$); Persistent AF: Baseline score: 55.4; 9-month follow up: 74.5 (< 0.001). SF-36: Physical component of SF-36 score improved significantly (PAF: Baseline: 58.31; 9-month follow up: 75.92 ($p < 0.001$); Persistent AF: Baseline: 59.67; 9-month follow up: 70.28 ($p < 0.001$). SF-36: Mental component: PAF group had significant ($p < 0.01$) improvement in scores in ablation arm. Persistent group had significant ($p < 0.05$) improvement in scores in ablation arm. The AAD group did not have significant changes in AFEQT scores (PAF: Baseline score: 63; 9-month follow up: 64.89 ($p = 0.17$)). No significant changes were noted with the Persistent group: (AFEQT: Baseline score: 61.0; 9-month follow up: 64.4 ($p = 0.07$)). AAD group: SF-36: Mental component of SF-36 score improved significantly (PAF: Baseline: 60.98; 9-month follow up: 63.30 (**p** = 0.03); Persistent AF: Baseline: 59.2; 9-month follow up: 61.84 (**p**=0.14). SF-36: Physical components score: PAF group had non-significant improvement (62.05 at baseline to 64.31 at follow up) in scores in AAD arm. Persistent group had non-significant improvement (from 59.72 at baseline to 62.06) in scores in AAD arm.	Single-centre study with expertise may have led to the higher than normal effectiveness scores (-). Short follow up period (-).
Freeman et al. (2015) USA	AF (n=10,087)	Observational	AFEQT; EHRA	EHRA symptom class inversely correlated with the AFEQT score (Spearman correlation coefficient = −0.39).	Study representative of AF population. May not be generalisable to other populations (-).
Inohara et al. (2017) Japan	N=1,874	Multicentre AF registry assessing performance	AFEQT	Groups split into achievement (n= 479) and non-achievement (n= 492) groups. Results re: HRQoL. Similar results between groups at baseline. However, significant higher scores reported at follow up (one year) in	Not randomised (-). As registry is ongoing, there may be potential

	(PAF, Persistent, unknown)	measures (such as anticoagulation adherence and quality of medication adherence for AF management)		most subdomains. Overall score: Non-achievement group: baseline: 77.1 (IQRs 64.8 – 88.0); follow up: 86.7 (IQRs 76.7 – 95.0). Achievement group: baseline 79.2 (IQRs 66.7 – 88.5); Follow up 89.2 (IQRs 78.5 – 96.6), (p = 0.021). All subdomain scores showed significant differences between groups at baseline and follow up (symptom [p= 0.014], treatment concern [0.163] and satisfaction [p= 0.001]) apart from daily activities [p= 0.163].	selection bias/ skewed results as only half of follow up data was available at time of publication (-).
Jackson et al. (2016) Multicentre	AF (n=9631): PAF, persistent and permanent; 1710 (17.7%) had the impression of Sinus node dysfunction	Multicentre registry (174 sites)	EHRA score; AFEQT	Lower AFEQT scores noted in those study participants with SND: 80 (67–93) at 12 months compared to those without 85 (72–94) (p=0.0008).	Not randomised, observational methodology (-). Specific cohort so results are not generalisable (-).
Looi et al. (2013) USA	PAF (n=203)	Catheter ablation	AFEQT (CCS-SAF)	Similar scores noted between groups after treatment (not significant; p=0.35). Reoccurrence of AF after treatment was associated with significantly lower AFEQT scores (72.1±26 and 84.7±21; p<0.002).	Mean AFEQT scores only taken at follow up, so no comparison scores available (-). Low proportion of patients on AAD at follow up may impact scores (-).
Magnani et al. (2017) USA	N=31	Use of mobile health technology	AFEQT; Patient activation with the Patient Activation Measure (PAM); Medication Adherence Scale (MMAS-8).	HRQoL global scores using AFEQT improved significantly (64.5 [22.9] at baseline and 76.3 [19.4] at day 30 [p<0.01]). Improvements were noted in subdomains (Symptoms 74.6 [24.1] at baseline and was 80.7 [21.4] at day 30 [p<0.07]; daily activities 56 [27.8] at baseline and noted as 65.2 [26.1] at day 30 [p<0.1]; Treatment concern 66.7 [26.2] at baseline and 74.6 [22.6] [p<0.71] at day 30; Treatment satisfaction 71.2 [25.4] at baseline and 72.9 [27.6] [p<0.71] at day 30.) **Only significant improvement noted in global score and daily activities.** Significant small improvements noted in medication adherence.	Small convenience sample – not randomised (-).
Peleg et al. (2017) Spain	=n19; AF	Implementation of mobile health device in patients' daily life.	AFEQT; EuroQoL	The overall score of the AFEQT pre-MobiGuide was 72.3 ± 18.7 and post-MobiGuide was 67.8 ± 11.1. The treatment satisfaction subscale score was reported as 72.3 ± 18.7 and the post-MobiGuide was 71.9 ± 21.7. The EuroQoL utility coefficient pre-MobiGuide was 77.6 ± 0.23 and 78.4 ± 0.23. The analogue score was reported as 67.5 ± 18.6 and	Limited in size (-). Mobile health device not fully implemented within the hospital (-).

				post-MobiGuide was 80.1 ± 13.0. EuoQoL showed improvement in HRQoL pre- and post-MobiGuide. However, AFEQT shows decrease in HRQoL pre- and post-MobiGuide.	
Raine et al. (2015) Newcastle, UK	PAF (n=44) Persistent AF (n=36)	Catheter ablation: types of ablation technologies: PVI (n=45) PVI+Linear (n=17) PVI+CFAE (n=8) PVI+Linear+CFAE (n=10)	AFEQT SF-36 V2	Significant improvement in HRQoL scores were greater when measuring HRQoL with AFEQT (25.4 ±19) compared to measuring HRQoL with SF-36 (MCS: 8.5±7.9; p<0.01; PCS: 6.8 ±6.4; p<0.01). Improvements correlated closer with AF-specific measure (AFEQT r=0.55; PCS r=0.26; MCS r=0.30).	Indicates AF-specific measure has higher sensitivity to changes compared to generic HRQoL measure (+). Short follow-up period (-). Not randomised (-).
Sandhu et al. (2017) Canada	AF (n=100)	Follow up of patients with an electrical cardioversion	SF-36; AFEQT	Significant improvement (p=< 0.0001) in mean (± SD) global scores of the AFEQT from a baseline of 55.6 (24.4) to 68.7 (23.6) at 3-month follow up. Significant improvement in the following domains: symptoms: 66.2 (26.6) at baseline and 77.9 (23.5) at 3-month follow up (p<0.0001); daily activities: 48.5 (29.5) at baseline and 61.9 (29.7) at 3-month follow up (p<0.0001); treatment concerns: 57.6 (25.8) at baseline and 71.8 (25.3) at 3-month follow up (p<0.0001); treatment satisfaction: 56.7 (26.1) at baseline and 65.2 (29.2) at 3-month follow up (p=.02). Significant improvements (p<0.0001) (indicating improved HRQOL) were noted in all domains of AFEQT at 3-months follow up in those who maintained sinus rhythm after electrical cardioversion. At 3-month follow up, most of the subdomains of the SF-36 showed significant improvements when patients were in sinus rhythm (physical functioning p=0.001; physical role p<0.0001; emotional role p=0.03; vitality p<0.0001; mental health p=0.002; social functioning p<0.0001; physical summary score p<0.0001; mental summary score <0.0001. Body pain scores improved but this change was not significant (p=0.42); general health scores reduced slightly from 57.9 (SD 21.8) at baseline to 57.8 (22.8) at 3-month follow up, but this change was not significant (p=0.96). Although improvements were noted in most AFEQT domains at 3-month follow up after cardioversion, changes were not significant (global score p=0.10; symptoms p=0.10; daily activities p=0.78; satisfaction p=0.07) in those who were in AF at 3-month follow up except for treatment concerns which improved from 61.2 (27.3) at baseline to 69.0 (26.9) at 3-month follow up (p=0.02). Significant improvement in SF-36 scores in those who were in AF after cardioversion was observed only in one domain of the SF-36 (emotional role), from 50.4 (43.0) at baseline to 71.1 (39.3) at 3-month follow up (p<0.001). Improvements to other domains (mental summary	First study using AFEQT in cardioversion population. Small study size (-). Mostly healthy individuals enrolled (-). ECG not taken at follow up (-). Symptom questionnaire not used so asymptomatic population not considered. (-). Short follow up period (-).

				score; body pain; social functioning; physical functioning) were noted, but these were not significant. Significant reduction in scores using the SF-36 were noted in one domain (general health), from 61.9 (20.9) at baseline to 55.7 (20.3) at 3 months (p=0.02). Reduction in other domains (physical role; vitality; mental health; physical summary score) was not significant.	
Särnholm et al. (2017) Denmark	N=19	Examining the impact of CBT	AFEQT, Atrial Fibrillation Effect on Quality-of-Life. AFEQT-13, AF-specific worry and symptom fear SF-36-MCS (Mental Health component score) and SF-36-PCS, (Physical component summary score) GAD-7, Generalized Anxiety Disorder 7-item. PHQ-9, Patient Health Questionnaire. PHQ-15, Patient Health Questionnaire. 15-Item Somatic Symptom Severity Scale. SCL frequency/severity, Symptoms Checklist; Frequency and Severity Scale. PSS-10, Perceived Stress Scale.	Global AFEQT score improved from 56.9 (SD 19.6) at baseline to 82.0 (10.7) after treatment (p<0.001). AFEQT (item 13), mean score improved from 4.6 (1.5) at baseline to 2.0 (1.4) after treatment (p<0.001). Item 13 on the AFEQT reported to have significant large effects sizes at 6 months follow up (ES; 95% CI); (1.81; 1.06, 2.68) was significant (p<0.001). SF-36-PCS improved from 44.3 (11.1) at baseline to 49.5 (6.5) after treatment (p<0.05). However, the effect size (95% CI) 0.66 (0.21, 1.17) was not significant (p=0.018). SF-36-MCS mean scores improved from 37.1 (9.9) at baseline to 45.2 (9.0) after treatment (p<0.05). However, the effect size (95% CI) 0.73 (0.25, 1.25)] was not significant (p=0.014). The frequency and severity of AF symptoms showed large significant improvements.	Not all the subdomain results are reported (-). Small number of participants (-). No control group (-).
Siddoway et al. (2015) USA	PAF (n=100)	Cryoballoon pulmonary vein isolation (PVI) versus radiofrequency (RF) PVI	AFEQT (baseline and 3 months)	Although HRQoL AFEQT scores recorded as part of study, results are not reported in publication.	HRQoL scores not reported (-).
Wynn et al. (2014) Liverpool, UK	AF (n=362)	Observational	AFEQT; EQ-5D; mEHRA	Validation of the mEHRA (which is a symptom classification measure). EHRA class one: AFEQT mean score (SD); 78.4 (+19.0); mEHRA does not discriminate between those with low symptoms (-). Class 1: 78.4 (+19.0) (p=n/a); Class 2: 63.6 (+20.0) (p<0.0001); Class 3: 42.1 (+21.1) (p<0.0001); Class 4: 31.3 (+18.6) (p=0.01).	Scores did not differentiate between PAF and non-PAF groups (-).

NB: Full text articles reviewed. Only articles which have used the AFEQT were included (protocols for future research/abstracts/literature reviews were not presented)

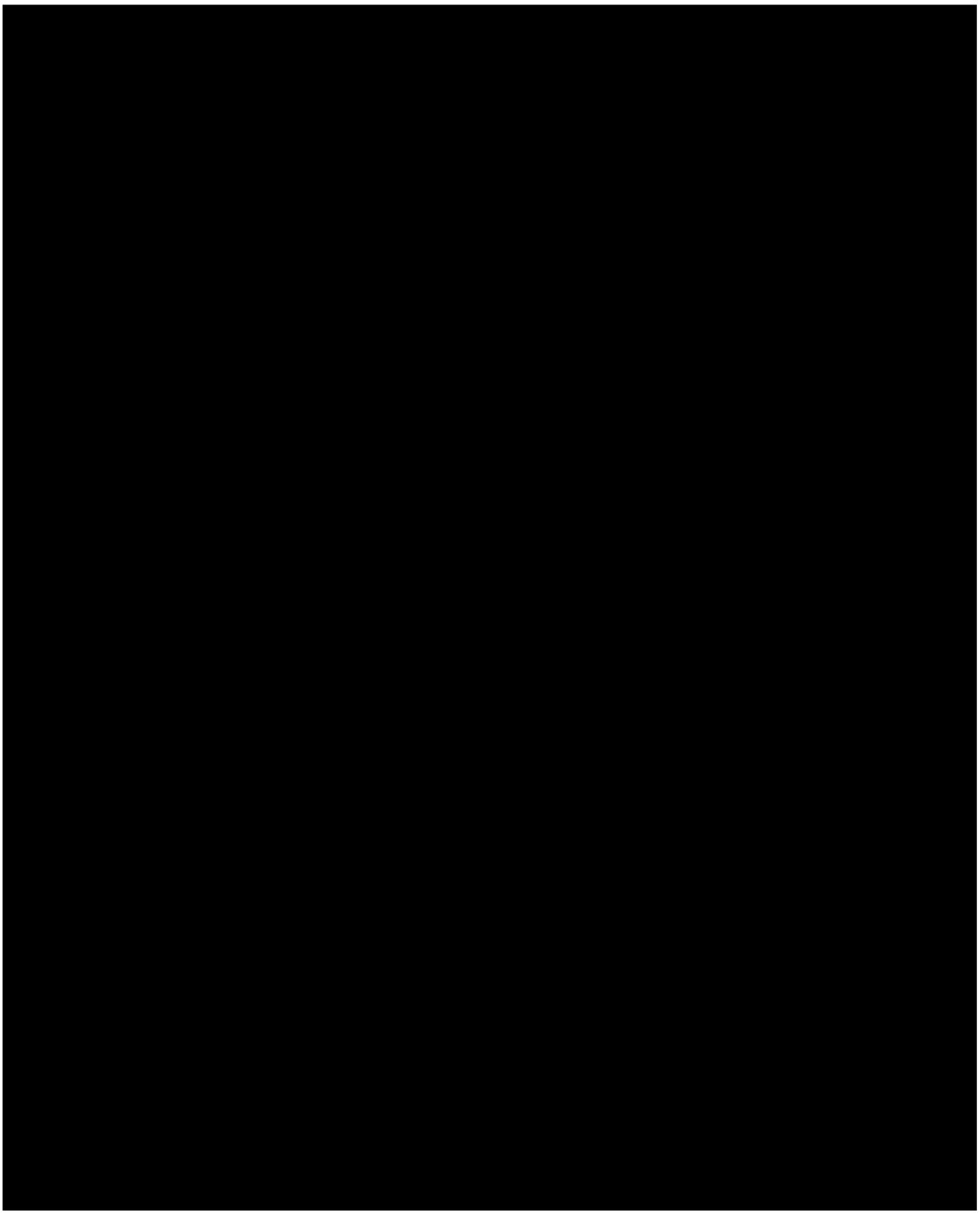
Table 3.5 PubMed results of AFQLQ. searched October 2017: Updated September 2018.					
Study	**Population**	**Study**	**Questionnaire**	**Results in relation to HRQoL**	**Critique**
Kodani et al. (2013) Japan	Persistent AF (n=11) Permanent AF (n=2)	Impact of drug (Carvedilol) treatment	AFQLQ	No improvement in AFQLQ scores.	Small study size (-). Not randomised (-).
Moreira et al. (2016) Brazil	Persistent AF (n=19) Permanent AF (n=21)	Validation of Version 2	SF-36 AFQLQ v.1 AFQLQ v.2	**Test-retest:** Bartko intraclass correlation coefficient: Total score = (≥ 0.90). Scores above 0.80 indicate desirability. All individual items >0.80 apart from dizziness item (0.56). **Reproducibility: i**nter- and intraobserver reproducibilities in total score ≥ 0.90, implying accuracy. **Internal consistency:** Cronbach's alpha coefficient > 0.82.	Requires further testing in patient population with interventions.
Shiga et al. (2017) Japan	Paroxysmal AF (n=45)	Multicentre, randomized, crossover study (AAD)	Short Form-36 (SF-36) AFQLQ (baseline, 12 and 24 months)	No significant difference in HRQoL scores between groups when using generic or disease-specific measures. Improvements noted in two domains: AFQLQ1 (symptoms frequency) and AFQLQ2 (symptoms symptom severity). AFQLQ did not significantly improve (AFQLQ 3: limitations on activities and anxiety) in either treatment group. Further psychometrics of AFQLQ were not reported.	Study size small (-). Low drug dose used in study may lead to results not being generalisable (-).
Tsuneda et al. (2006) Japan	AF β-blocker (n=19) vs. Ca antagonist (n=14)	Impact of drug treatment	AFQLQ SF-36	CAA improved role function-physical score of SF-36, and frequency and severity of symptoms of AFQLQ. No changes in SF-36 scores in Beta Blocker group. AFQLQ: scores in CAA group improved (Q1–6); however, no significant changes in BB group. Remaining 2 subscales in AFQLQ were unchanged in both groups.	Selection bias: Population recruited on digitalis > 6 months (-). Few women included (-).
Yagishita et al. (2017) Japan	Asymptomatic persistent AF post catheter	Non- randomised: observational study investigating the impact of AF ablation on QoL,	SF-36; AFQLQ (baseline and 6 months)	In those who did not have reoccurrence of AF episodes, all domains (AFQLQ1: frequency and variety of symptoms; AFQLQ2: symptom severity; AFQLQ3: limitations on daily life and anxiety) of the AFQLQ showed significant improvement ($p<0.0001$) while only some domains (five out of eight) of the SF-36 showed significant improvement after ablation.	Not randomised (-). Small study size (-). No control group (-). Short follow up (-). Shows AF-specific questionnaire may

	ablation (n=34)	exercise tolerance and BNP			capture more changes in AF population (+).
Yamamoto et al. (2014) Japan	PAF and HTN (n=233)	Observational	AFQLQ	Provides evidence for reduced HRQoL in patients with asymptomatic AF in domains AFQLQ2 and AFQLQ3, indicating that mental anxiety and limitation of daily and other activities were negatively impacted. Asymptomatic and symptomatic episodes of AF negatively impacted HRQoL when measured with disease-specific measure.	Considers asymptomatic population (+). Evidence for reduced HRQoL in asymptomatic population (+). However, no patients were completely asymptomatic (-). Whole population had other comorbidities such as hypertension (-). Short follow-up period (-). No generic HRQoL measure used (-).

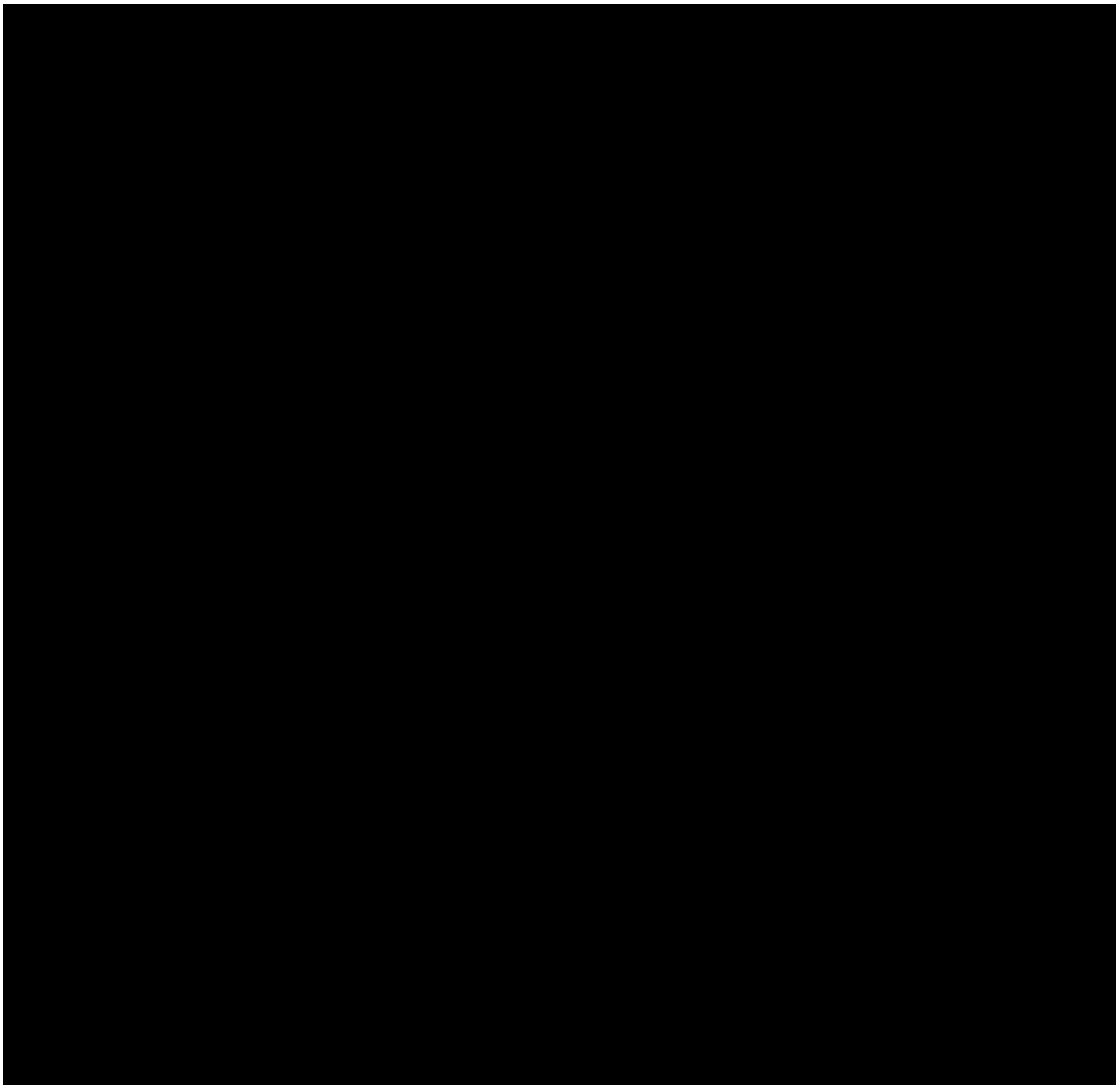
NB: PubMed results of AFQoL and QLAF: Developmental papers identified and noted in a systematic review of PROM in AF which is referred to throughout Chapter Three (Kotecha et al, 2001)

Appendix C Chapter Four

Appendix C 4.1 Poster for recruitment: Focus Groups



Appendix C 4.2 Map of St. Bartholomew's Hospital, London



Appendix C 4.3 Transcript for Focus groups

Hello and welcome. [Introduce self and co-moderator]

Thank you for agreeing to participate in our study of the effects of atrial fibrillation has on patient's quality of life. Everyone here today was invited because you share something in common related to atrial fibrillation.

We hope to learn from you how to better understand atrial fibrillation and how its effects can be measured with simple questions. We have a series of questions to ask you about how atrial fibrillation affects your quality of life. There are no right or wrong answers, and if you don't wish to answer any questions that is fine. We wish to understand how atrial fibrillation affects your quality of life. We are interested in getting a wide range of answers so please feel free to share your point of view even if it is different from what other people have said. The answers you give won't affect your treatment, and we won't be discussing the answers you give us with the doctors or specialists that you will see at a later date.

We anticipate this focus group to last around an hour and a half. We will be recording it for documentation purposes. We have placed name cards / badges on the table in front of you and we will be referring to you on a first name basis, if that is ok with you. If you prefer to be called something else please let us know. So that we can document properly the recording note taker or the research moderator will either comment who is speaking e.g. 'John has just spoken' or the moderator will speak directly to the you and say something to clarify who is speaking 'thank you for your contribution John, does anyone else have a similar experience/concern?'

My role is to ask questions and to listen. I will be summarising the information on the board at times and asking you to rate the themes on importance. I won't be actively participating in the group but only guiding it. I would like you feel free to talk to the other members of the group and not just me. We would like to hear about your personal experiences in relation to atrial fibrillation but as this is a research project, it would great if you could link your comments to the questions. I will move the discussion on if needed to keep us on track and make sure we get out on time. We have some guidelines so that everyone has the opportunity to speak and it will make our discussion more productive.

i) All information which is given by participants to the focus group will remain confidential and we would appreciate if you would show the same respect to the other participants and keep it confidential.

ii) One person speaking at a time.

iii) Please respect and listen to the other views of the participants, (even in circumstances where you may not agree with them).

iv) Please speak up and speak clearly; we're recording the session and we want to be able to hear all your comments so if anyone is having difficulty hearing any of the comments, please let the group know.

v) During the focus group; so we get a clear recording of the focus groups, it would be appreciated to keep the talk with the whole group and not break off in smaller groups.

vi) Please allow all participants the opportunity to speak.

Sometimes people in focus groups think of things after the focus group has moved onto other questions. If there is anything you would like to add, we will be around after the focus groups if you would like to talk privately.

You have all completed a consent form. I just want to check everyone is still happy to take part?

Has anyone got any questions before we begin?

(Introductory Topics = I; Main Content = C; Summary/Concluding/ Statements = S)

I1: How did you first notice your AF?

I2: What was the main thing that made you see your GP about it?

C1: What are the main ways that you find atrial fibrillation affects your quality of life?

Prompt/ clarify -

- activities of daily living;
- independence;
- psychological well-being;
- physical/ symptom related effects;
- social/ relationship related activities
- burden of treatment/ side effects**.**

- **Can I confirm these with you**? – list on the board .. individual verbal ranking – most/ least important.
- Provide opportunity to go through each point in turn and ask to expand on these areas.

C2: Are there any ways in which AF stops you doing the things you would like to be doing? Which ways in particular? (activities at home/ ADL; or recreational activities)

- **Which of these do you think is the most important for you?**
- **Can you expand on this?**
- **Do you ever not do things, for instance going out or taking part in an activity, because of your AF?**
- **Do you ever change your plans because of AF? How often**?

C3: Do you feel AF interferes with your social life and relationships? If so how? (Social relationships and social activities)

- **Are there any ways in which AF prevents you from being involved in social activities?**
- **Has your AF, or worry about AF, affected your personal relations?**

C3: Does AF affect your mood.. cause you worry (… affect your sleep … limit your concentration)?

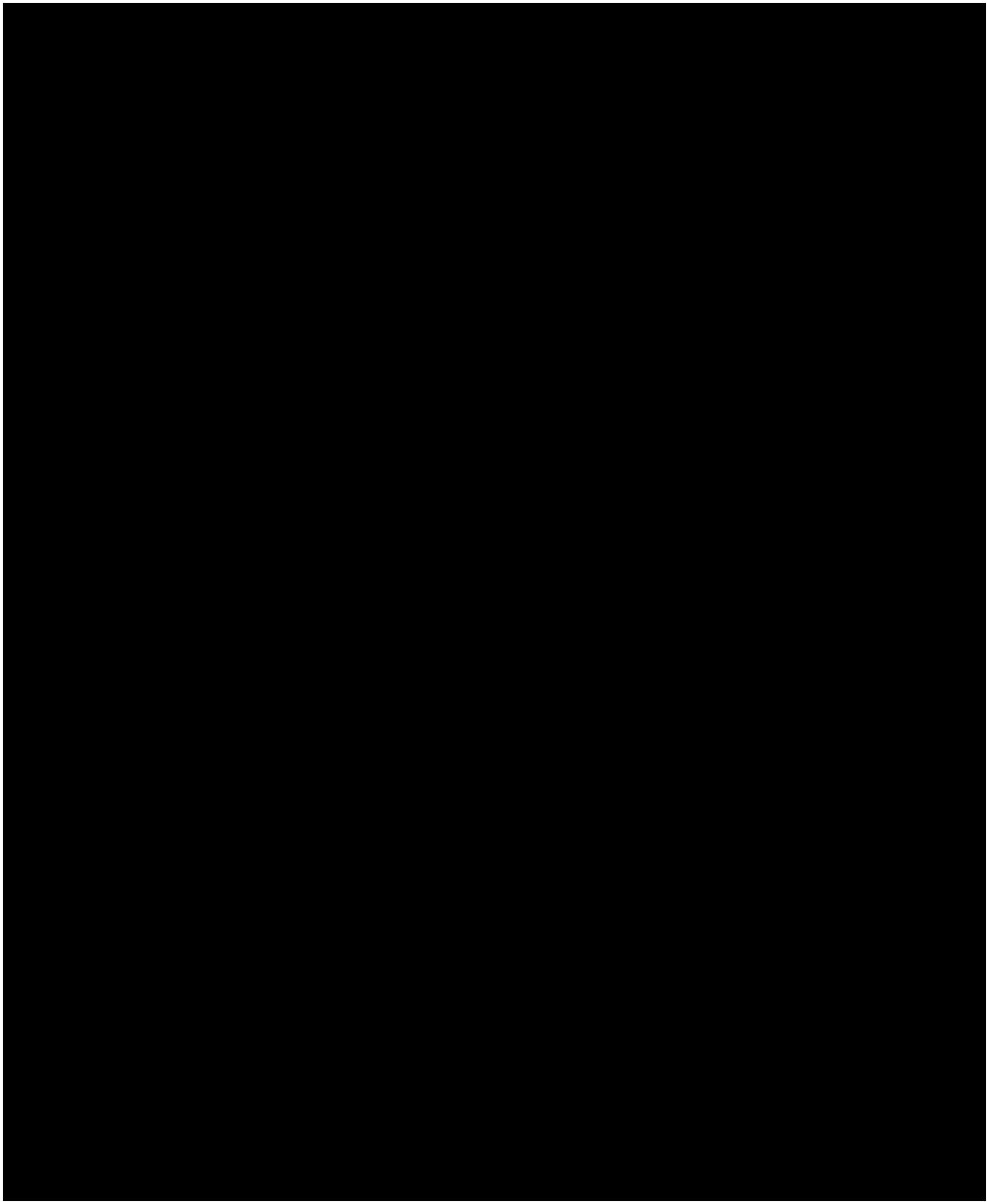
(Psychological well-being – anxiety, worry, acceptance, enjoyment, concentration,)

- **Do you have any worries about the future because of your AF?**
- **Do you feel down or depressed because of AF?**

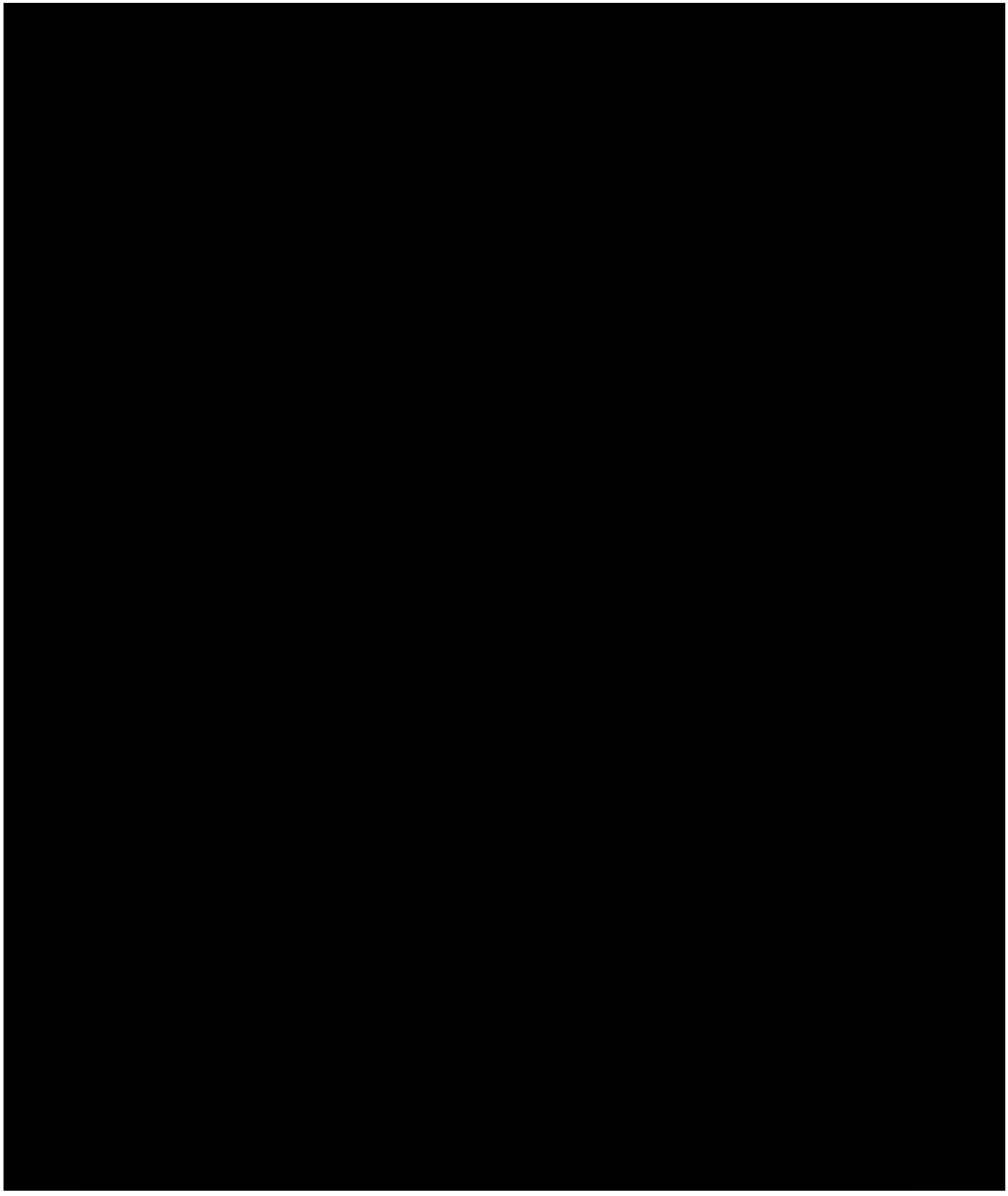
We've covered several different areas in how AF may affect you. Brief summary.

S1: Is there anything else anyone would like to say?

Are there any things we haven't covered that you think are relevant or important about how AF affects you? Thank you so much for taking part in this focus group.



Appendix C 4.5 Poster for recruitment: Pilot stage: Questionnaire and Interview



Appendix D Chapter Five.

This appendix covers the themes and subthemes identified from eight focus groups. Participants' quotes are listed under the title of each of the themes and sub themes and correlate to the theme and subtheme titles in Chapter Five. Please note there is no description for the themes and sub themes in this appendix.

Appendix D 5.1 Physical or symptom related effects

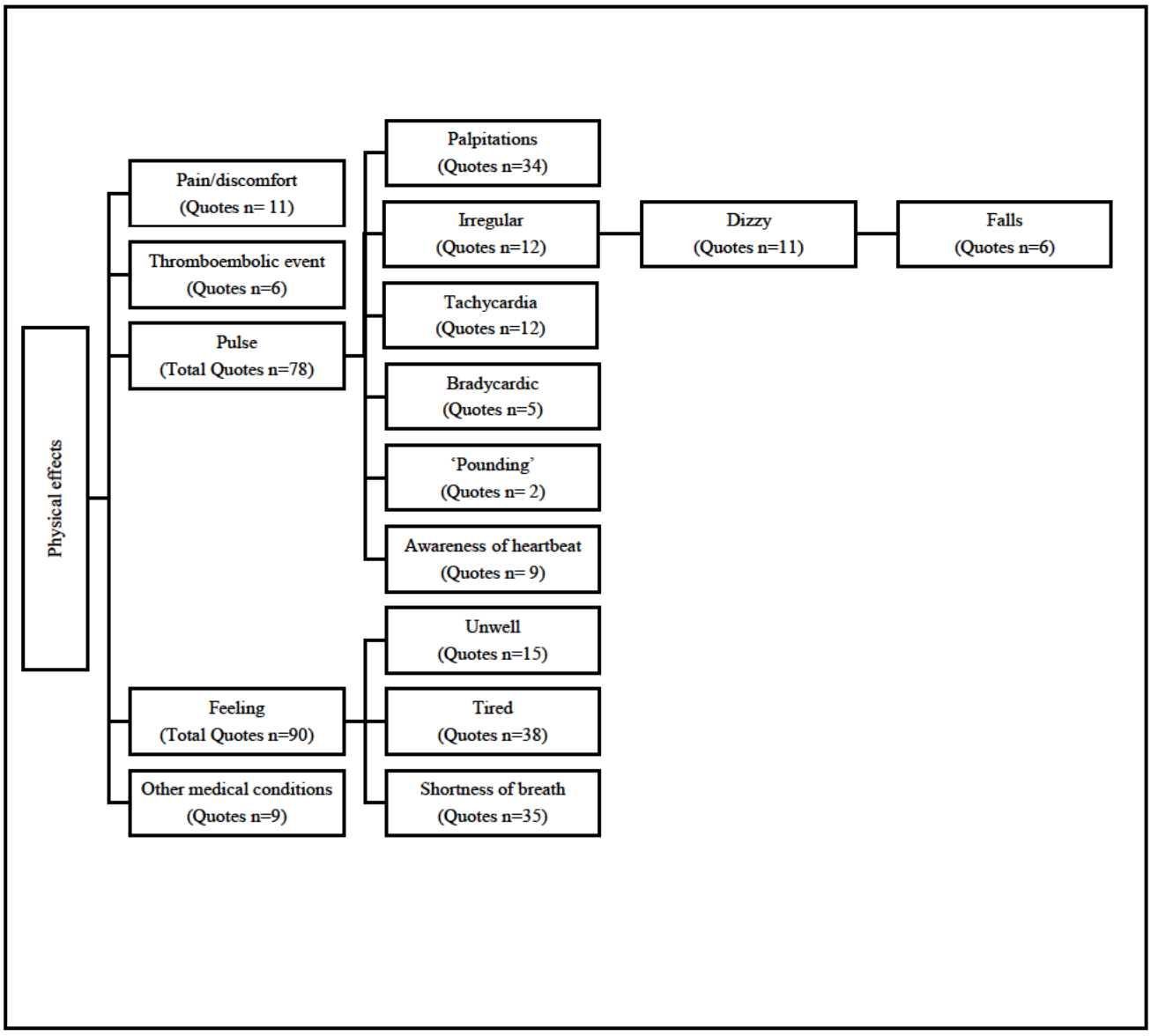
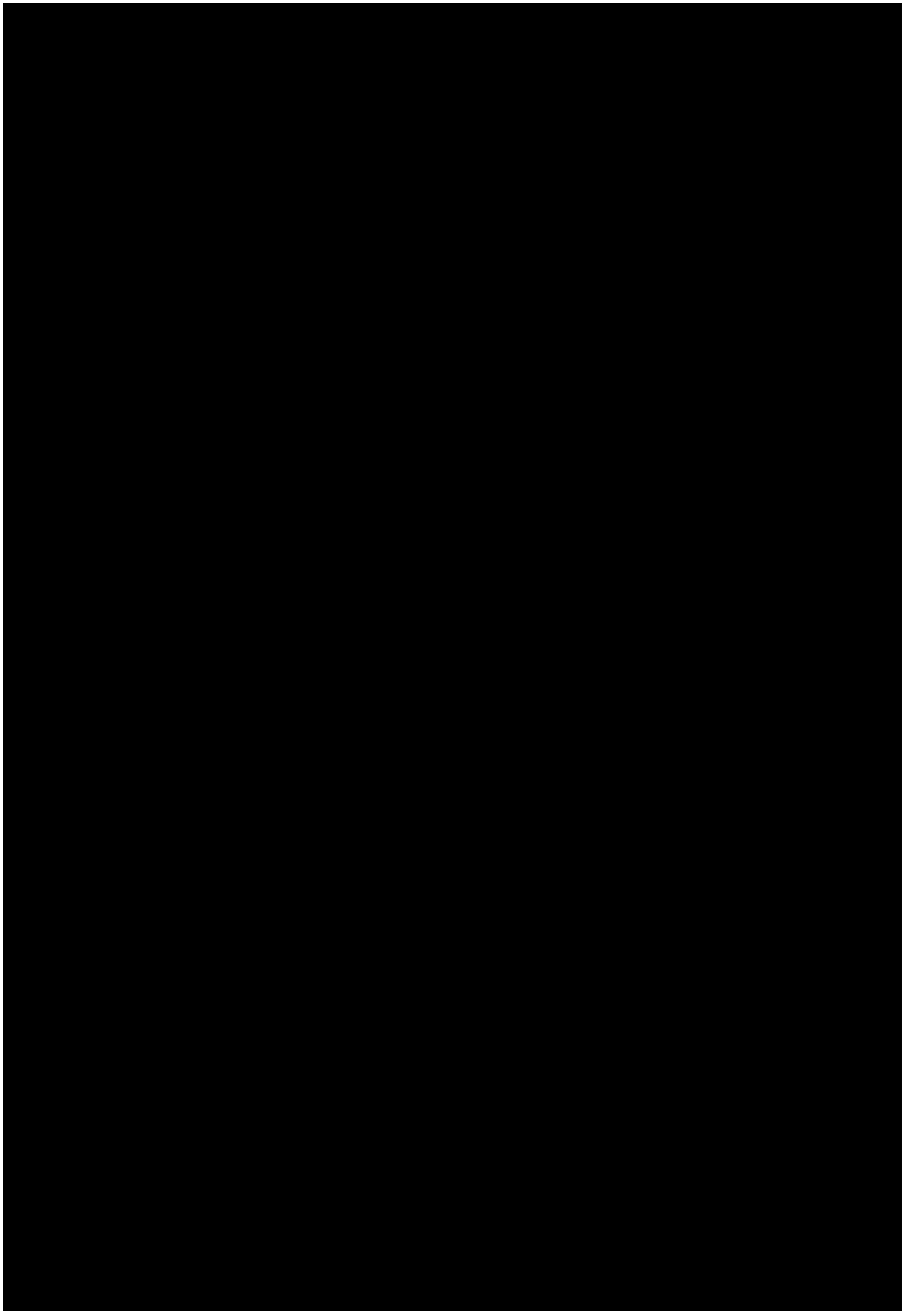


Figure 5.1 Overview diagram of themes noted: physical symptom effects of AF

Appendix D. 5.1.1 Pain discomfort

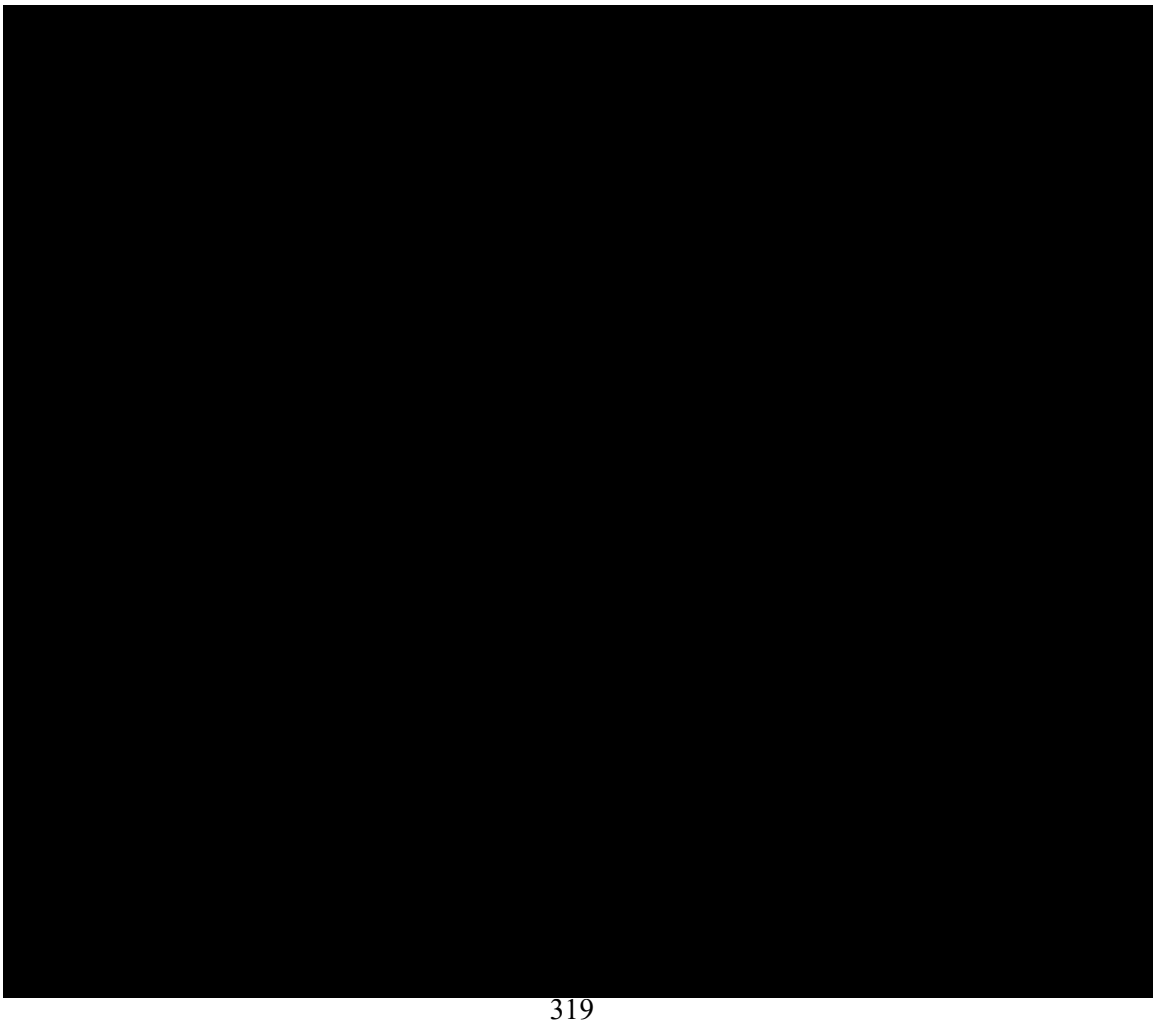


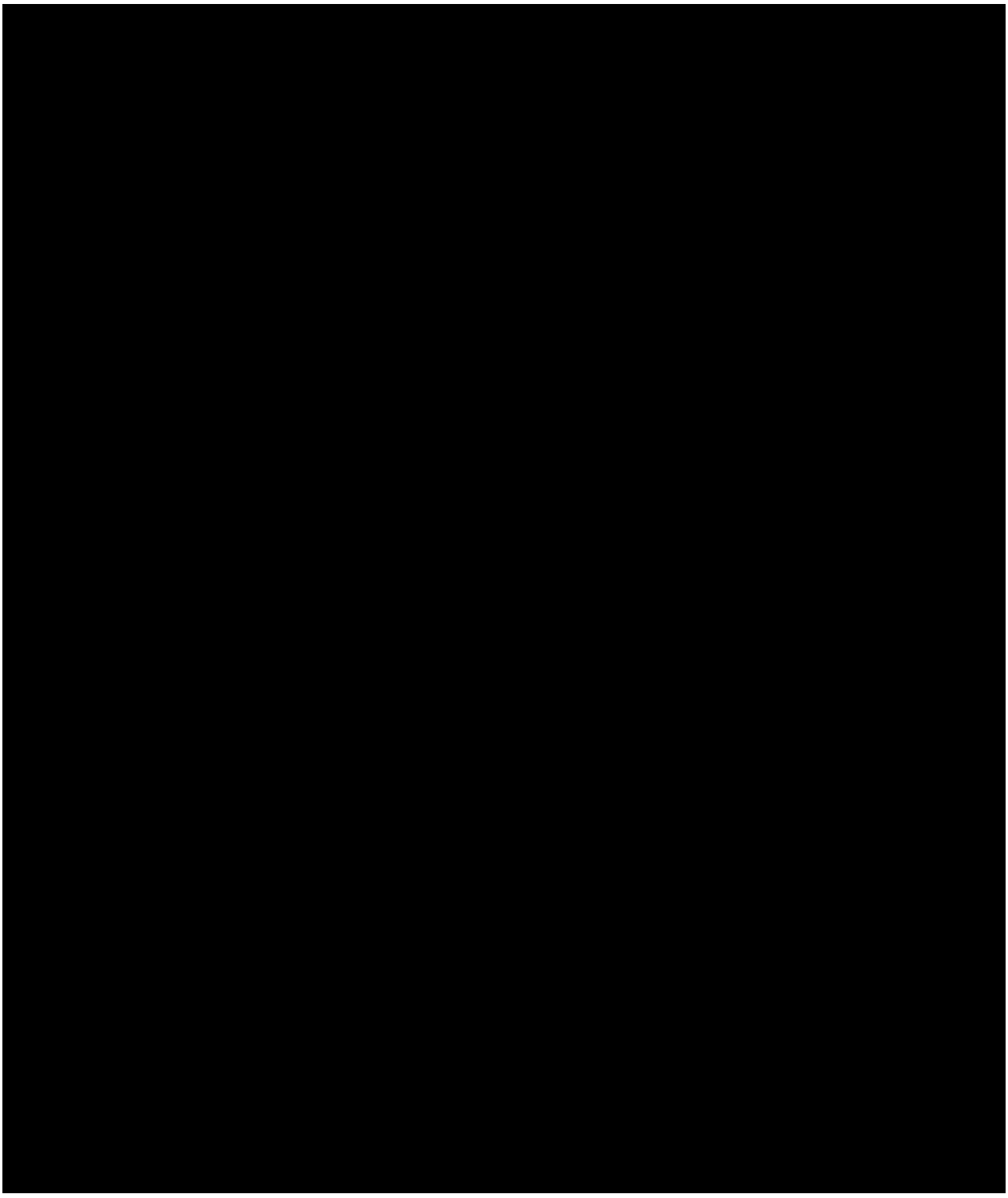
[redacted]

Appendix D. 5.1.2 Thromboembolic events

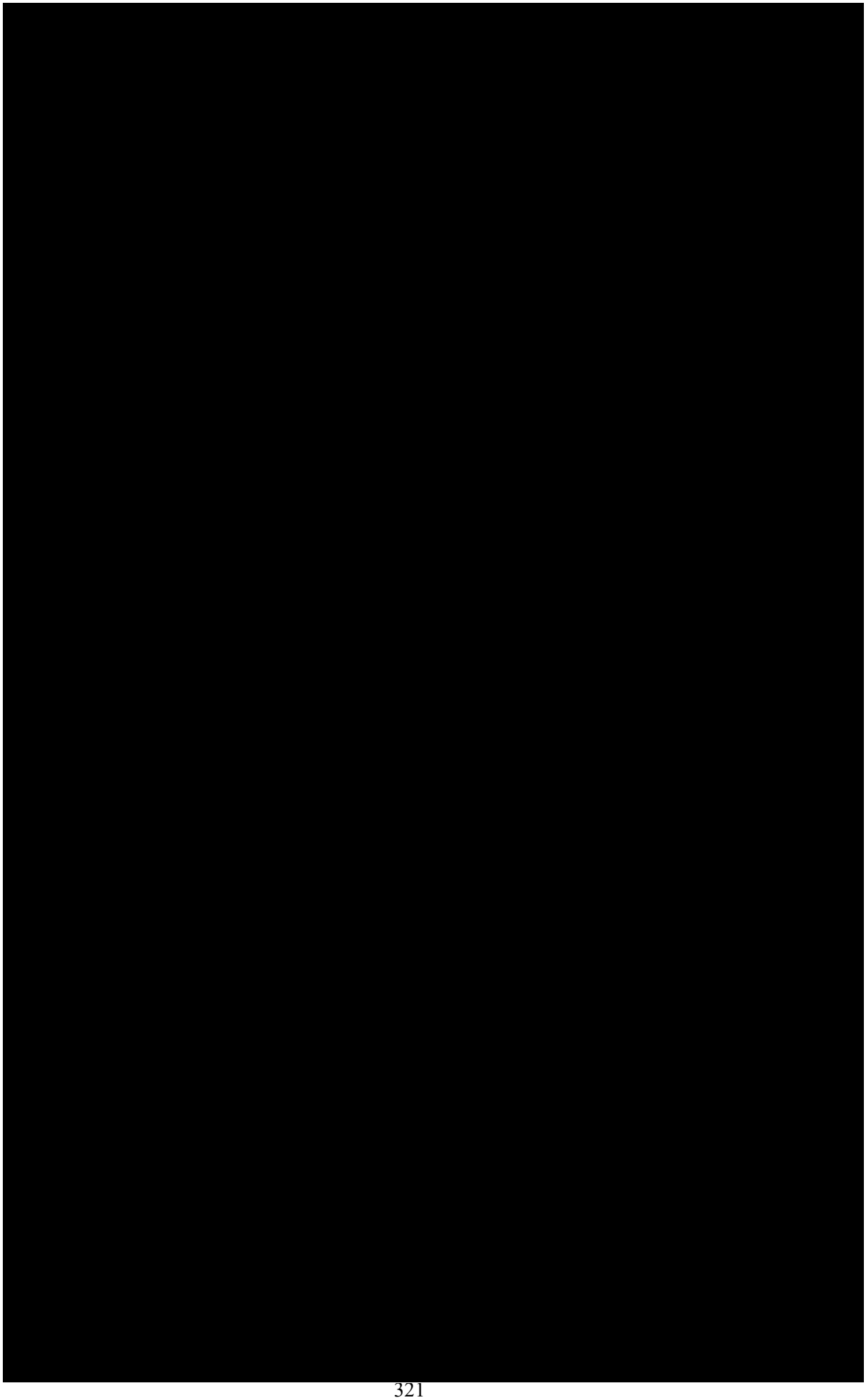
[redacted]

Appendix D. 5.1.3.2 ‘Irregular’



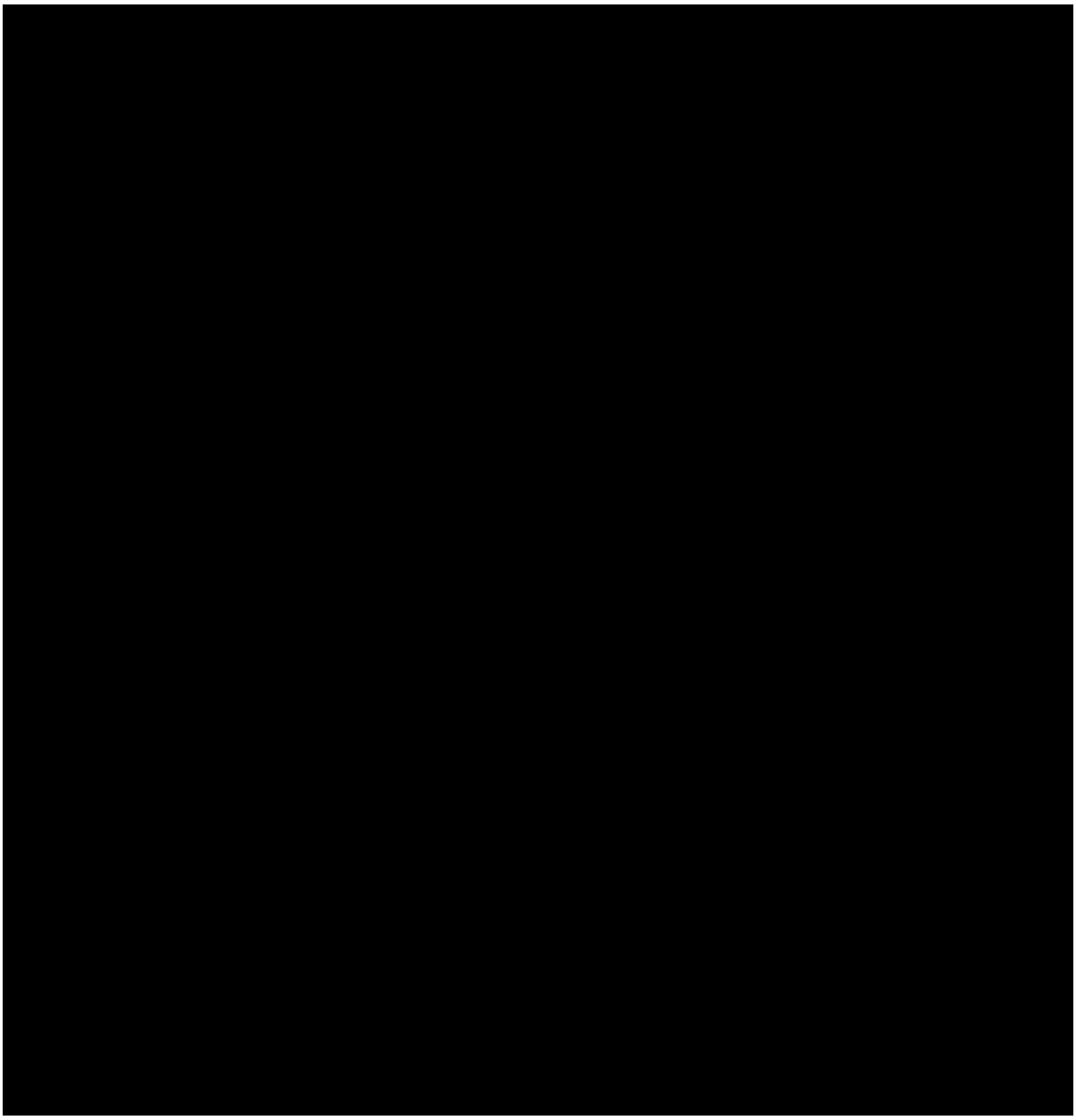


Appendix D. 5.1.3.2.1 Dizzy



Appendix D. 5.1.3.2.2 Falls

Appendix D. 5.1.3.3 Tachycardia (fast heart rate) or 'Racing'.



Appendix D. 5.1.3.4 Bradycardia (slow heart rate)

Appendix D. 5.1.3.5 'Pounding'

Appendix D. 5.1.3.6 Awareness of heart beat

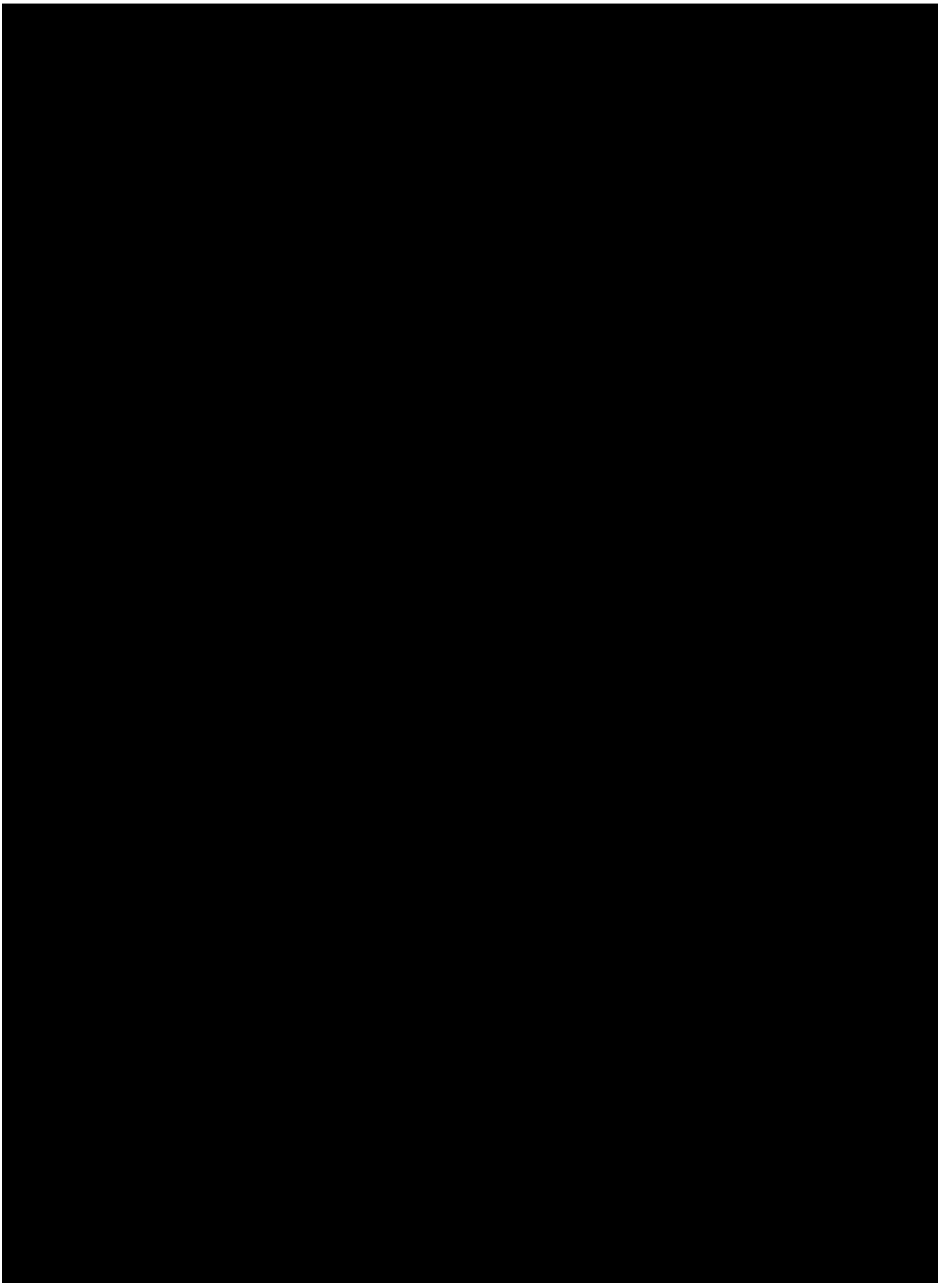
Appendix D. 5.1.4 Feelings

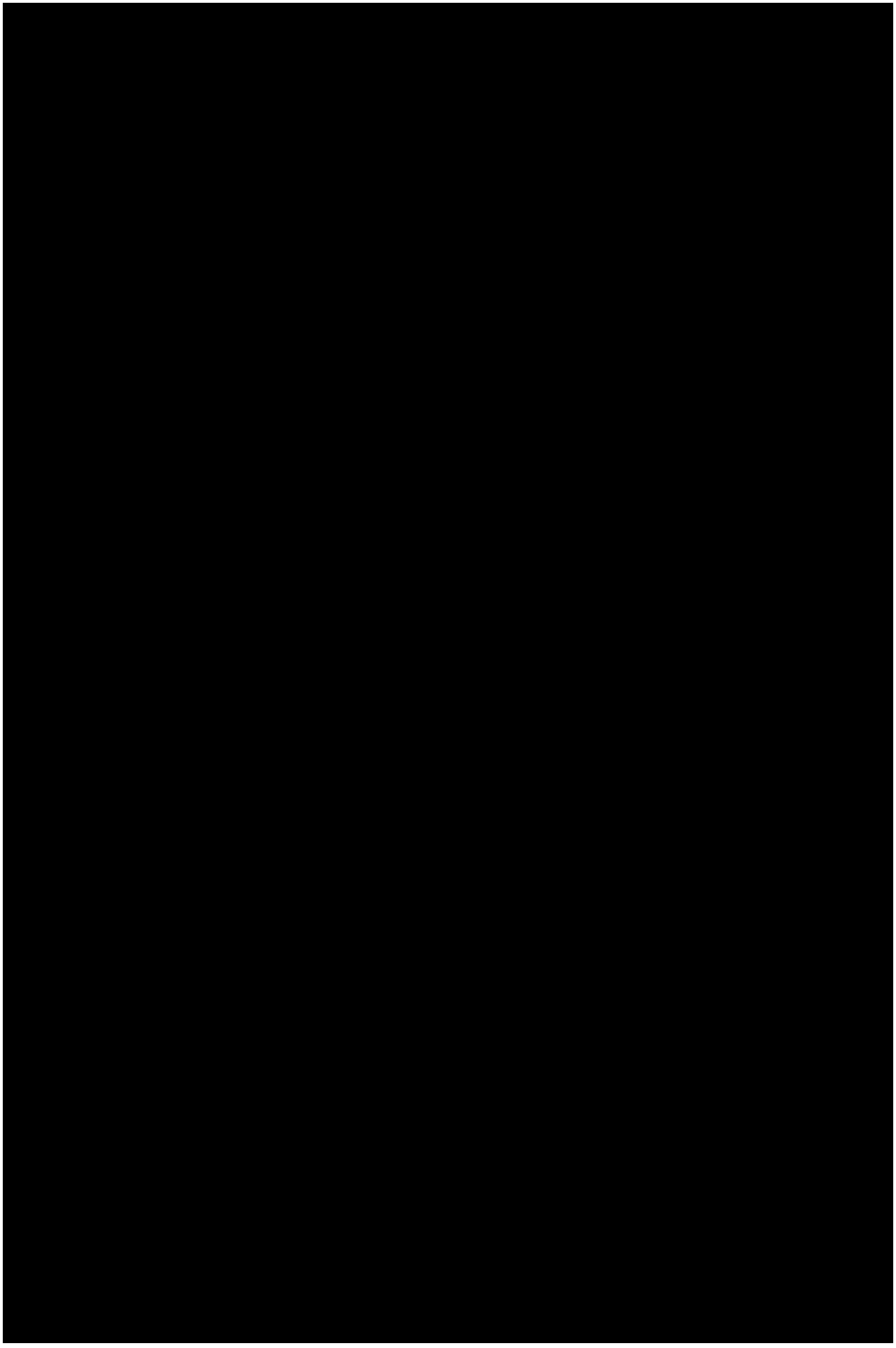
Appendix D. 5.1.4.1 'Feeling unwell'

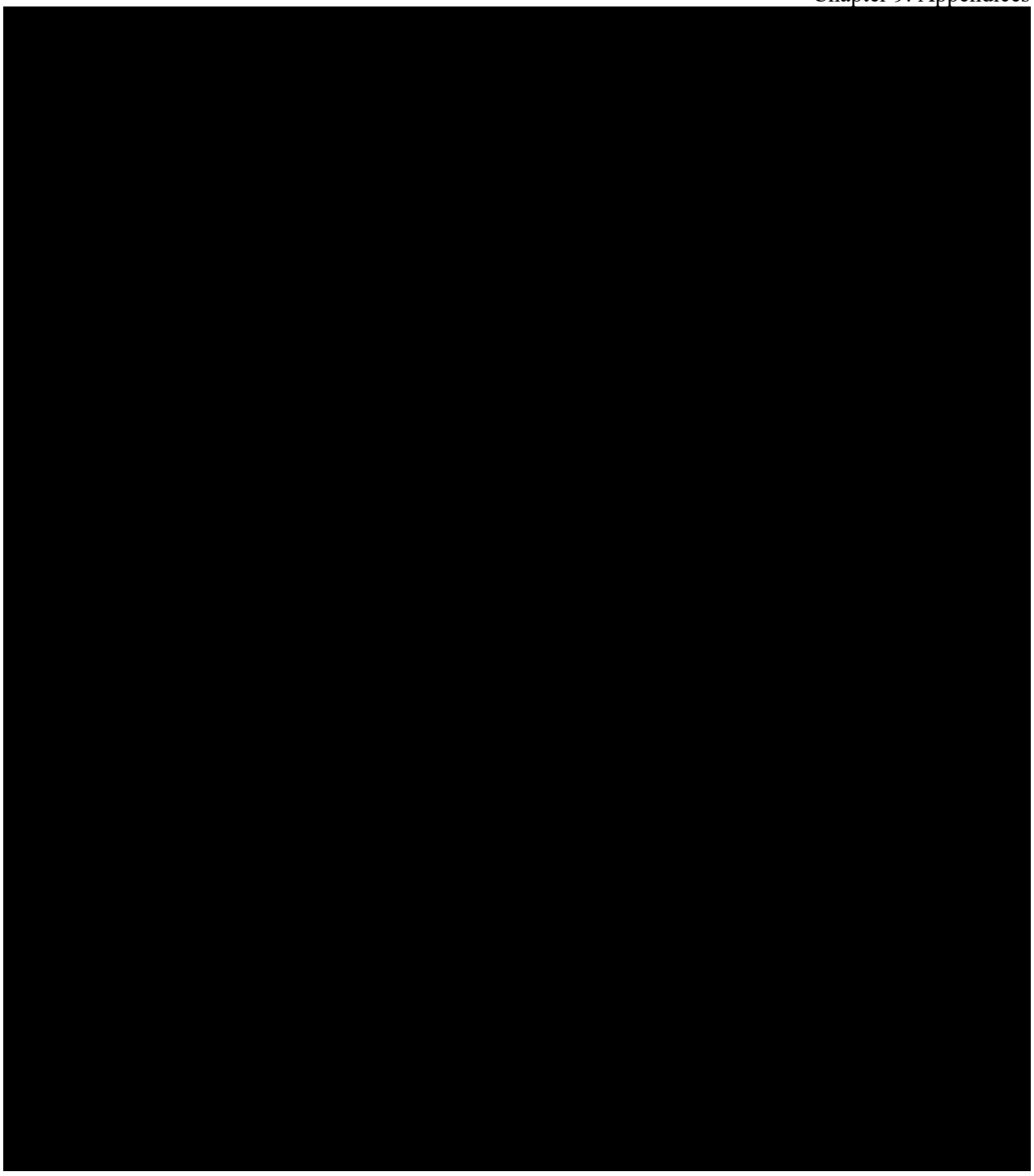
[redacted]

Appendix D. 5.1.4.2 Feeling Tired

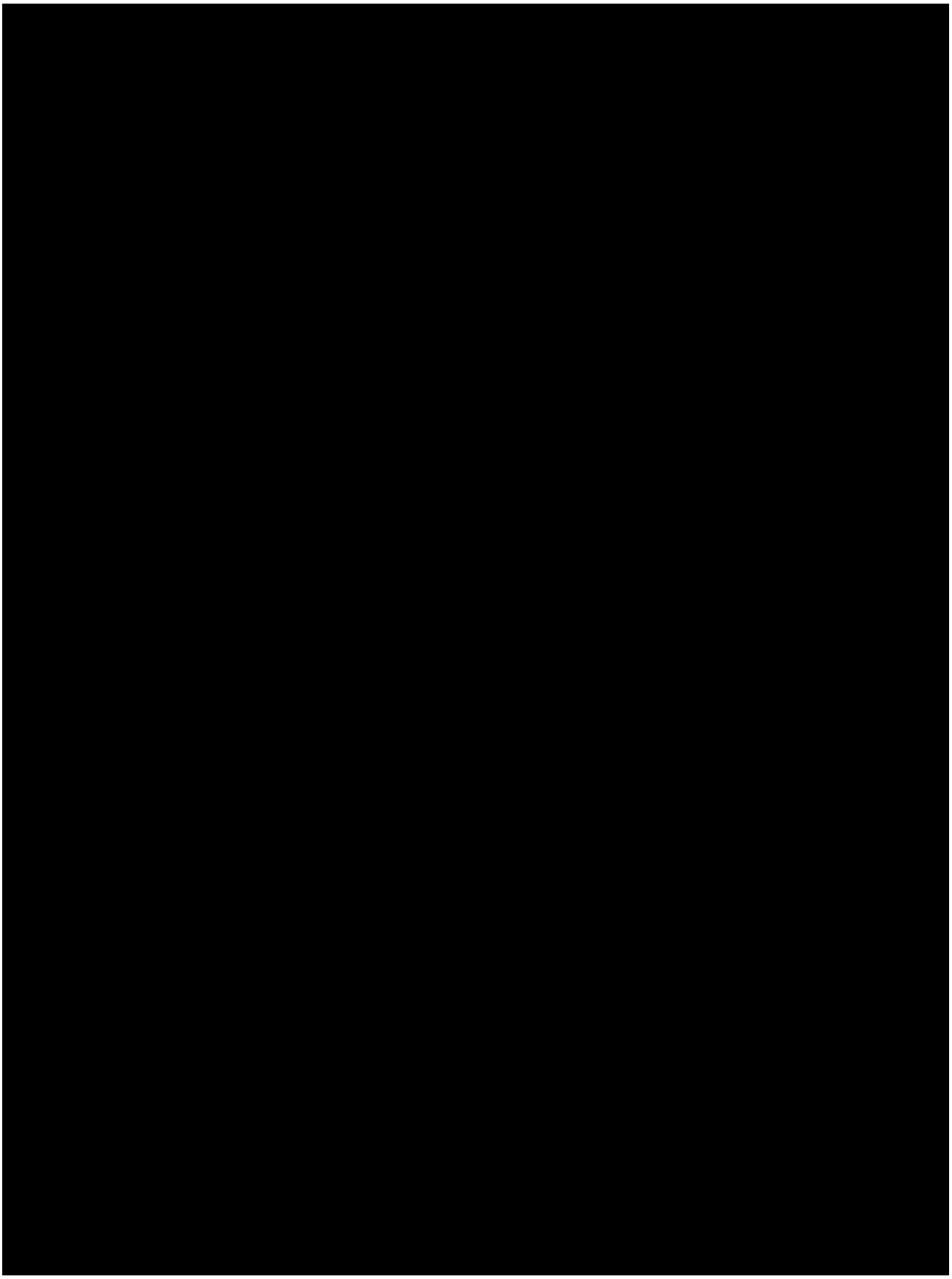
[redacted]

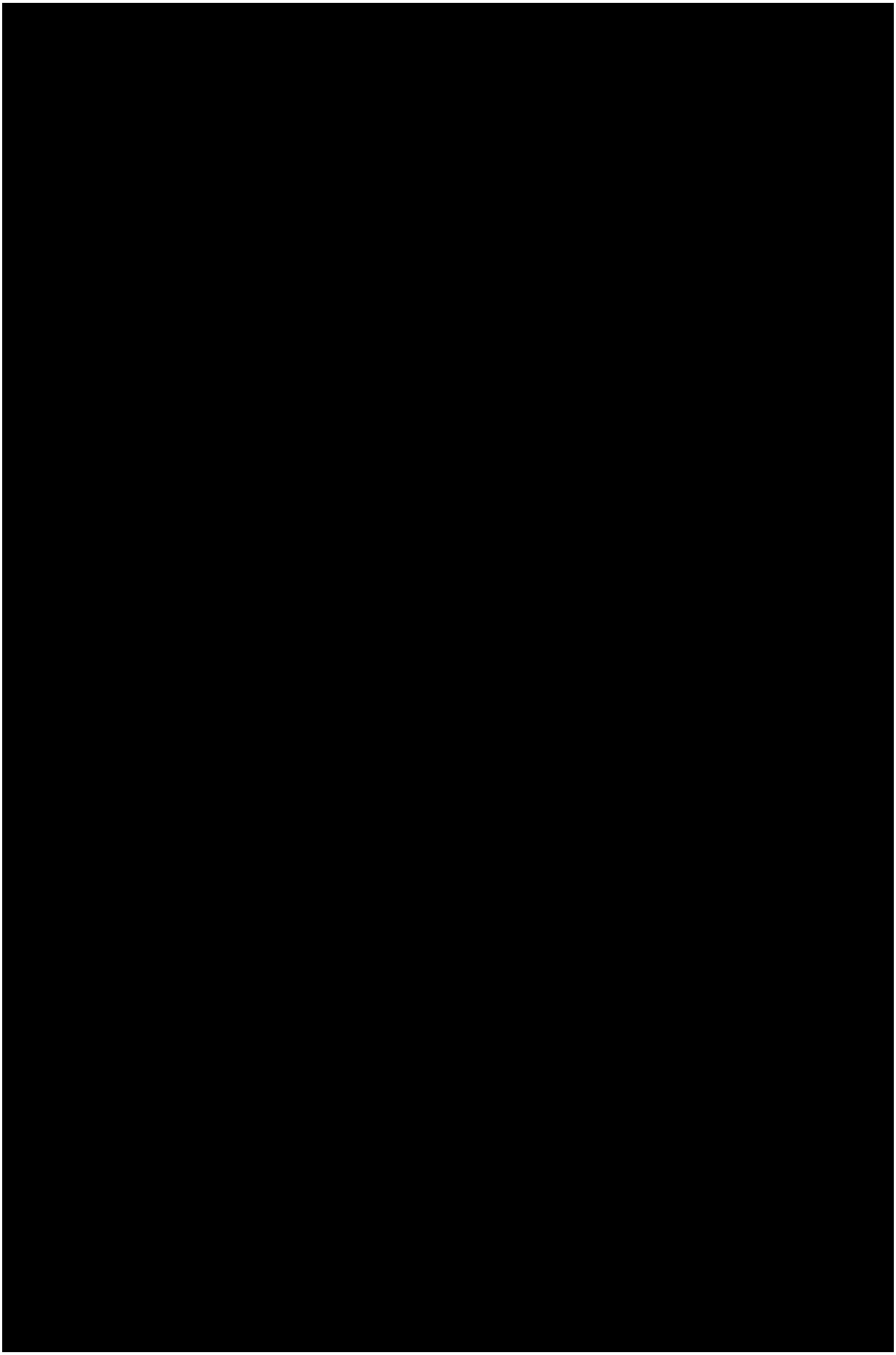


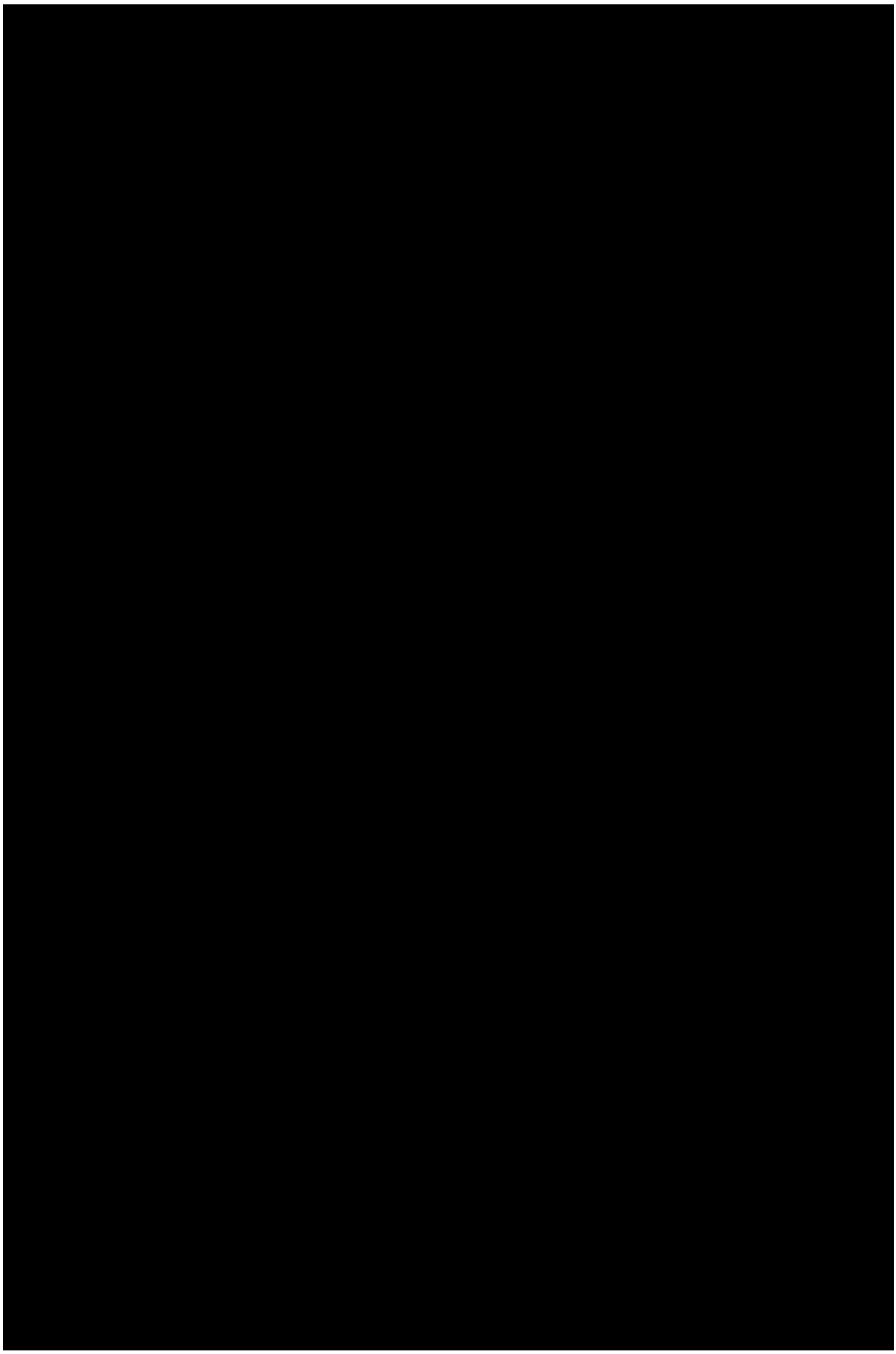




Appendix D. 5.1.4.3 Feeling shortness of breath







Appendix D. 5.1.4.3 Other medical conditions

Appendix D. 5.1.2.6 Sleep

Appendix D. 5.1.2.7 Ectopic beats.

Appendix D. 5.1.2.8 Alcohol

Appendix D 5.2 Psychological effects

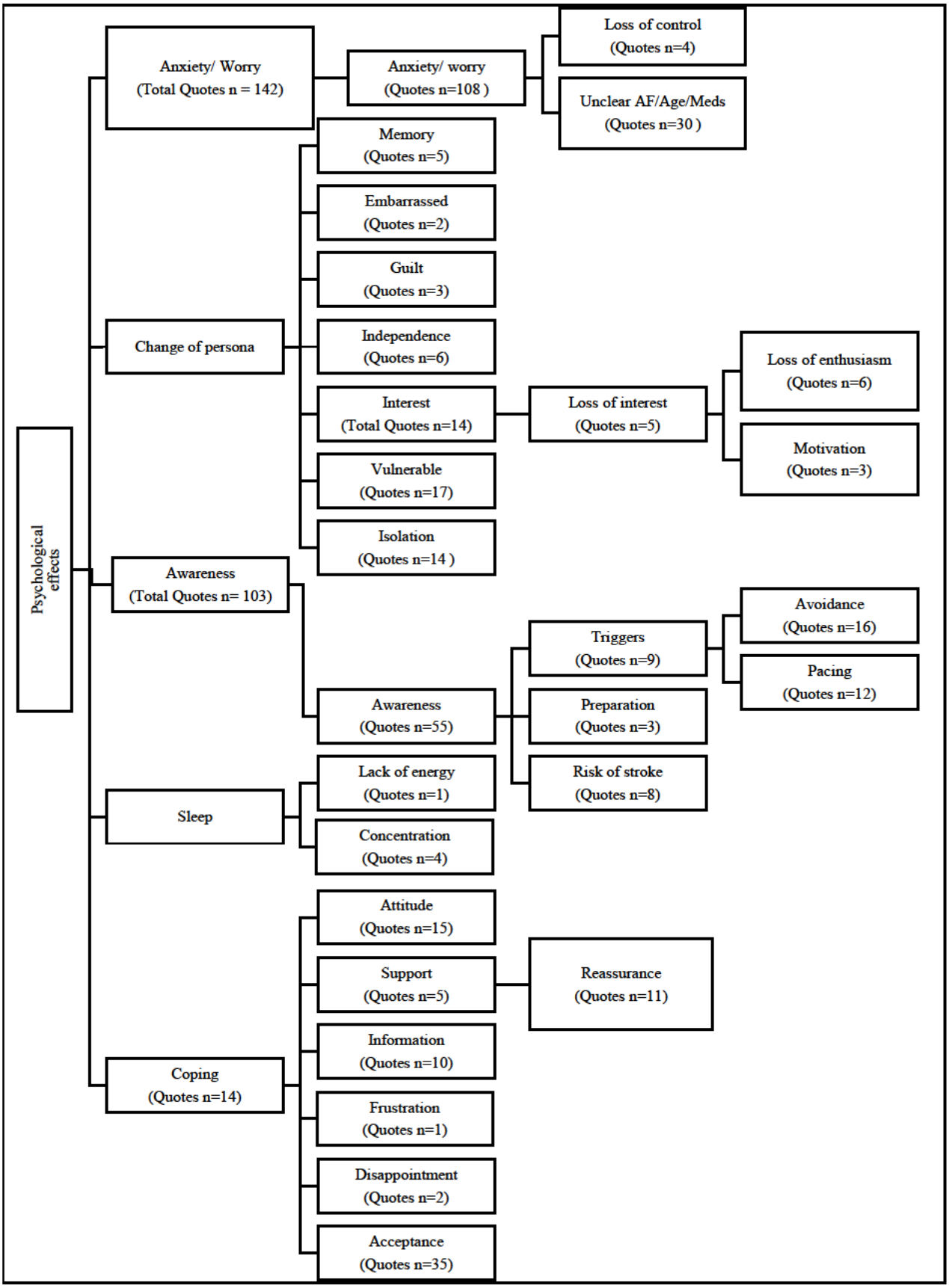
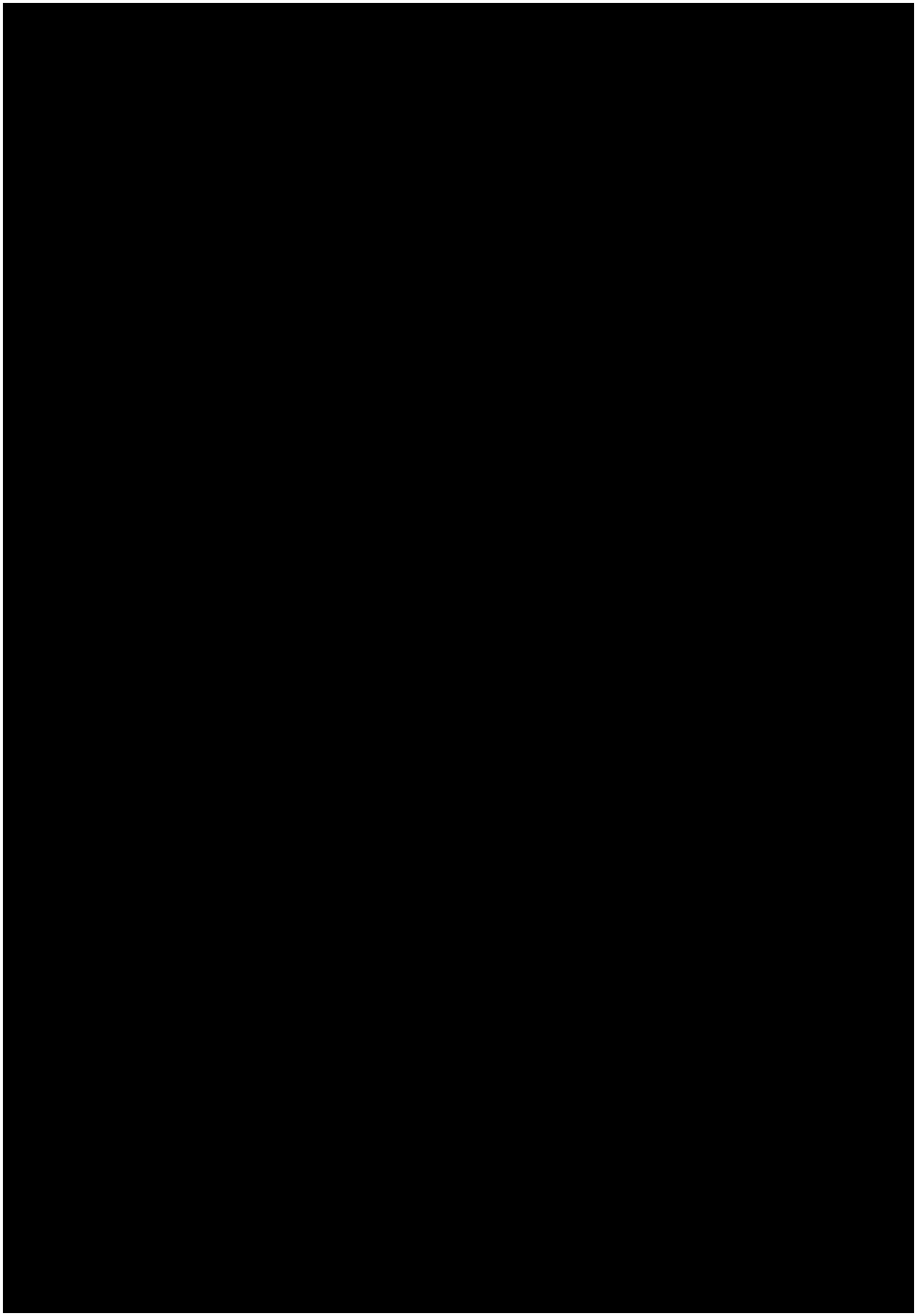
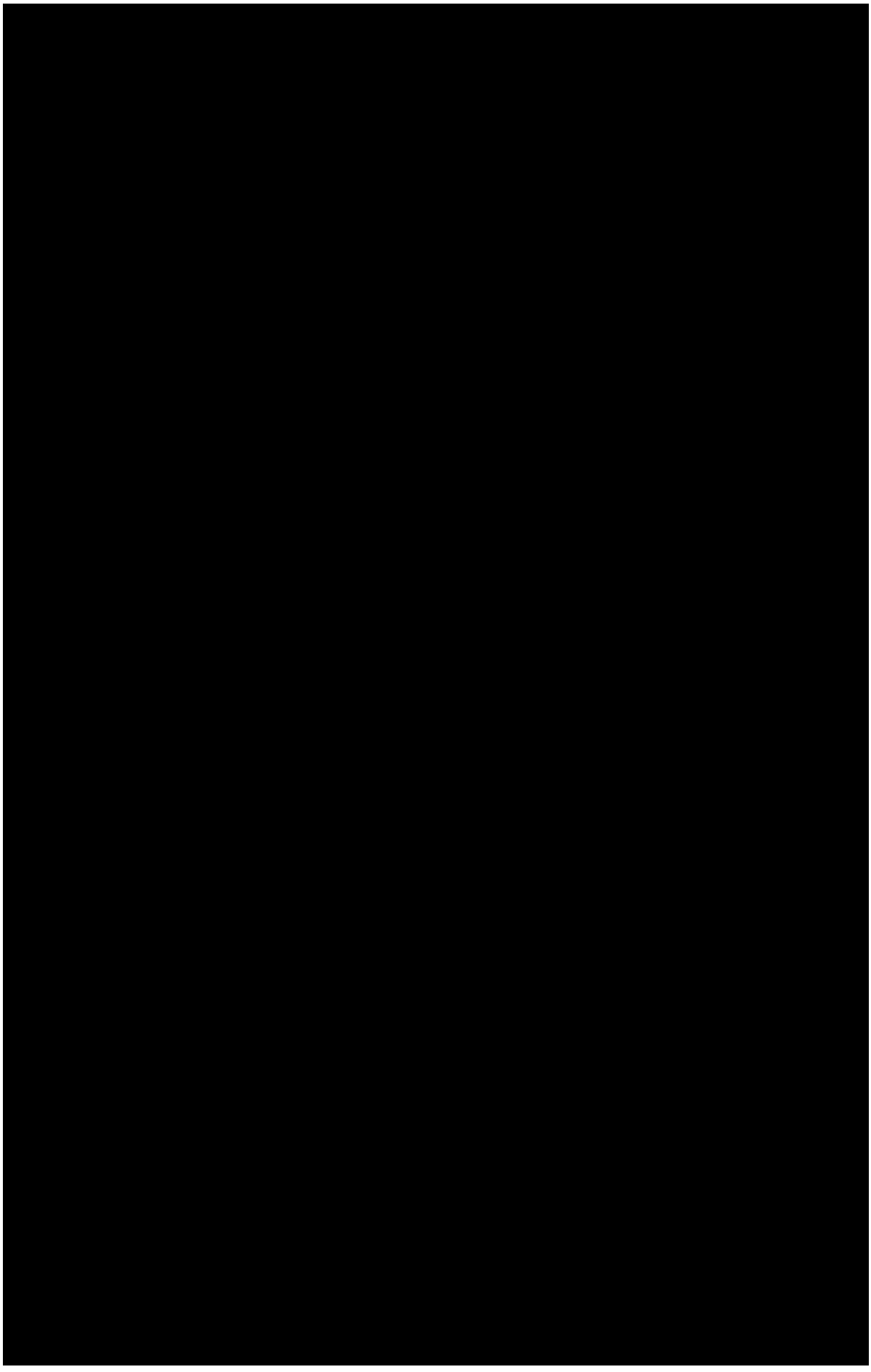


Figure 5.2 Overview diagram of main themes noted: psychological effect.

Appendix D. 5.2.1 Anxiety or worry



Appendix D. 5.2.1.1 Loss of control



Appendix D. 5.2.1.2 Unclear whether AF, Age or medications

Appendix D. 5.2.2 Change of persona

Appendix D. 5.2.2.1 Memory

Appendix D. 5.2.2.2 Embarrassed

Appendix D. 5.2.2.3 Guilt

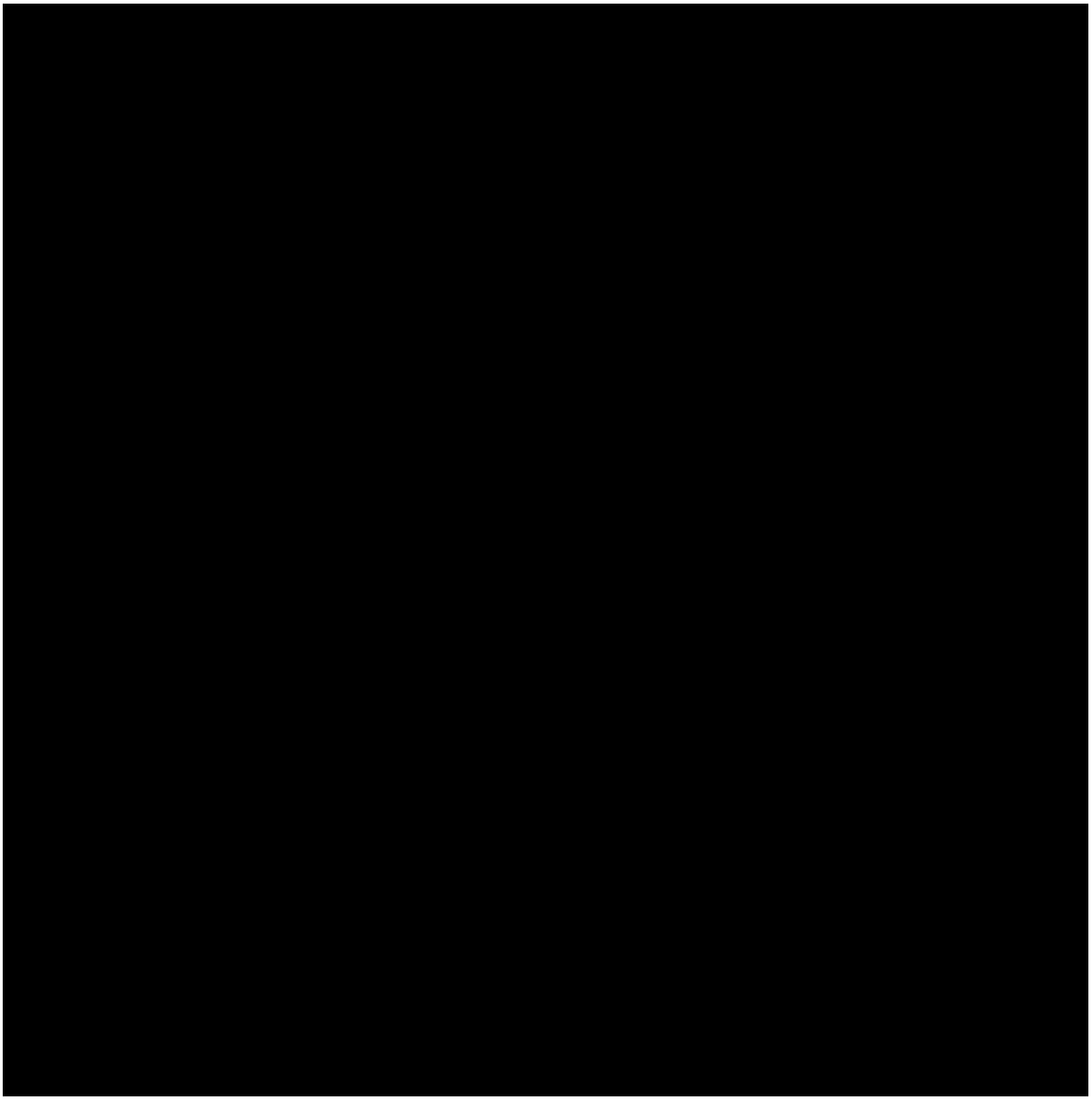
Appendix D. 5.2.2.4 Independence

Appendix D. 5.2.2.5 Interest

Appendix D. 5.2.2.5.1 Loss of interest

Appendix D. 5.2.2.5.1.1 Loss of enthusiasm

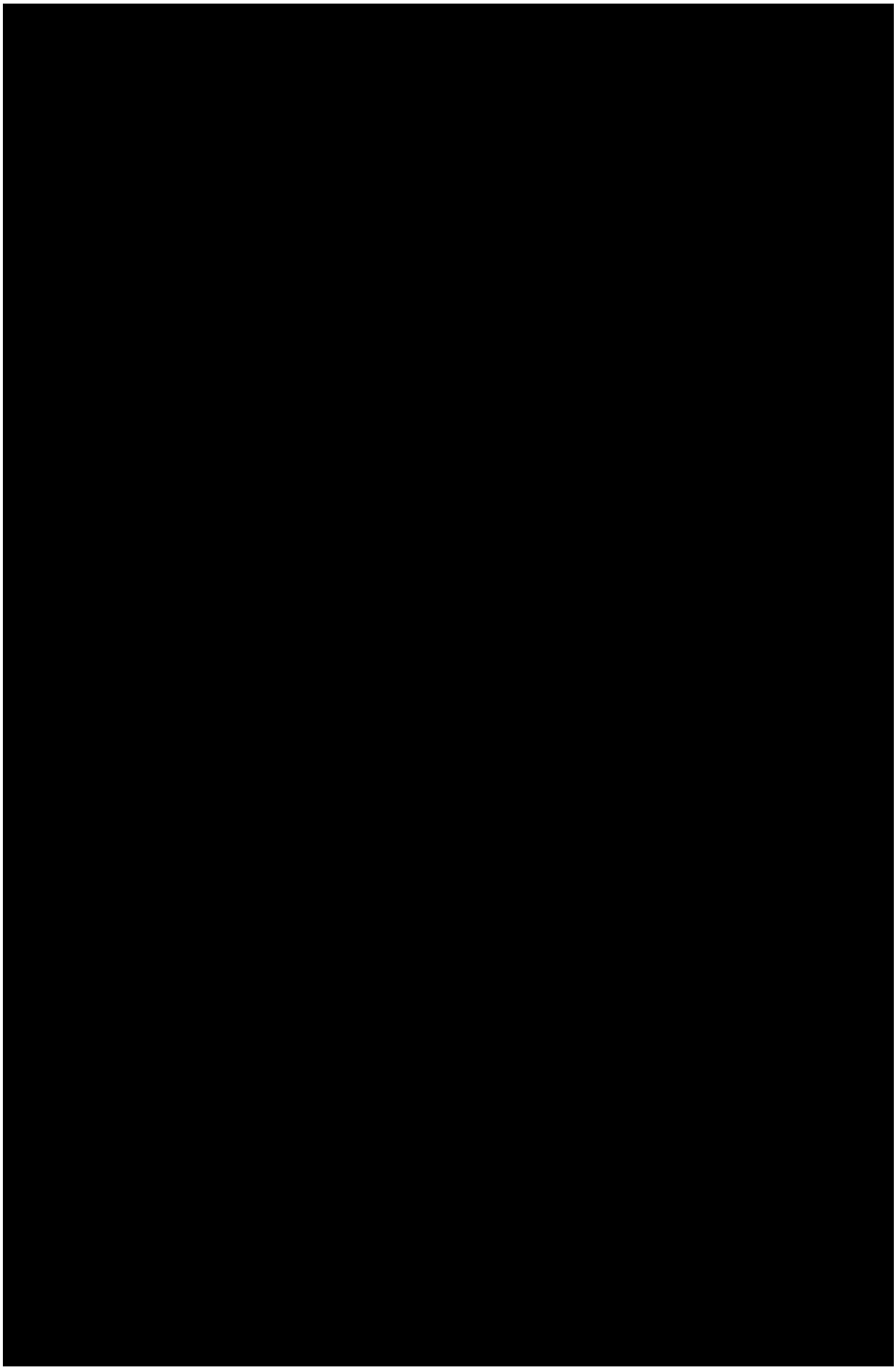
Appendix D. 5.2.2.5.1.2 Loss of motivation



Appendix D. 5.2.2.6 Vulnerable

Appendix D. 5.2.2.7 Isolation

Appendix D. 5.2.3 Awareness



Appendix D. 5.2.3.1 Triggers

Appendix D. 5.2.3.1.1 Pacing

Appendix D. 5.2.3.1.2 Avoidance

Appendix D. 5.2.3.2 Preparation

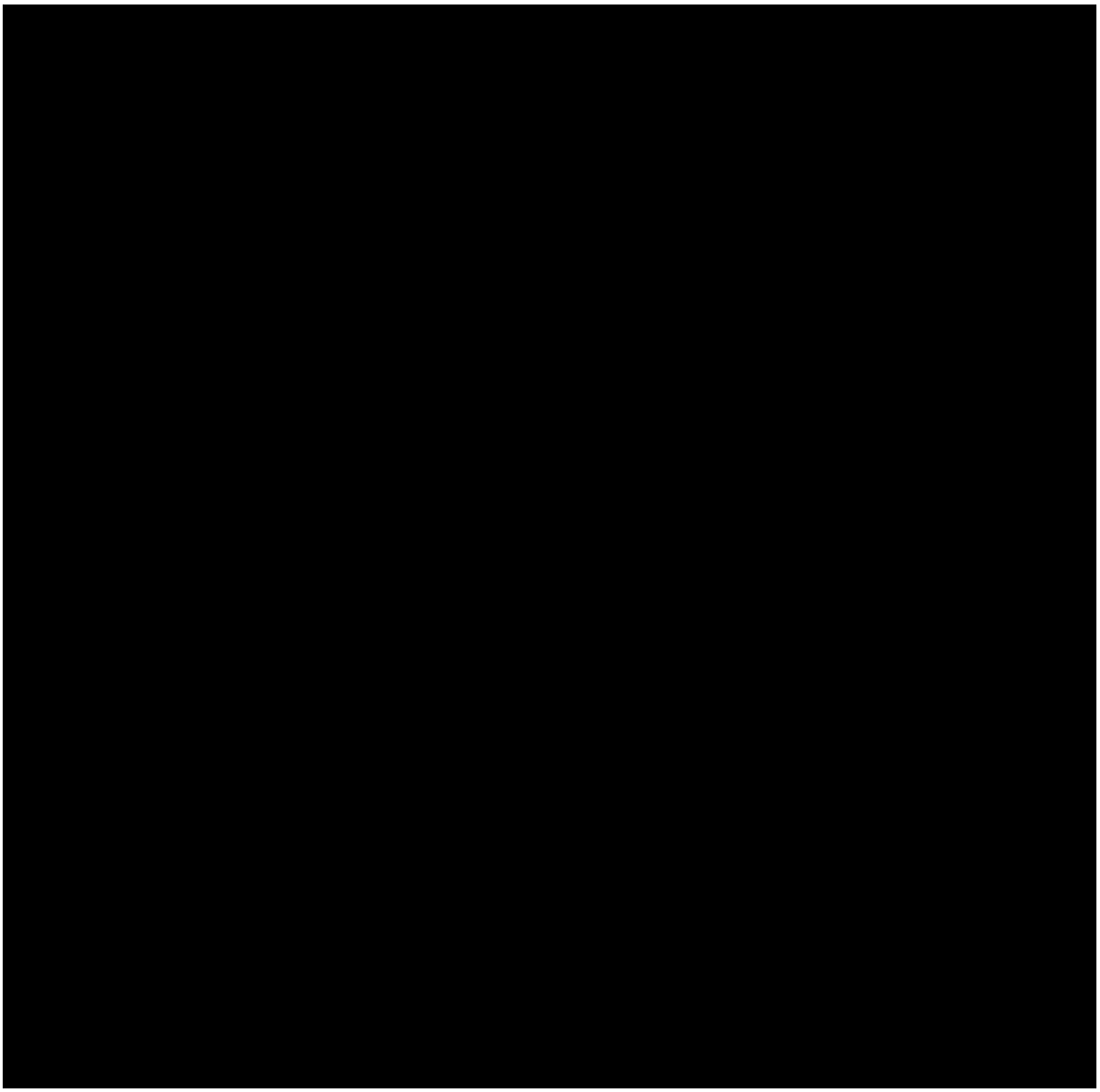
Appendix D. 5.2.3.3 Risk of Stroke

Appendix D. 5.2.4 Sleep

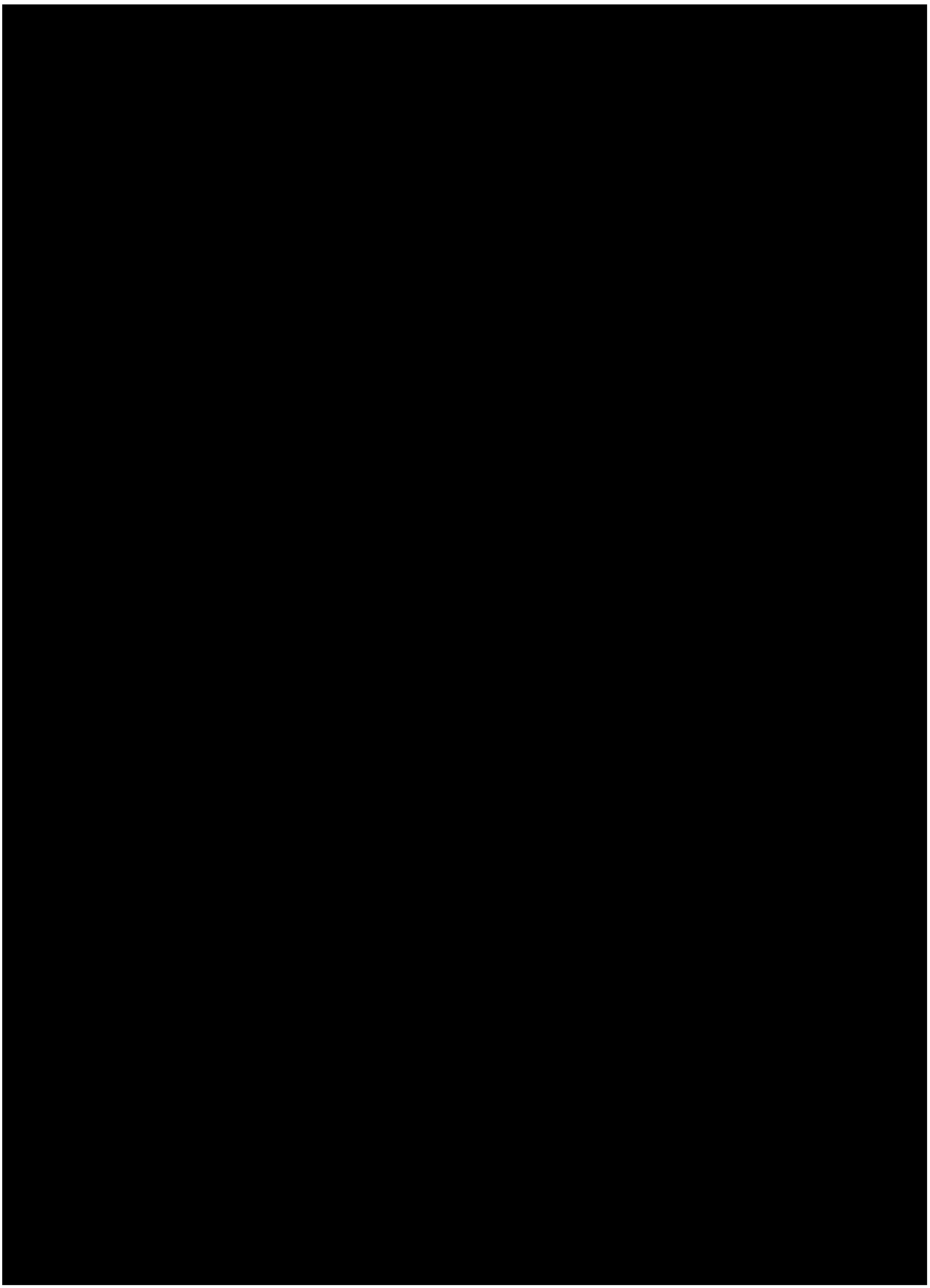
Appendix D. 5.2.4.1 Lack of energy

Appendix D. 5.2.4.2 Concentration

Appendix D. 5.2.5 Coping



Appendix D. 5.2.5.1 Attitude



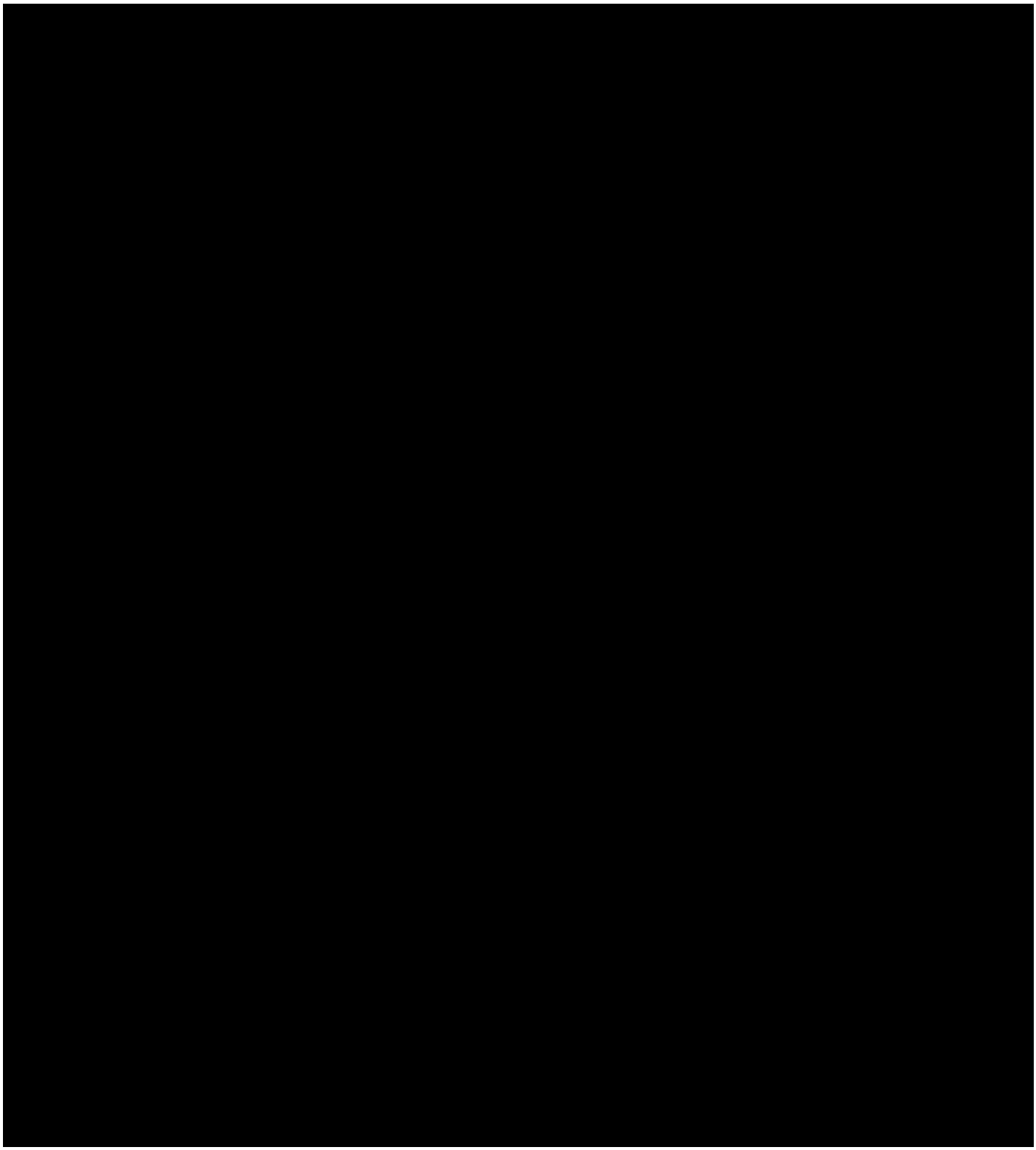
Appendix D. 5.2.5.2.1 Reassurance

Appendix D. 5.2.5.3 Information

Appendix D. 5.2.5.4 Frustration

Appendix D. 5.2.5.5 Disappointment

Appendix D. 5.2.5.6 Acceptance



Appendix D 5.3 Activities of Daily Living

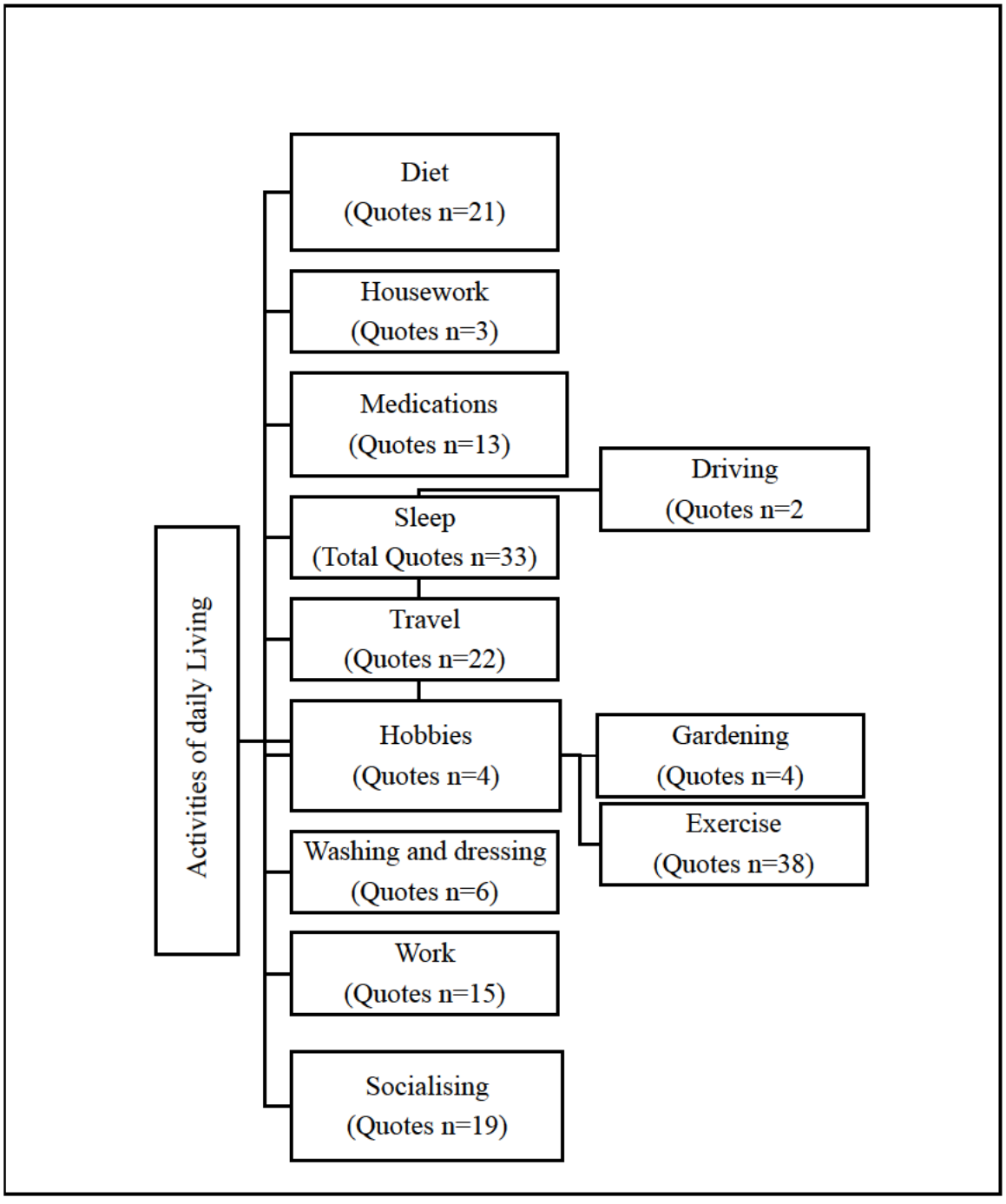
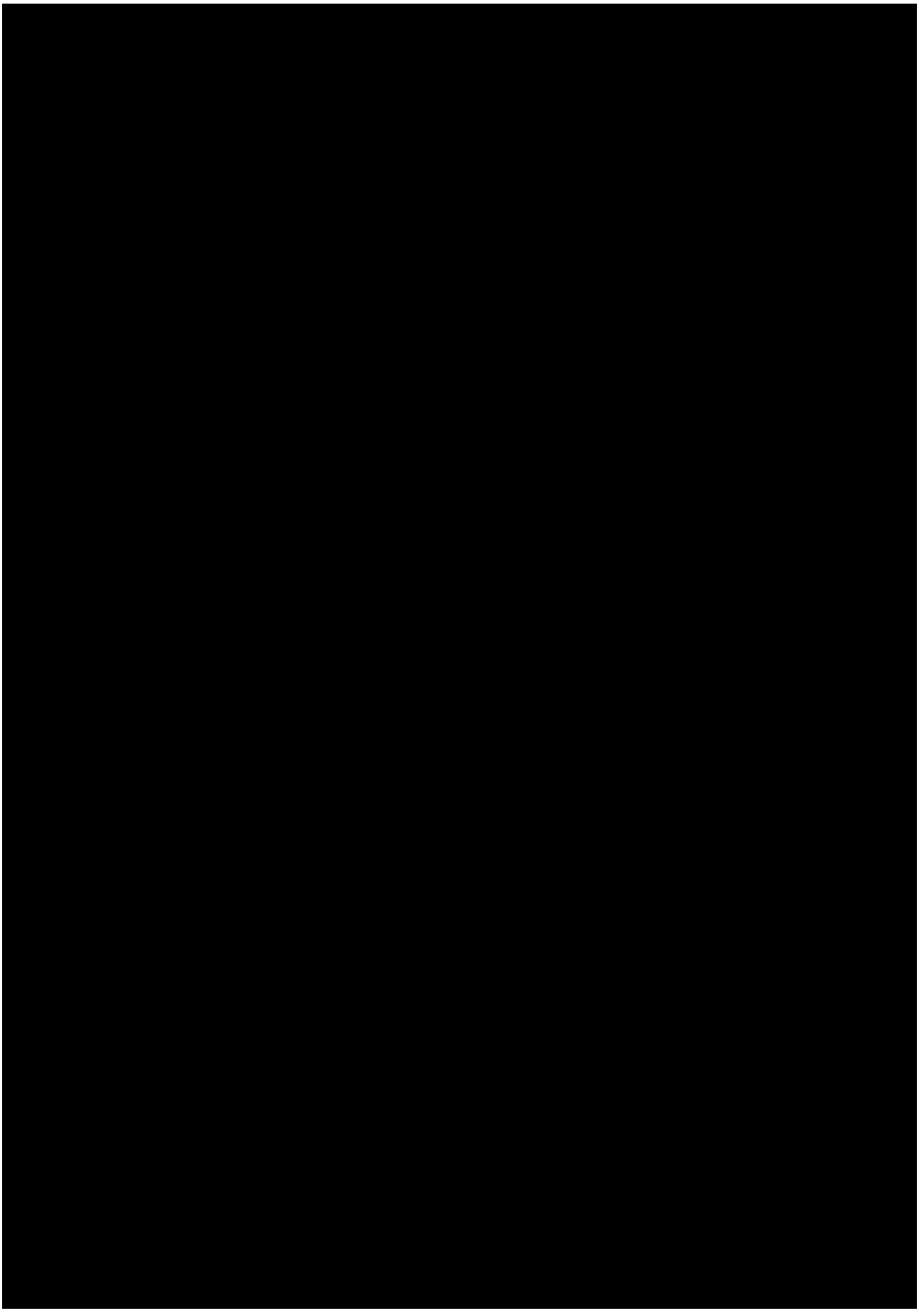
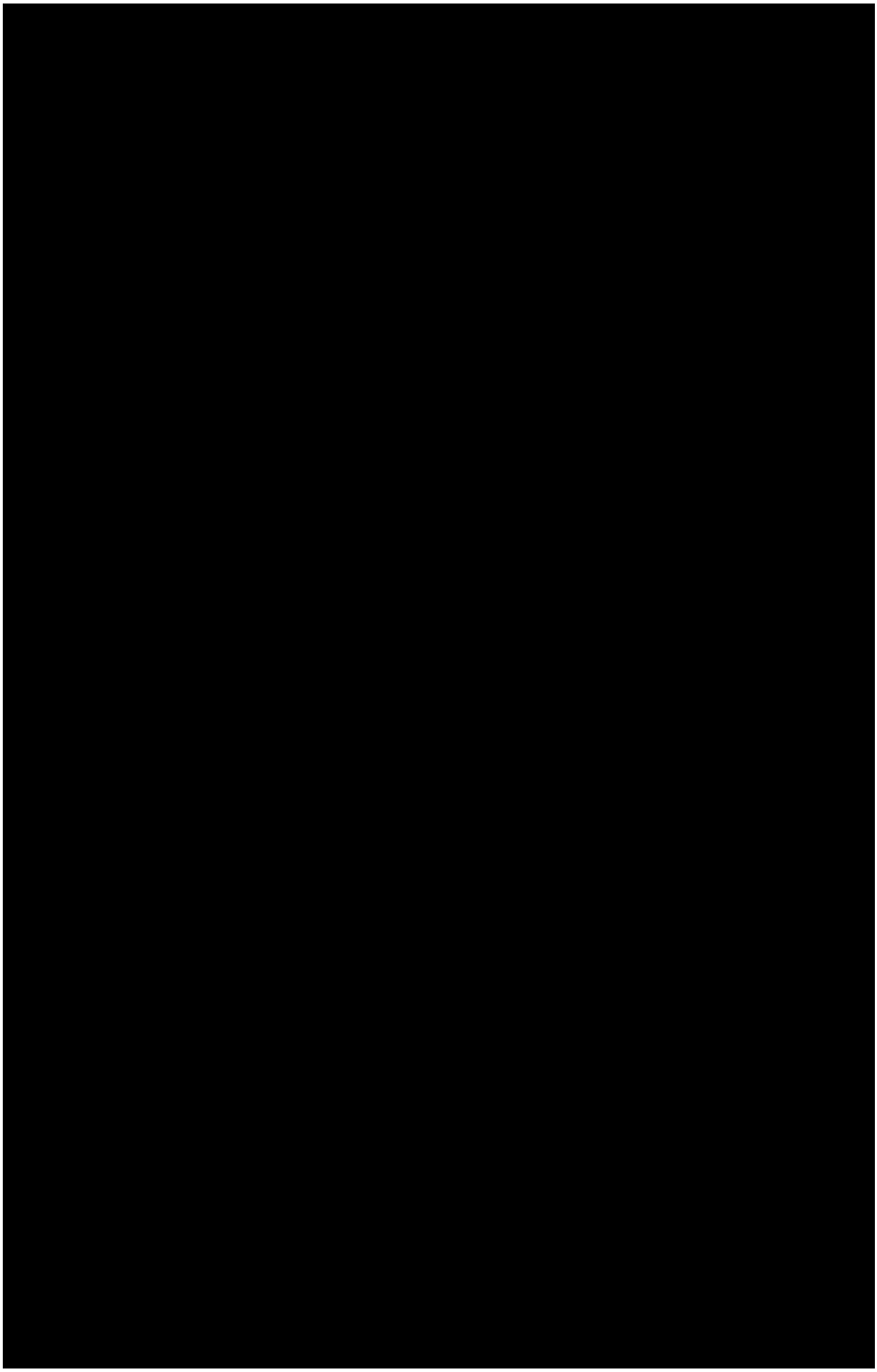


Figure 5.3 Overview diagram of main themes noted: Activities of daily living

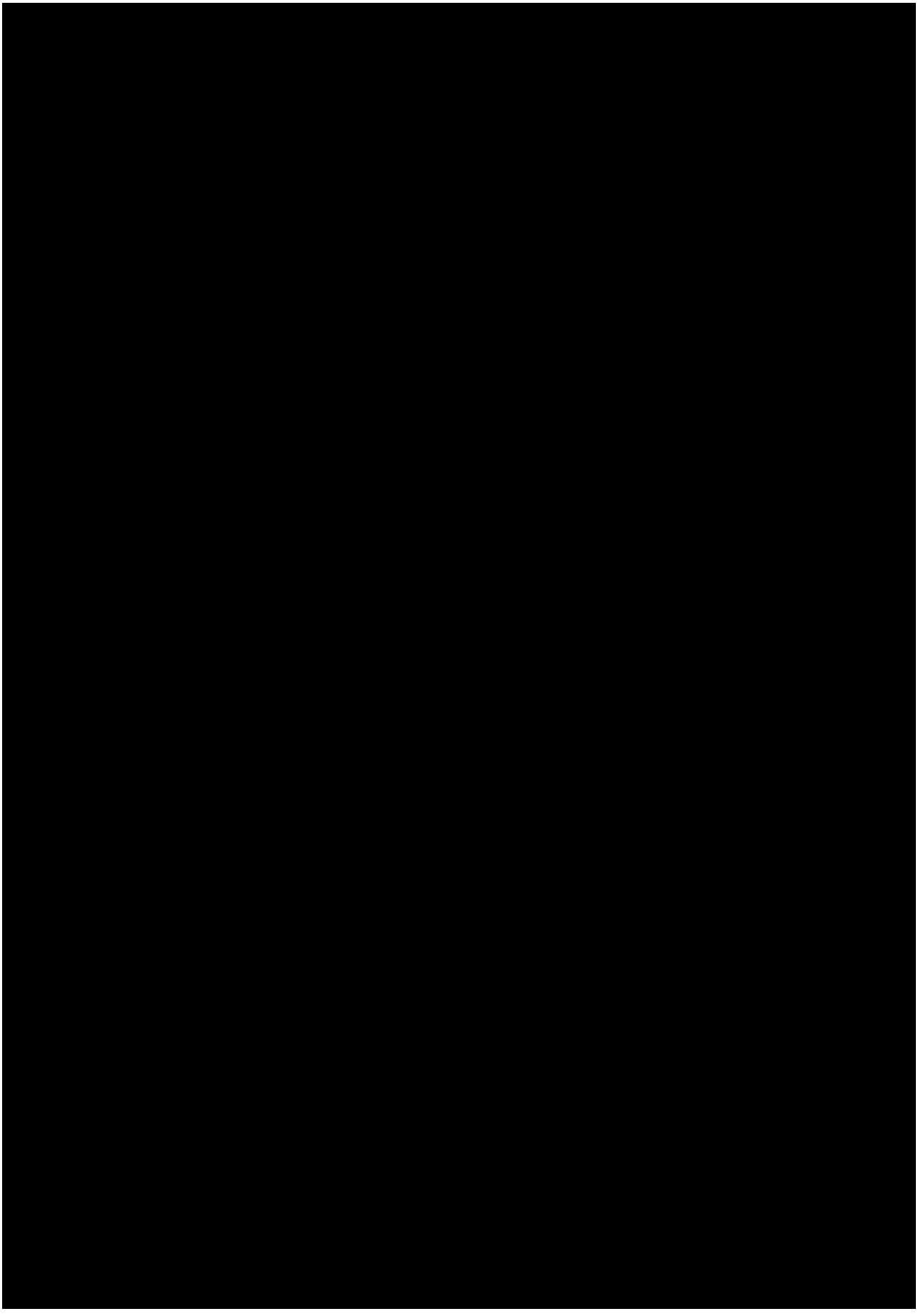
5.3.1 Diet including Food and Alcohol

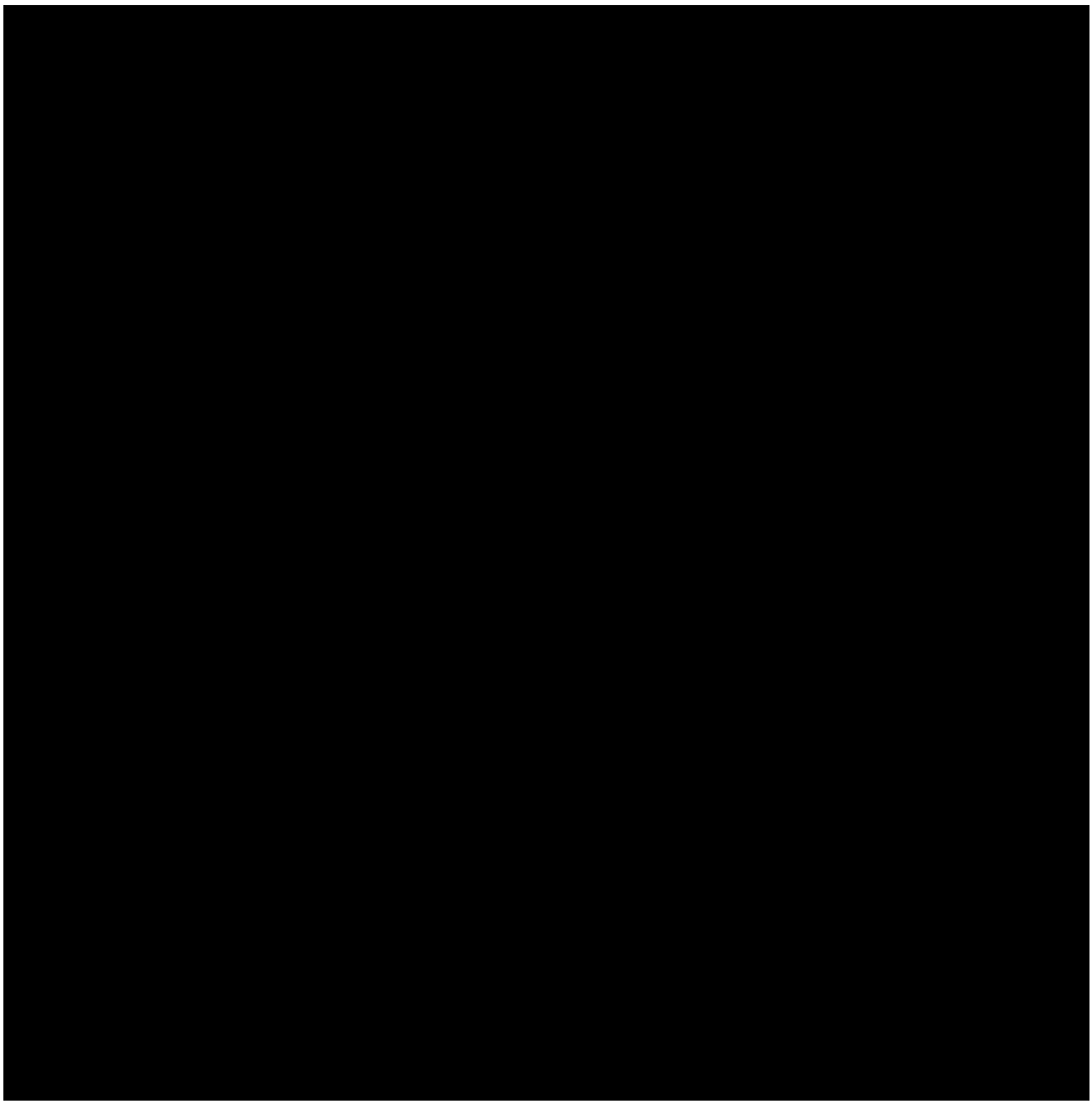




Appendix D. 5.3.2 Housework

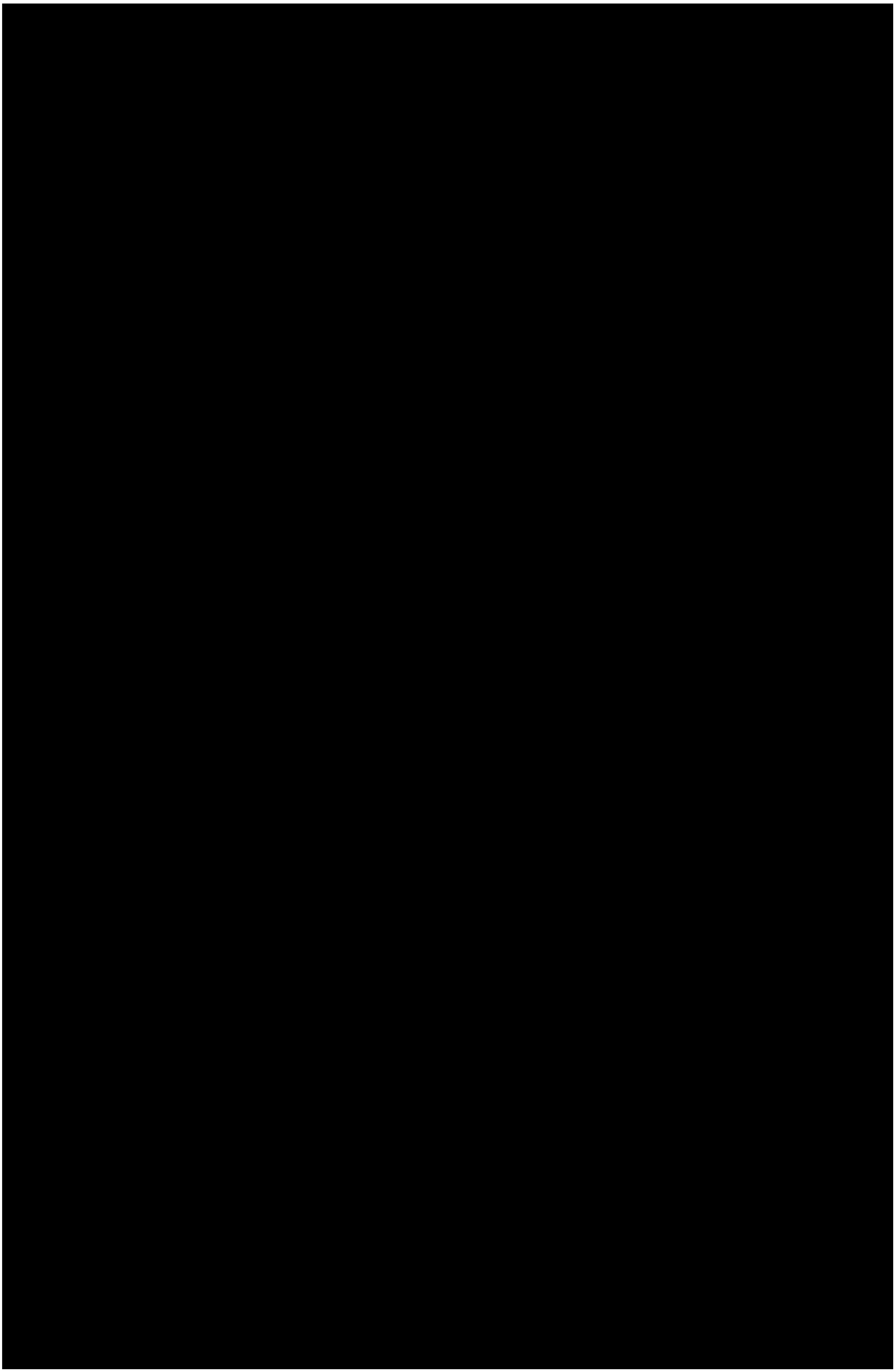
Appendix D. 5.3.3 Medications

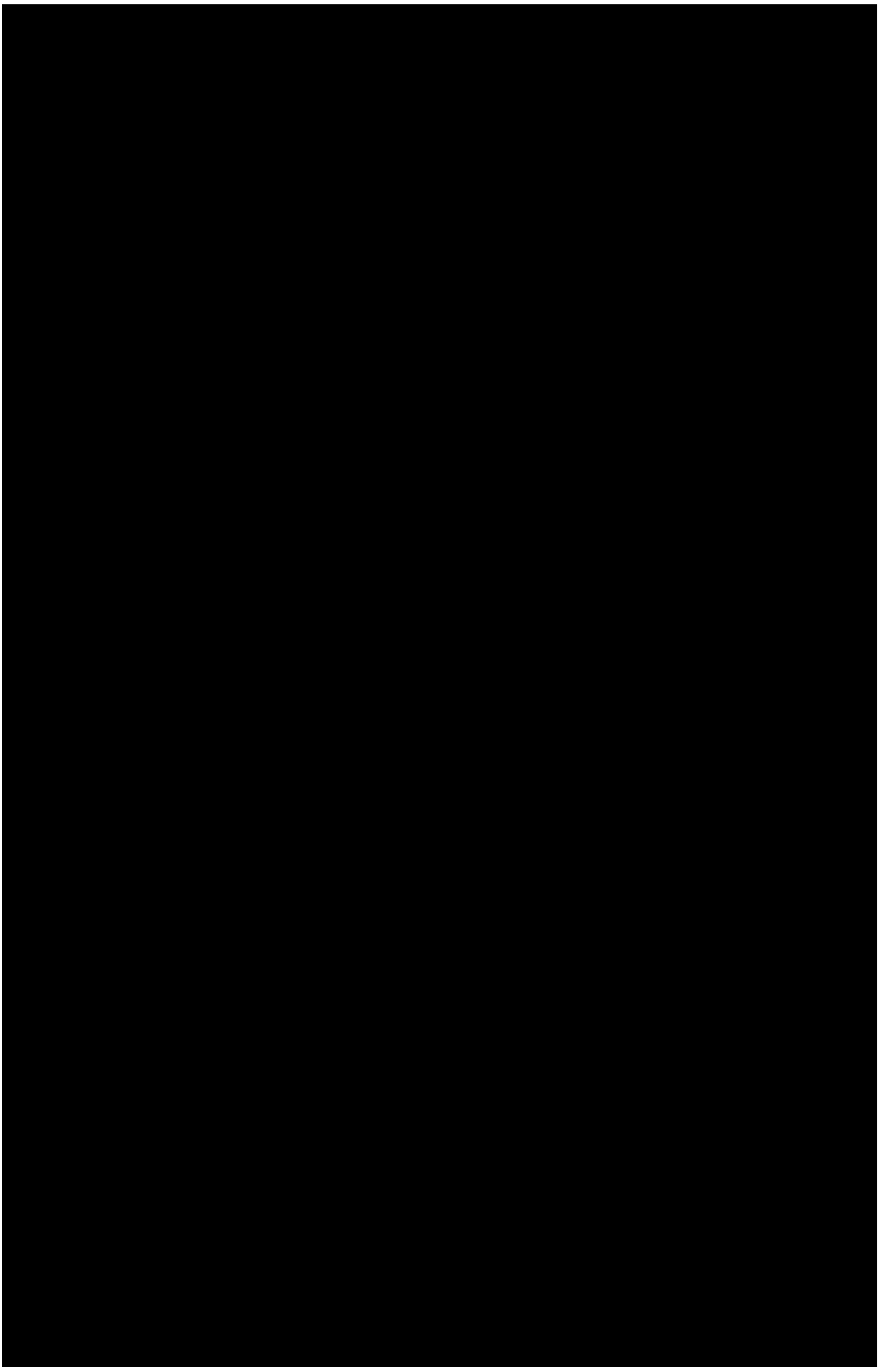




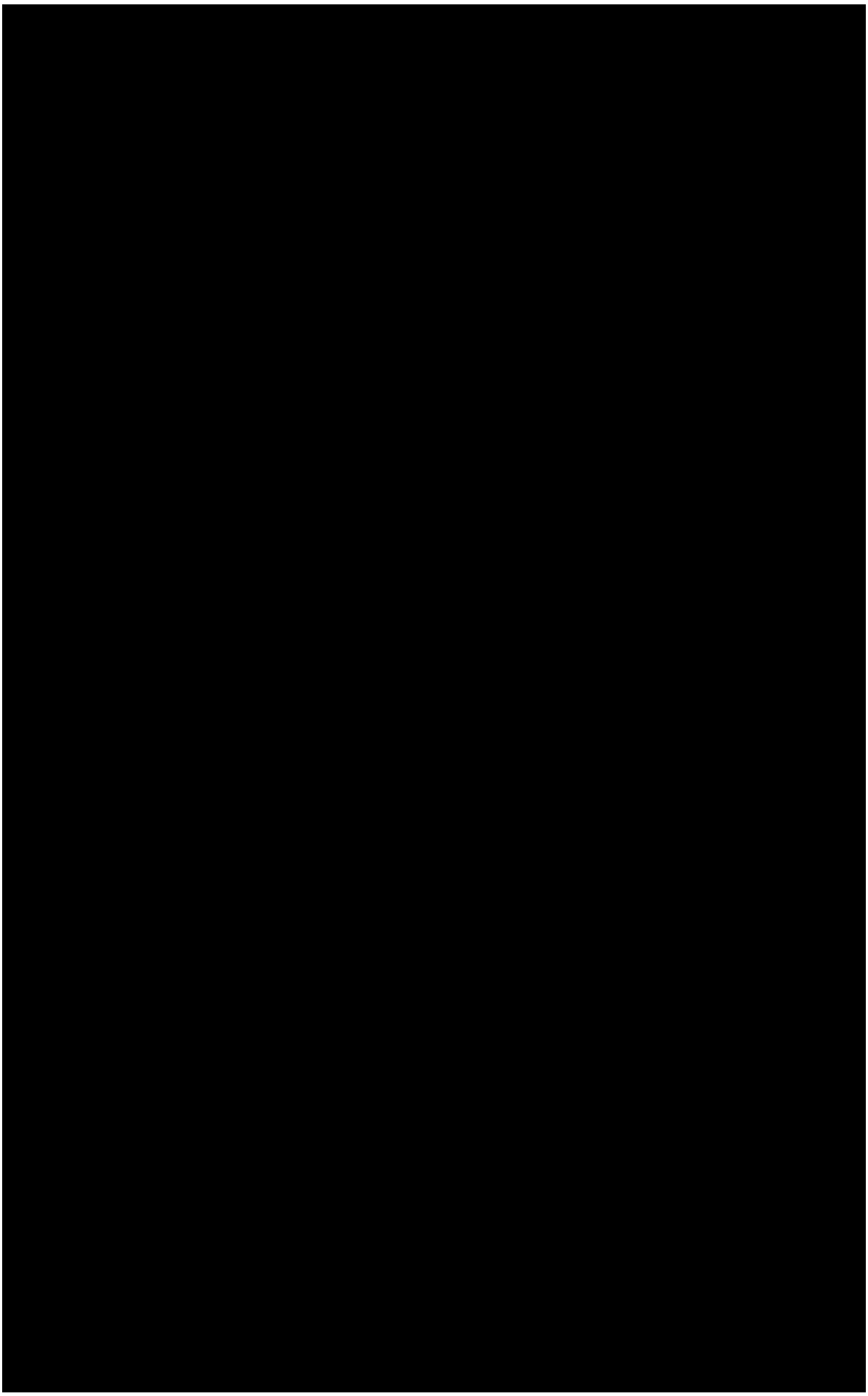
Appendix D. 5.3.4 Sleep

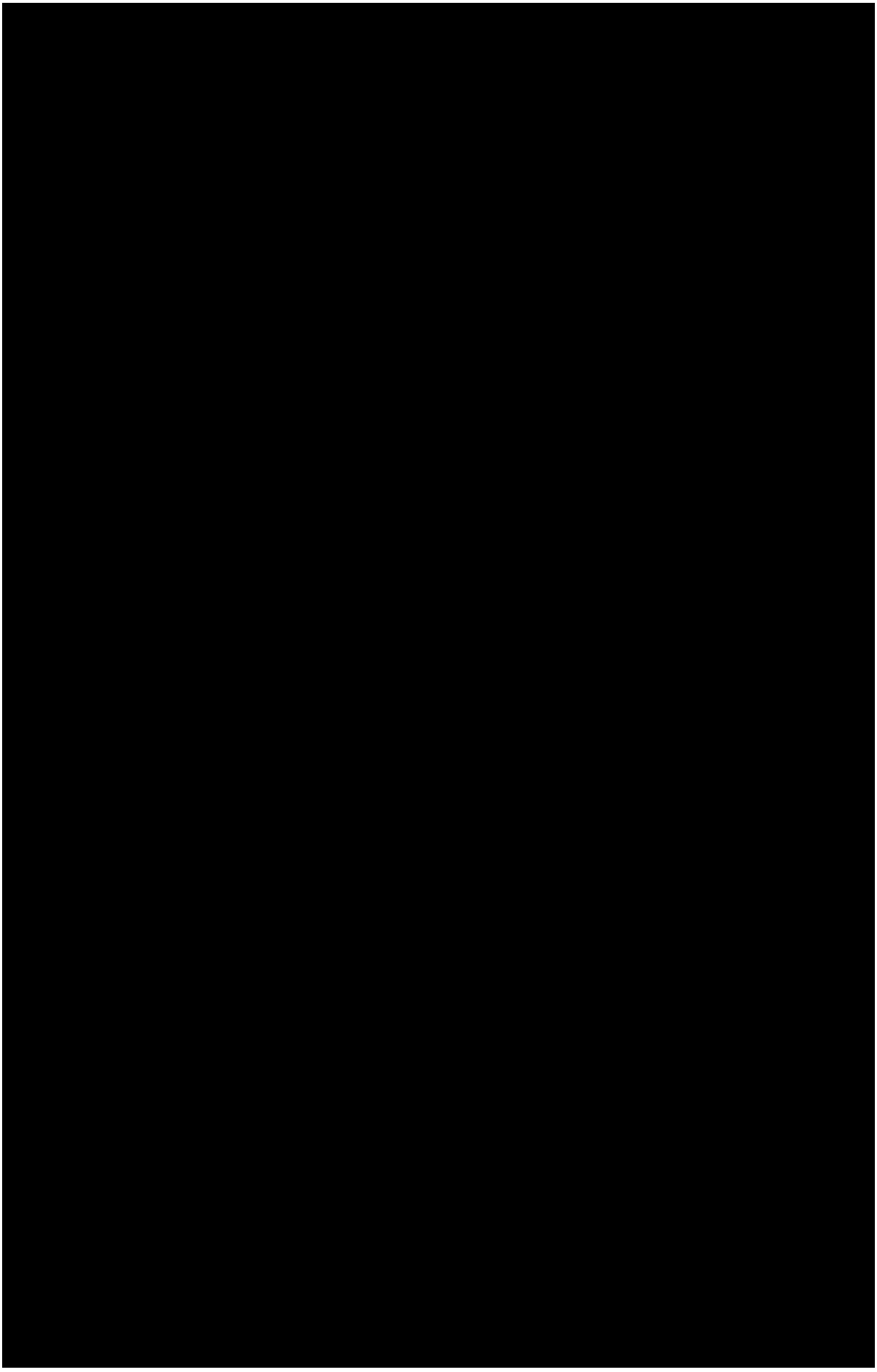
Appendix D. 5.3.5 Travel





Appendix D. 5.3.6 Exercise





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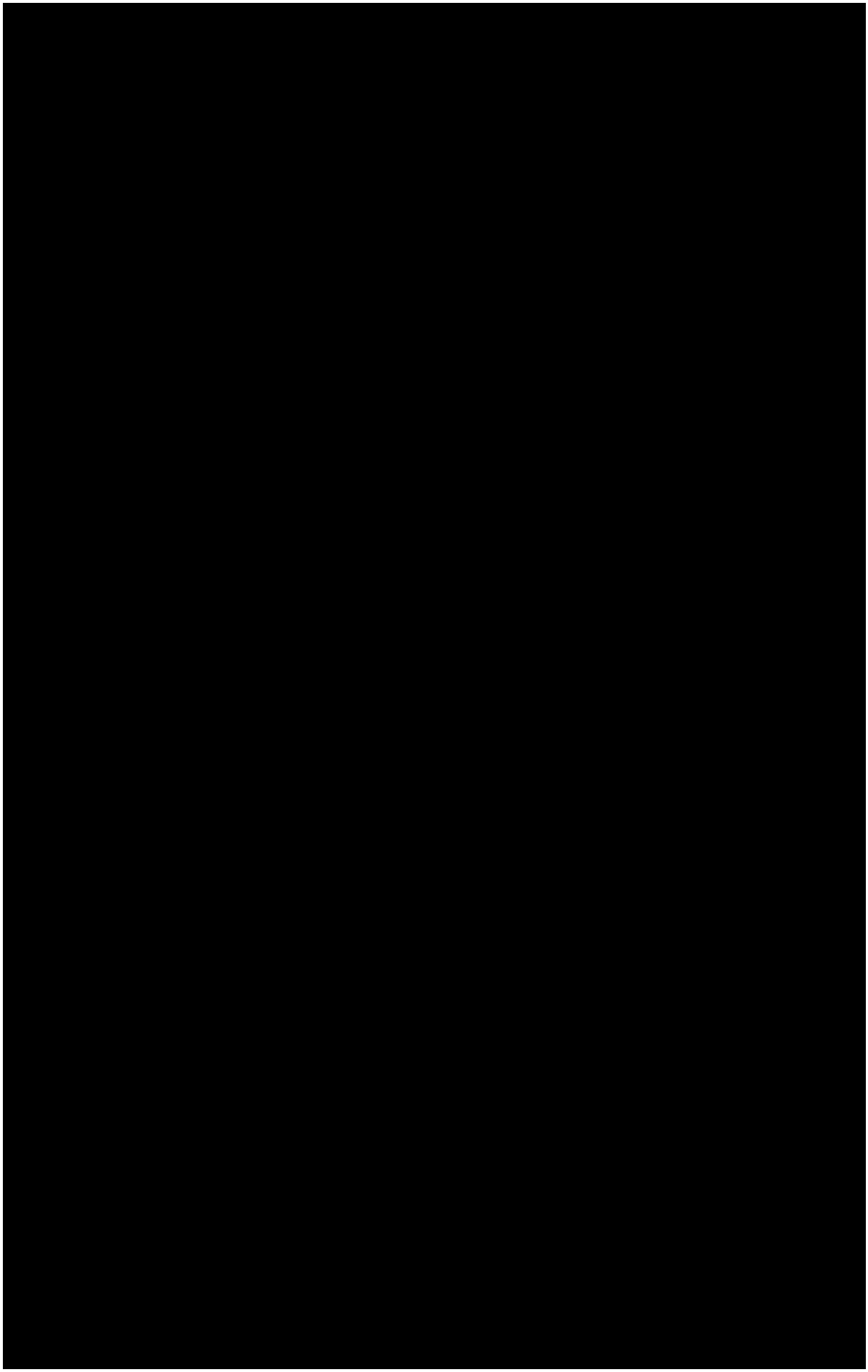
Appendix D. 5.3.7 Hobbies

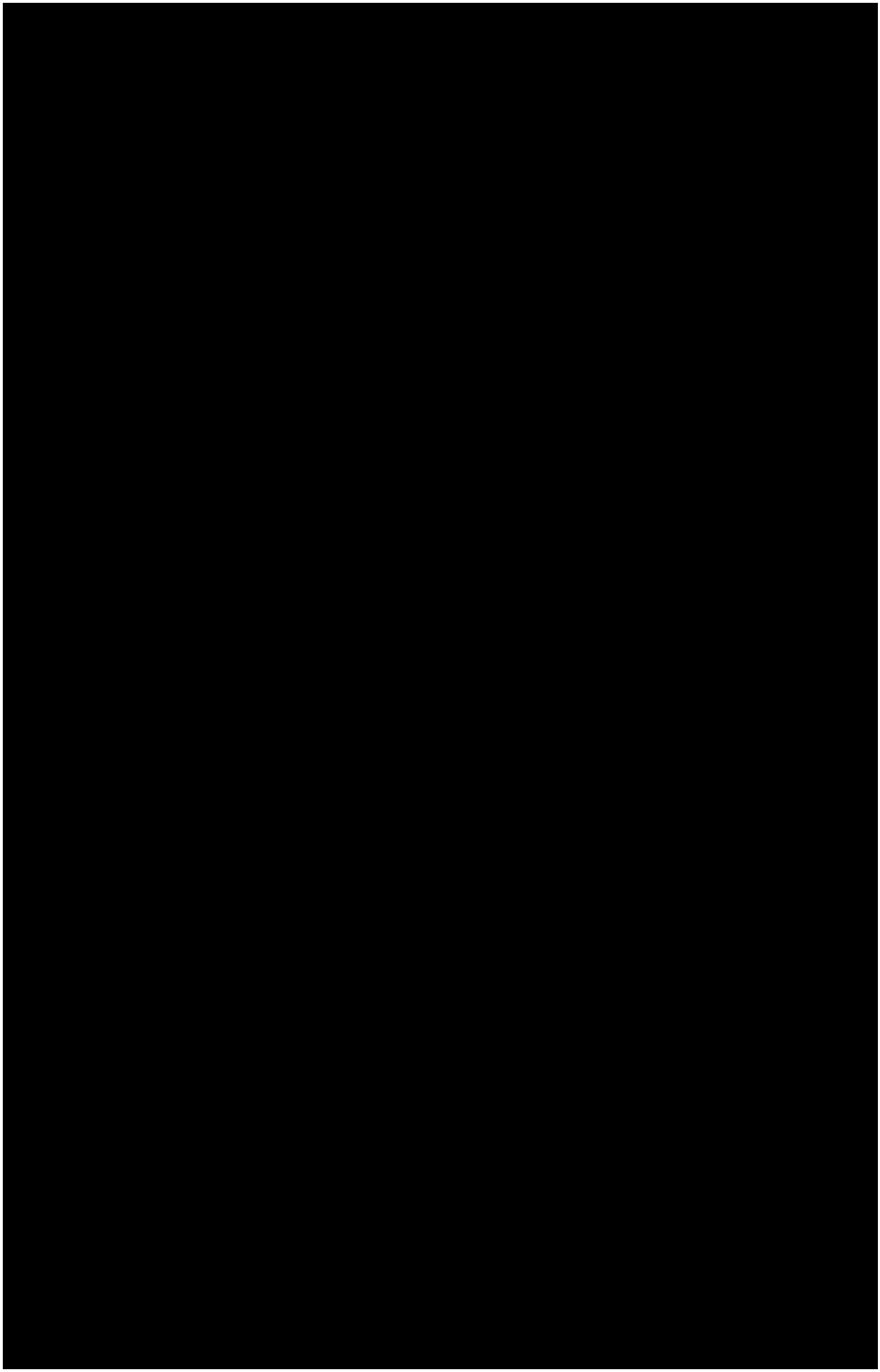
[redacted]

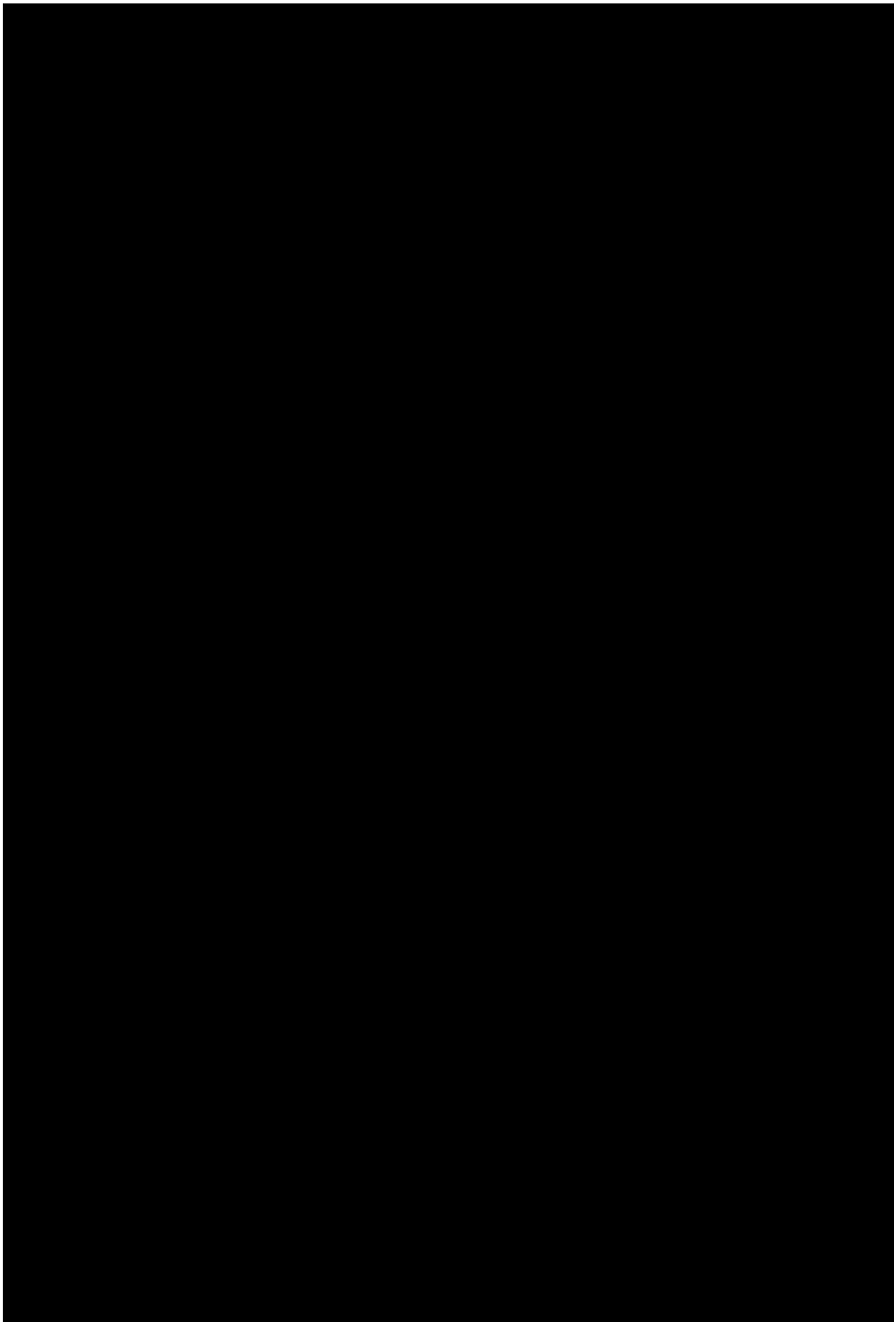
Appendix D. 5.3.8 Washing and Dressing

Appendix D. 5.3.9 Work



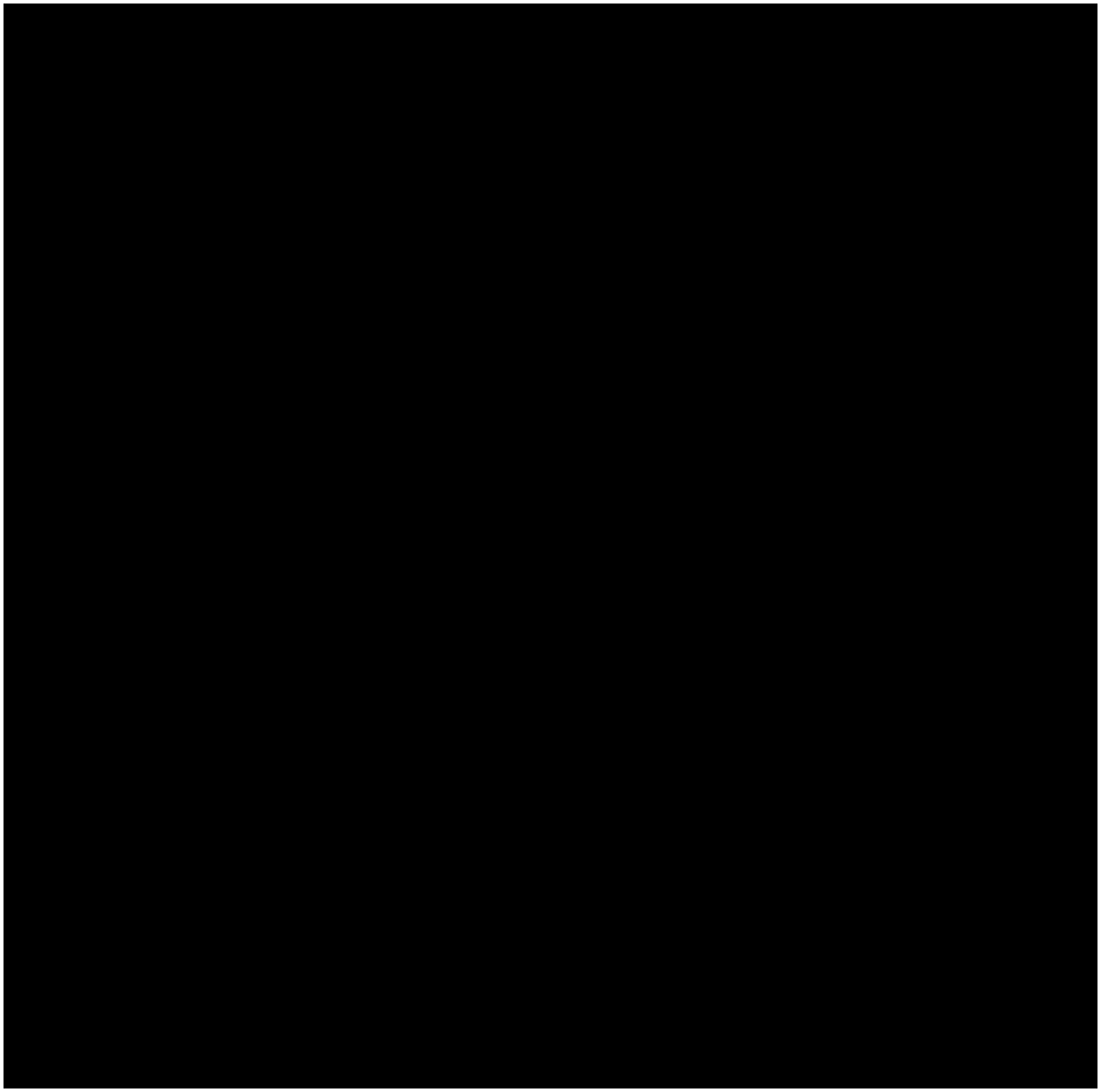
Appendix D. 5.3.10 Socialising





Appendix D. 5.3.11 Driving

Appendix D. 5.3.12 Gardening



Appendix D 5.4 Relationships

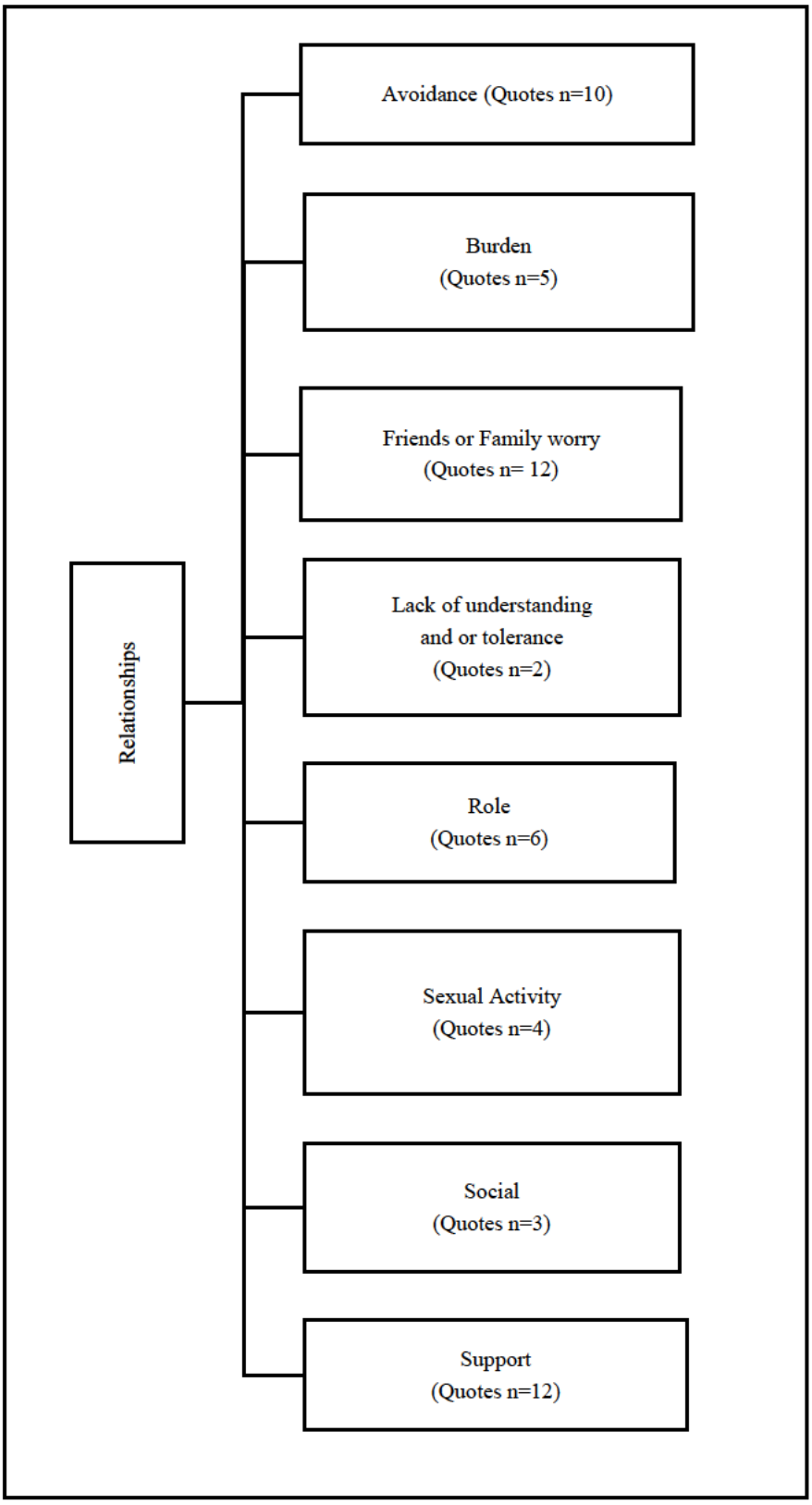


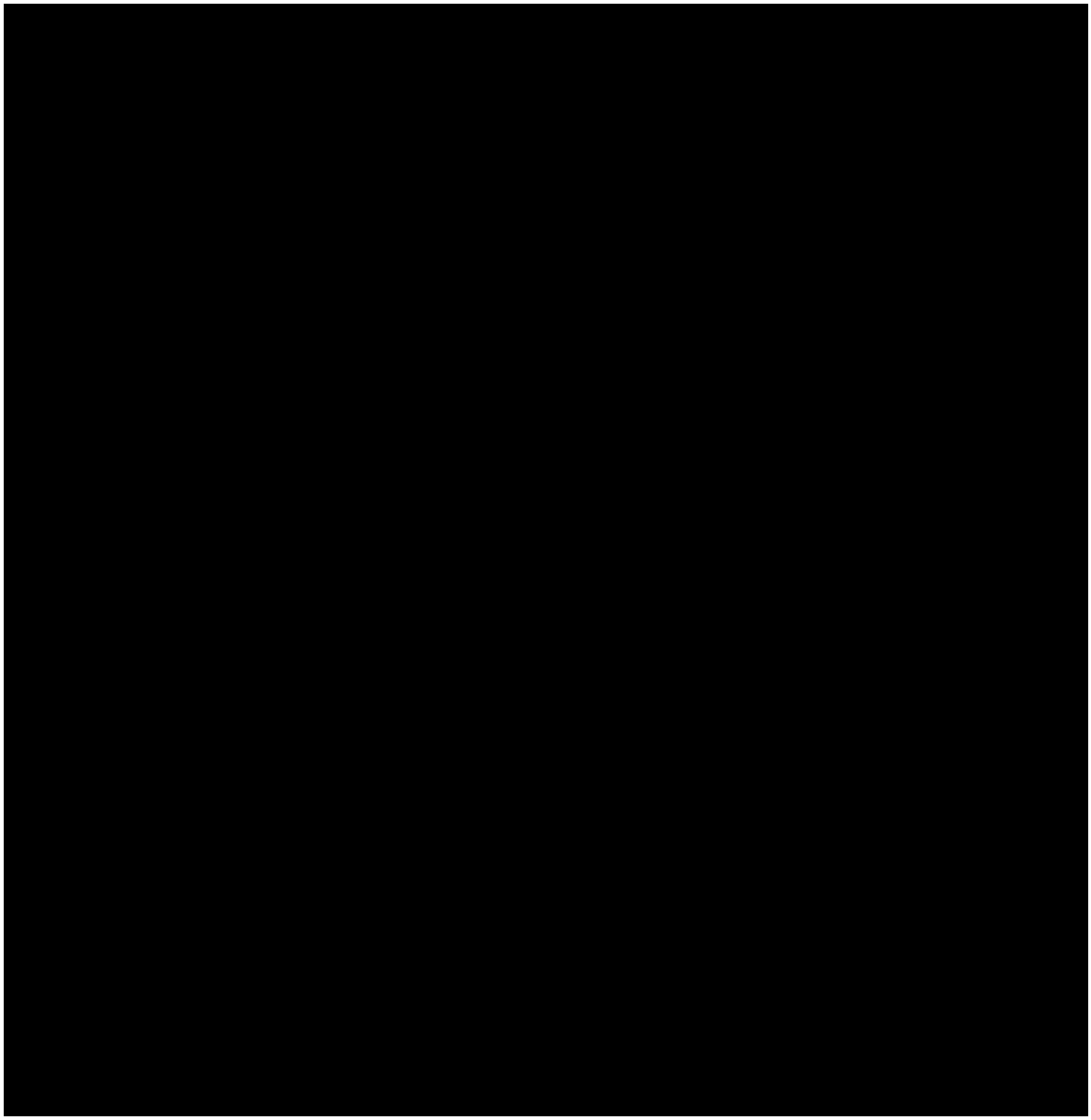
Figure 5.4 Overview diagram of main themes noted: Relationships

Appendix D. 5.4.1 Avoidance

Appendix D. 5.4.2 Burden

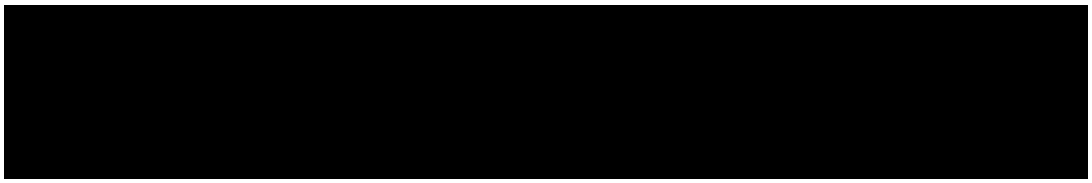
Appendix D. 5.4.3 Friends or Family worry

Appendix D. 5.4.4 Lack of understanding or tolerance

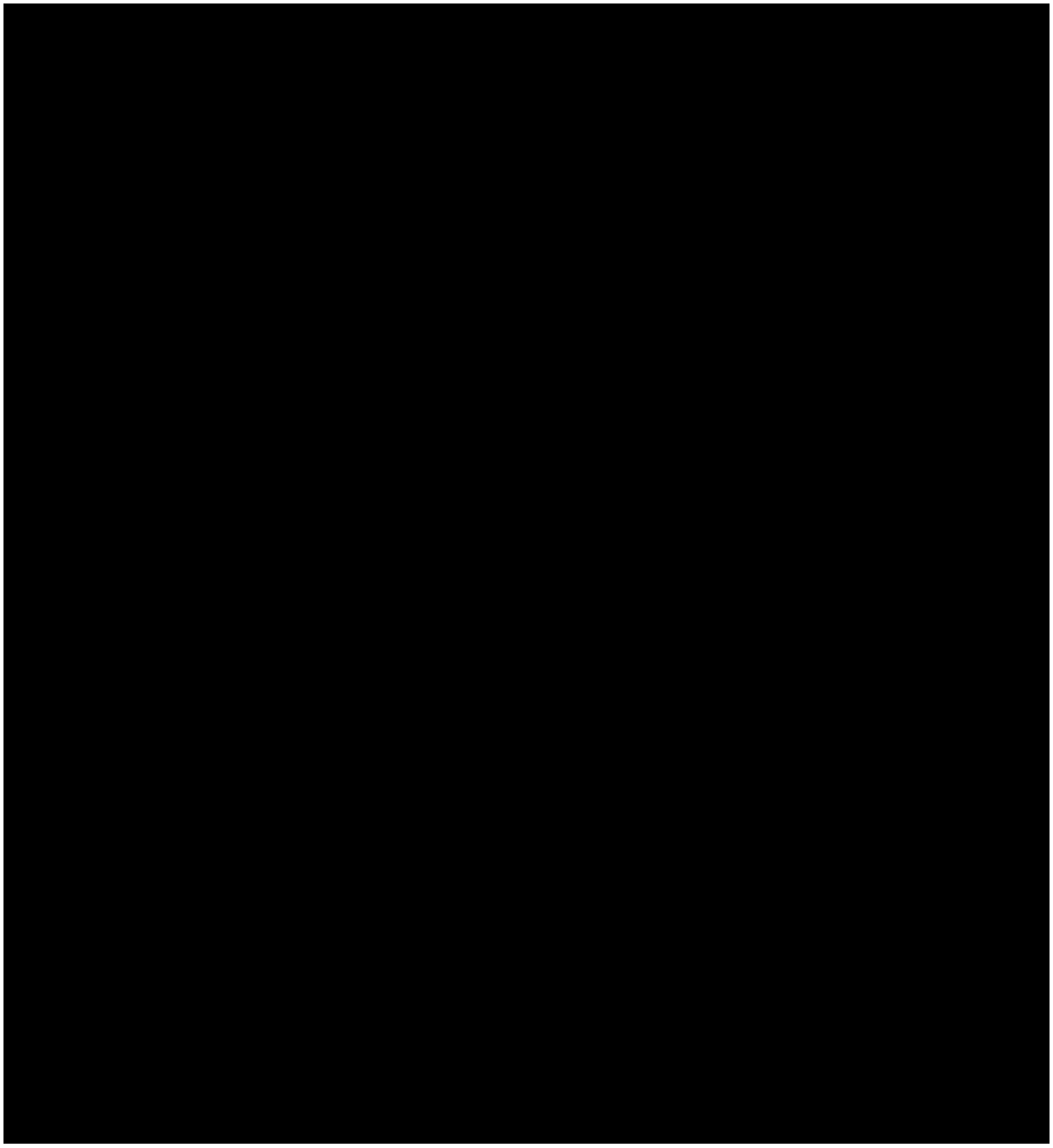


Appendix D. 5.4.5 Role

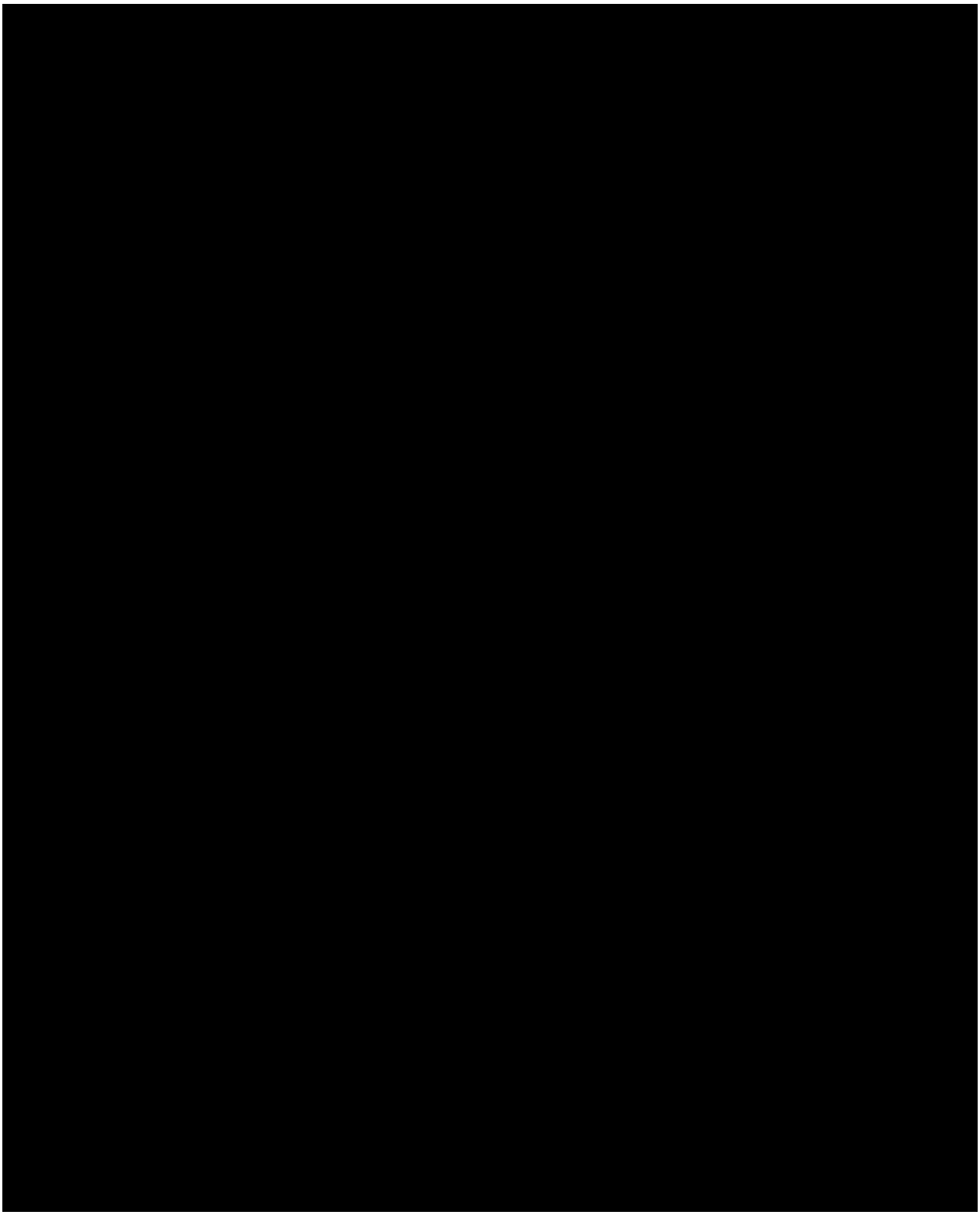
Appendix D. 5.4.6 Sexual Relationships



Appendix D. 5.4.7 Socialising



Appendix D. 5.4.8 Support



Appendix D 5.5 Treatment

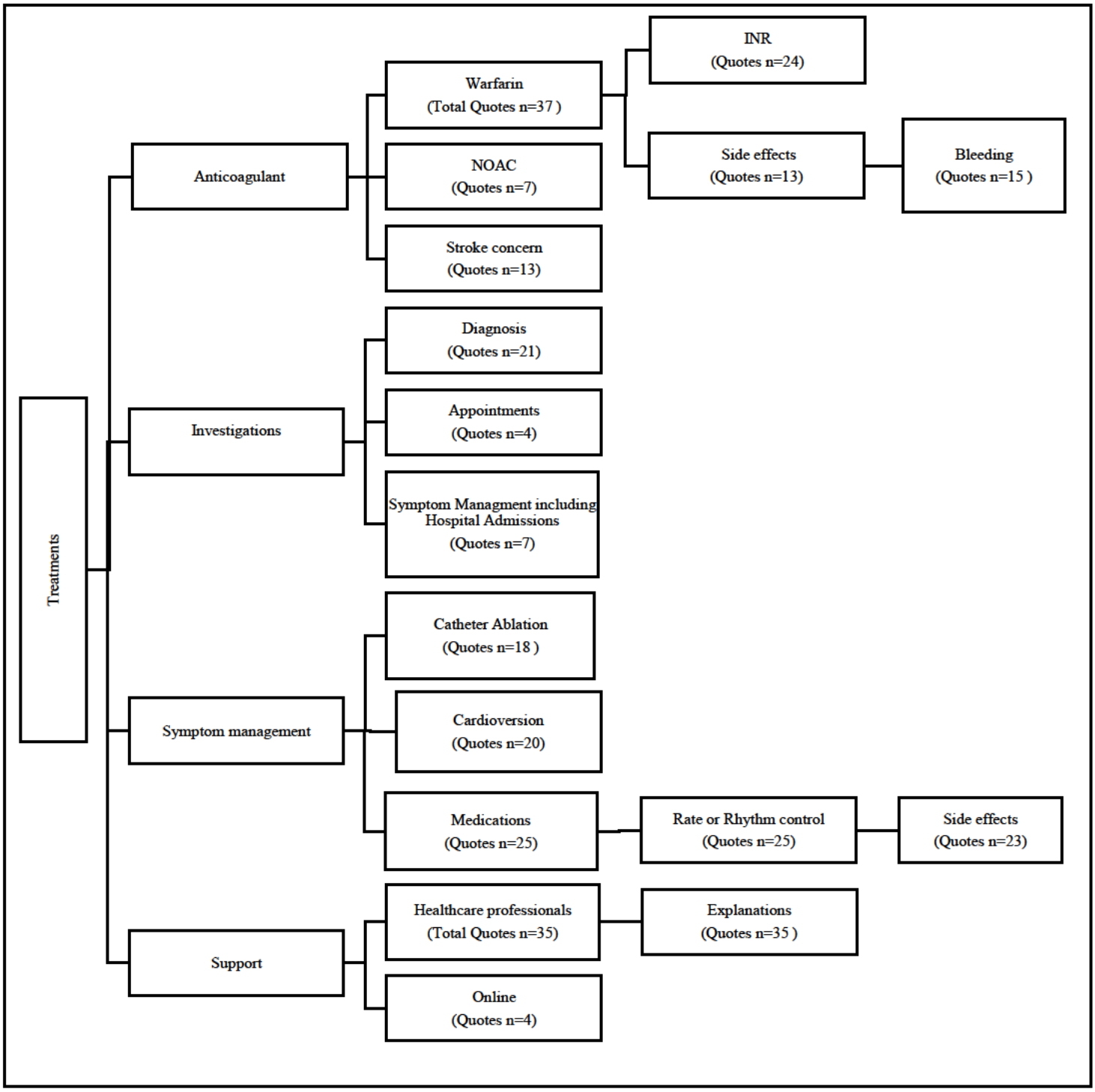


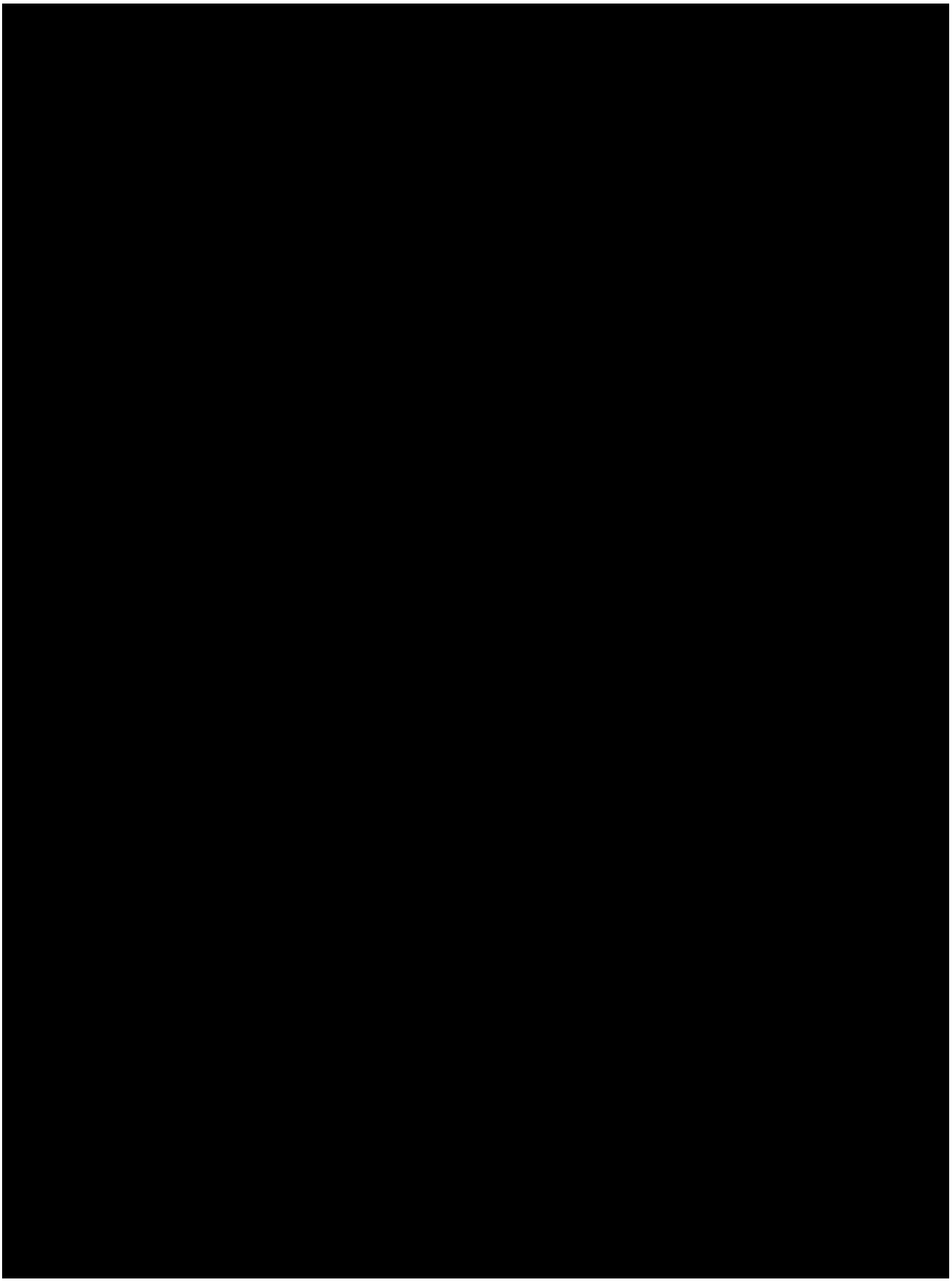
Figure 5.5 Overview diagram of main themes noted: Treatment

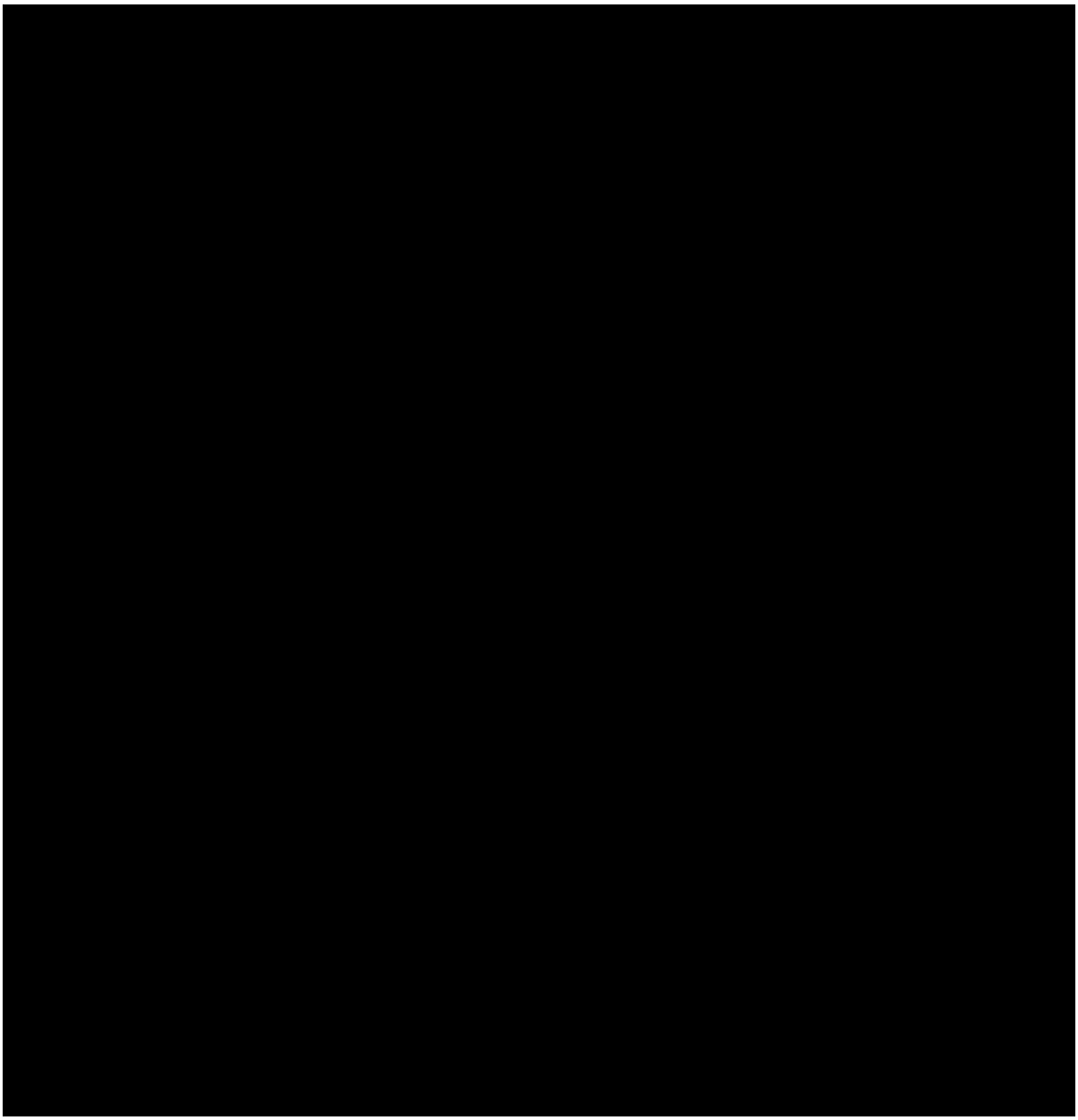
Appendix D. 5.5.1 Anticoagulant

Appendix D. 5.5.1.1 Warfarin

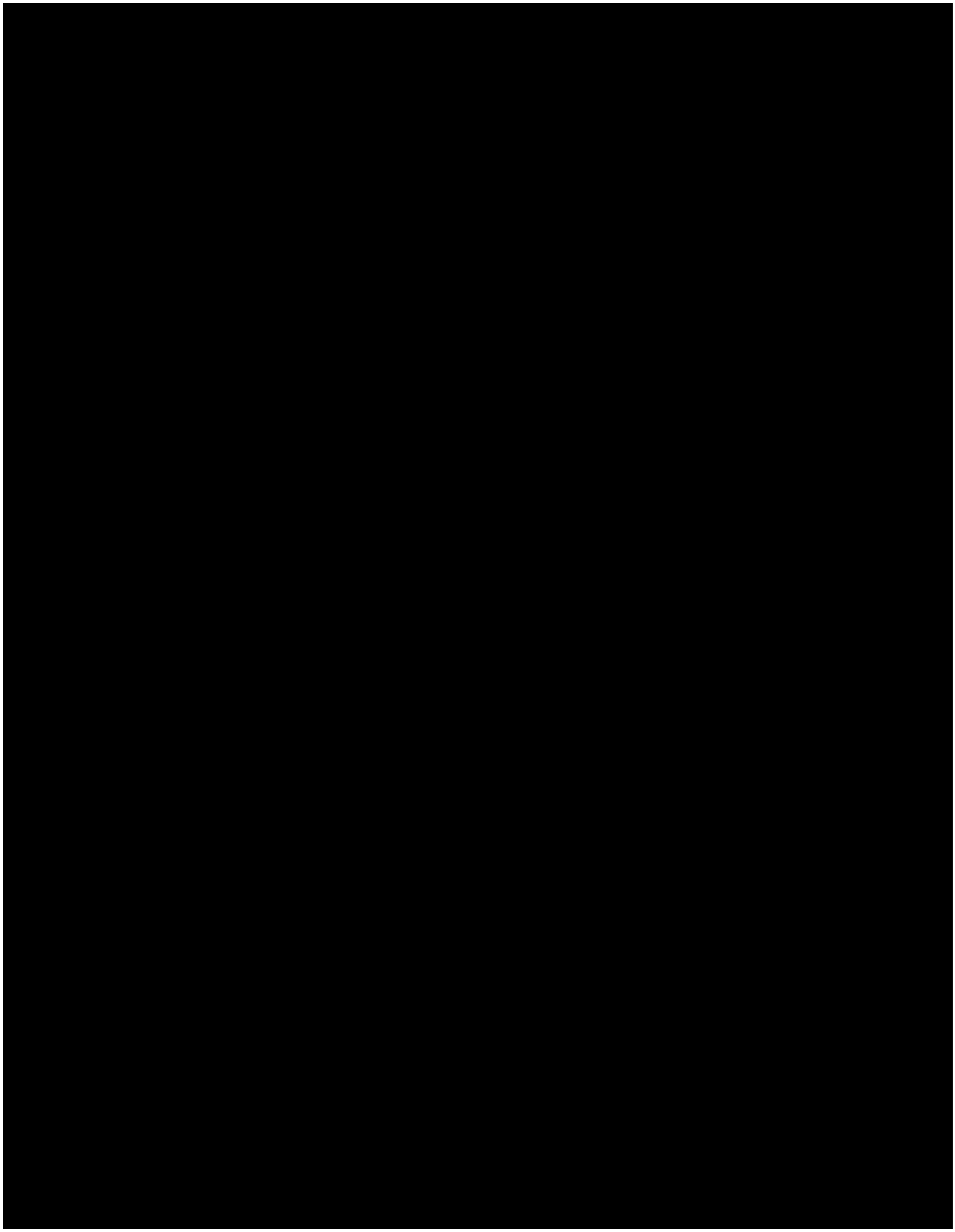
Appendix D. 5.5.1.1.1 INR

Appendix D. 5.5.1.1.2 Side effects

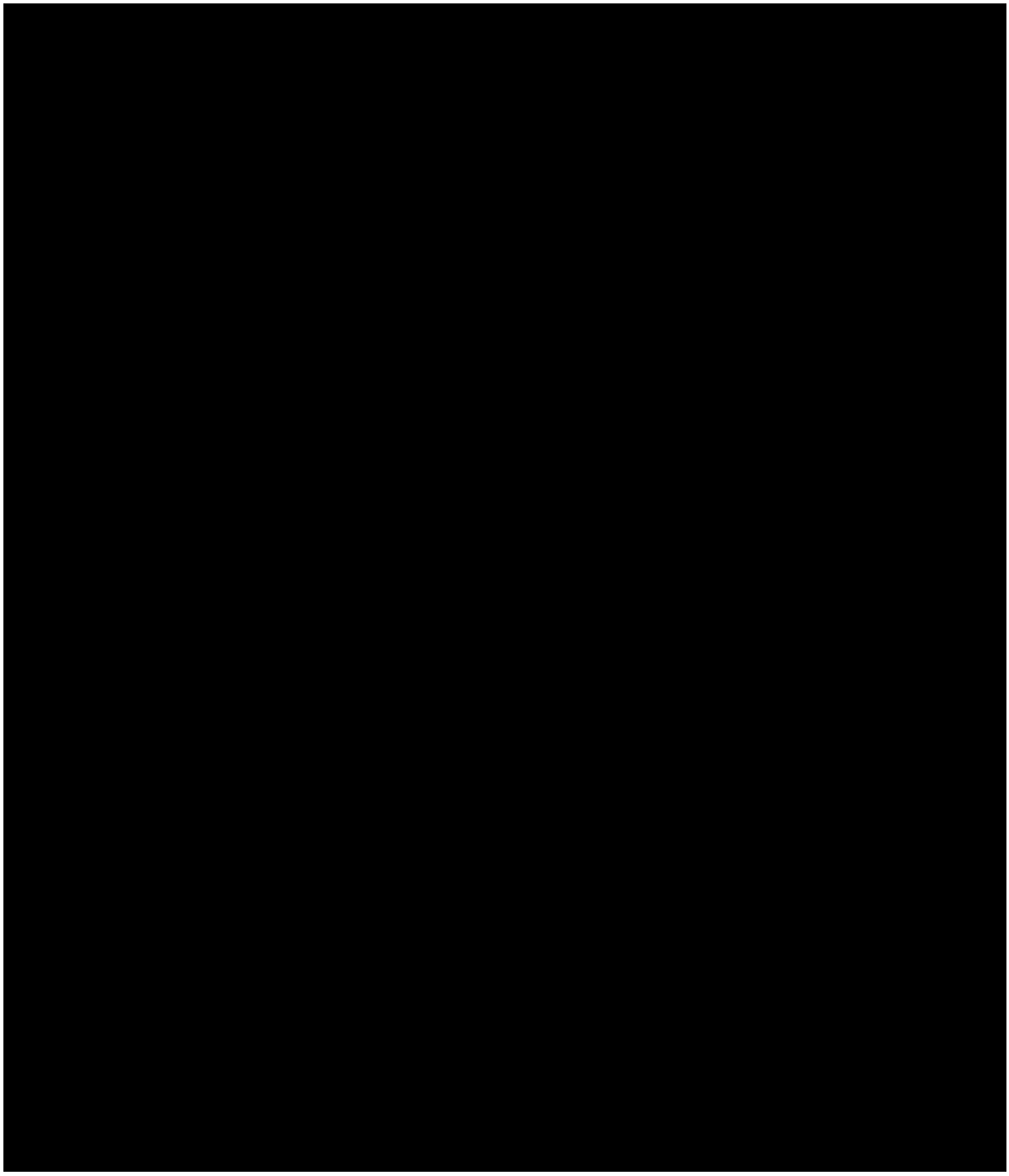




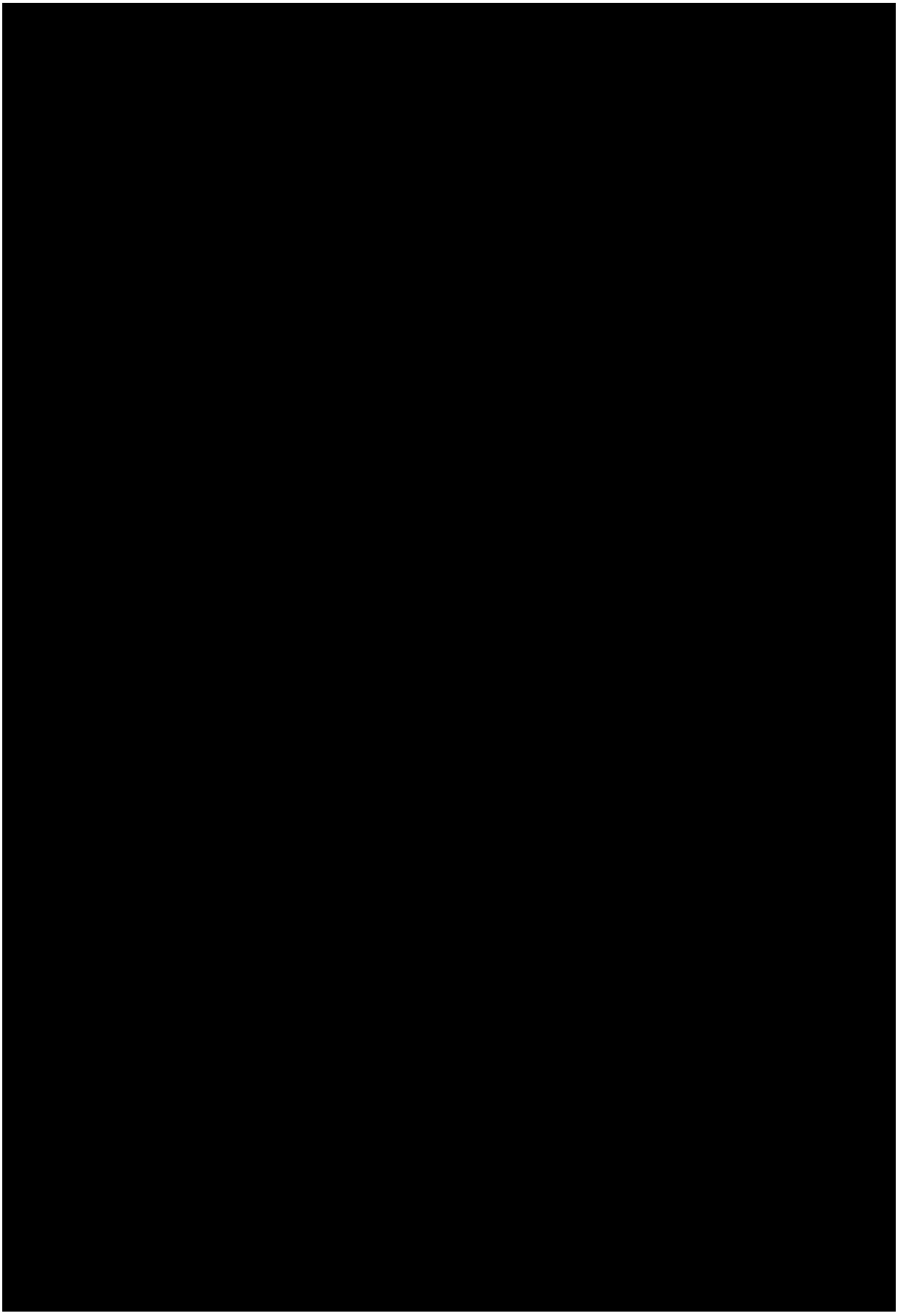
Appendix D. 5.5.1.1.2.1 Bleeding



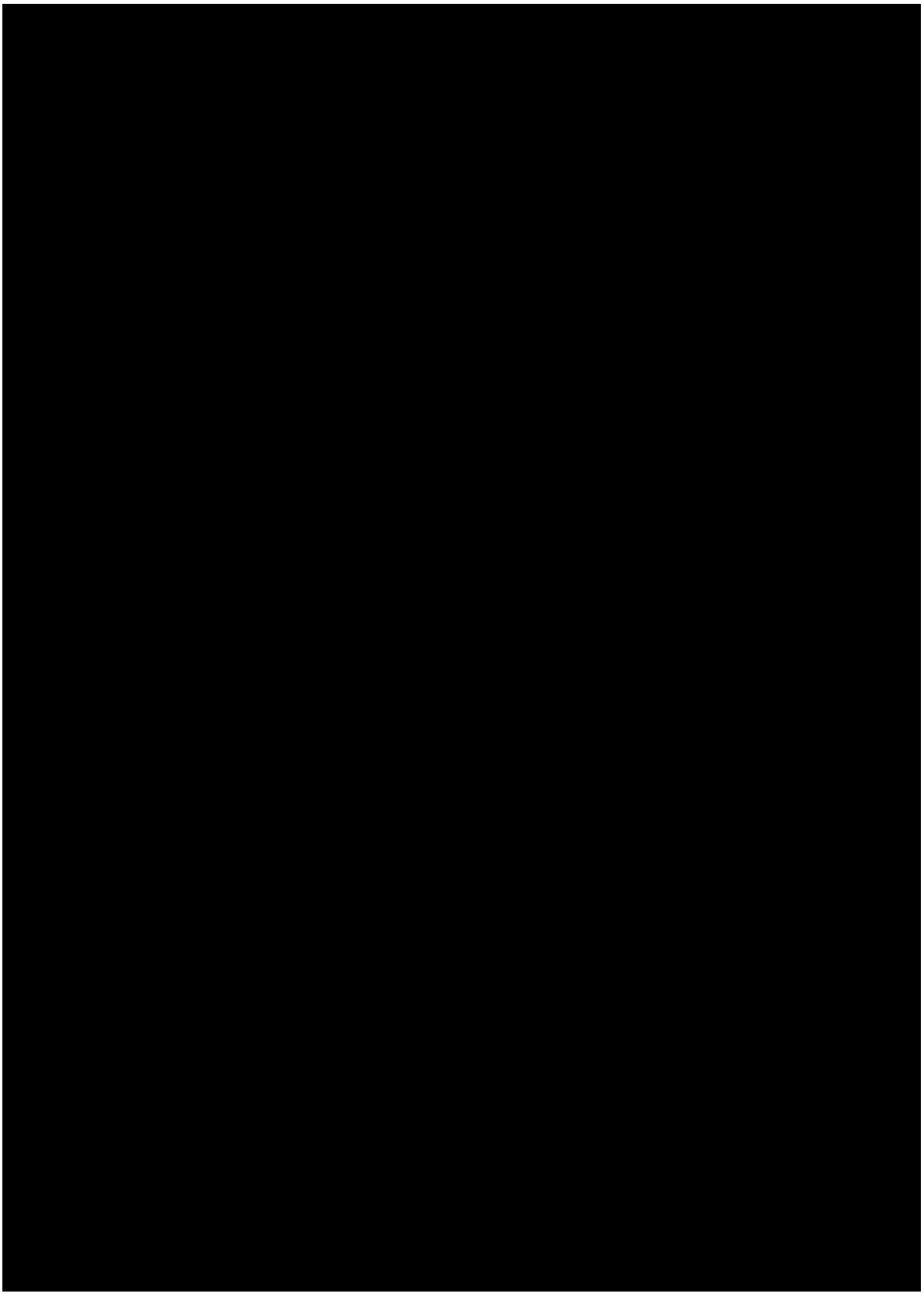
Appendix D. 5.5.1.2 NOAC



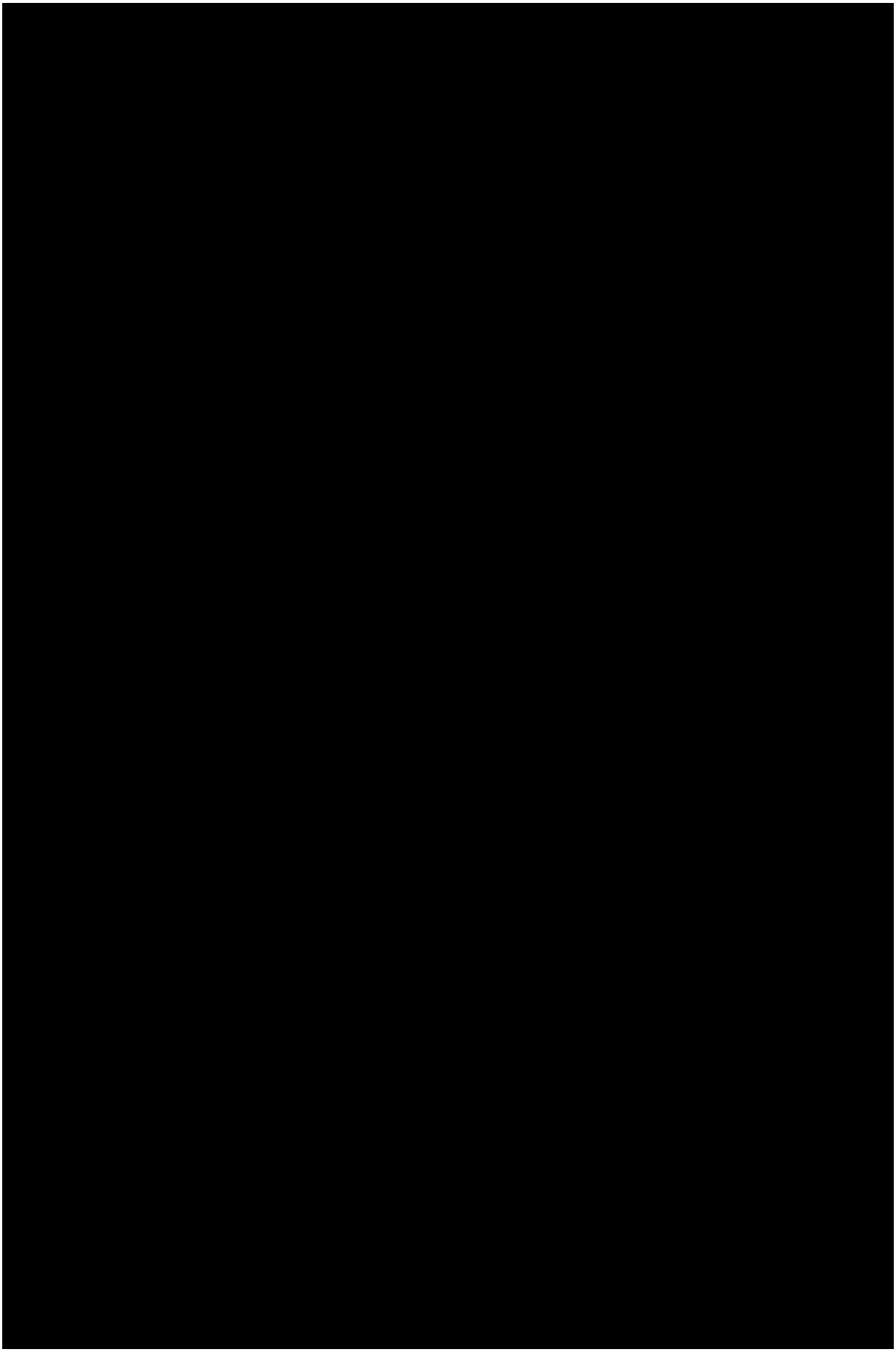
Appendix D. 5.5.1.3 Stroke Risk



Appendix D. 5.5.2 Investigations



Appendix D. 5.5.2.1 Diagnosis



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Appendix D. 5.5.2.2 Appointments

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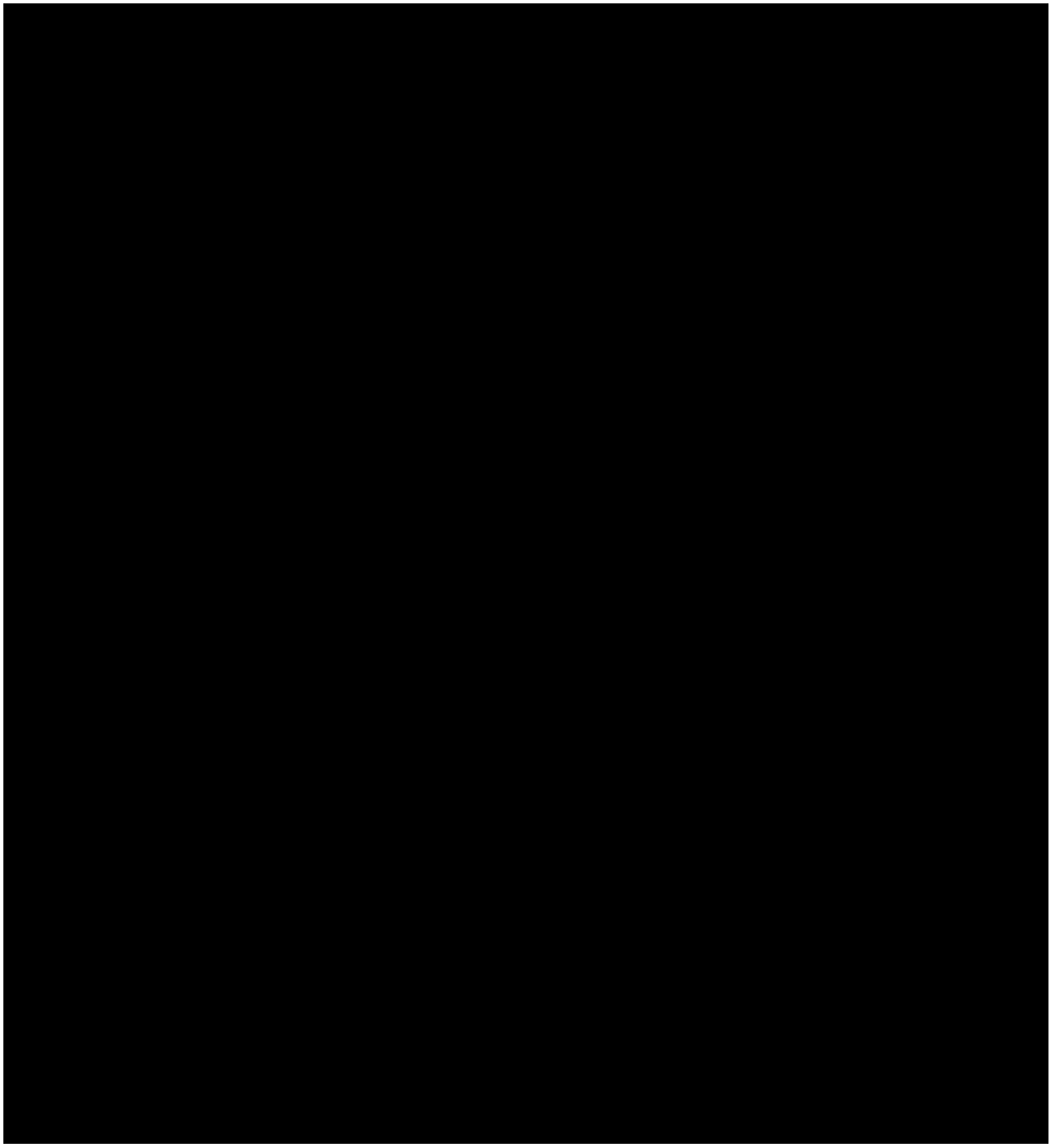
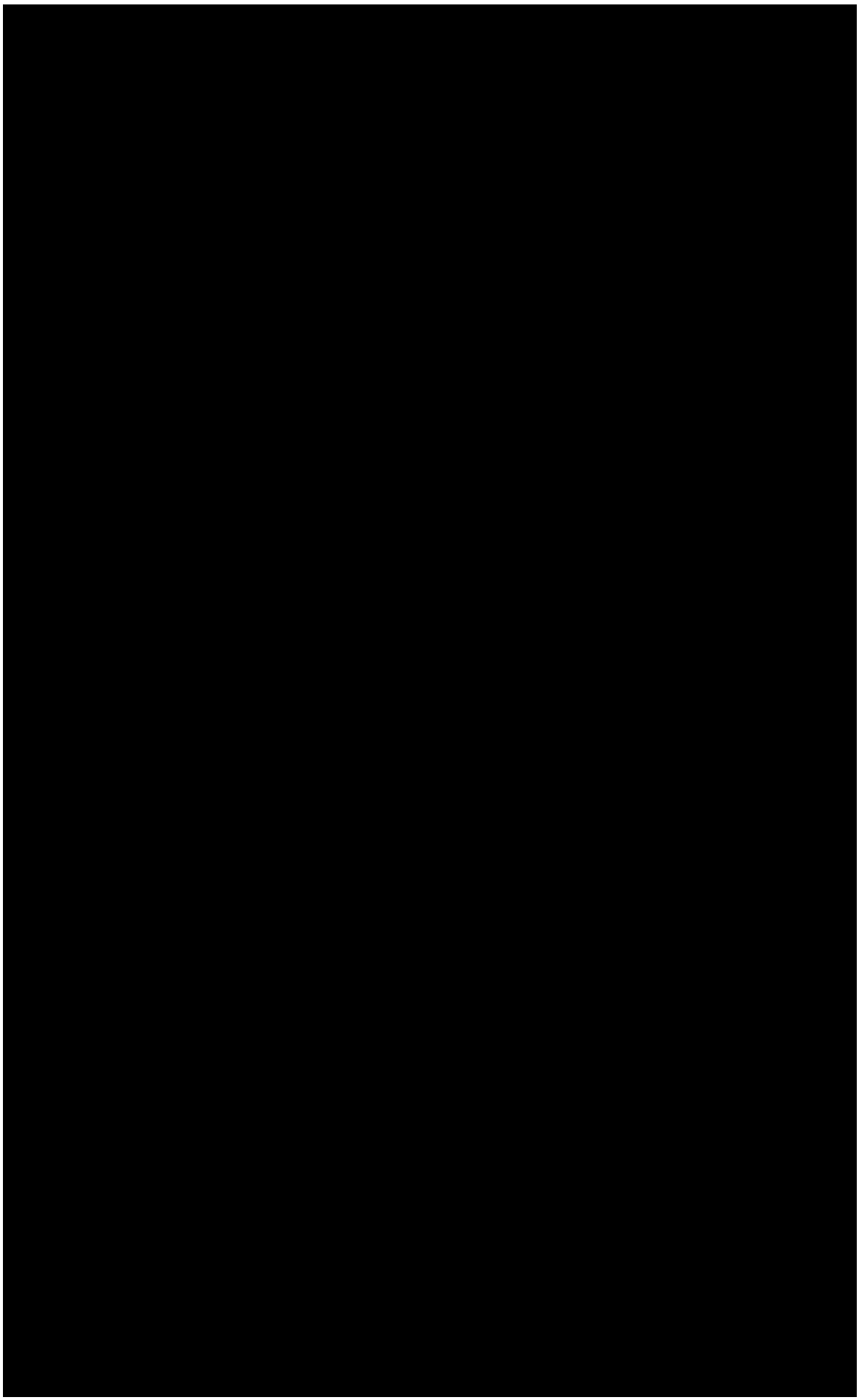
Appendix D. 5.5.3 Symptom management

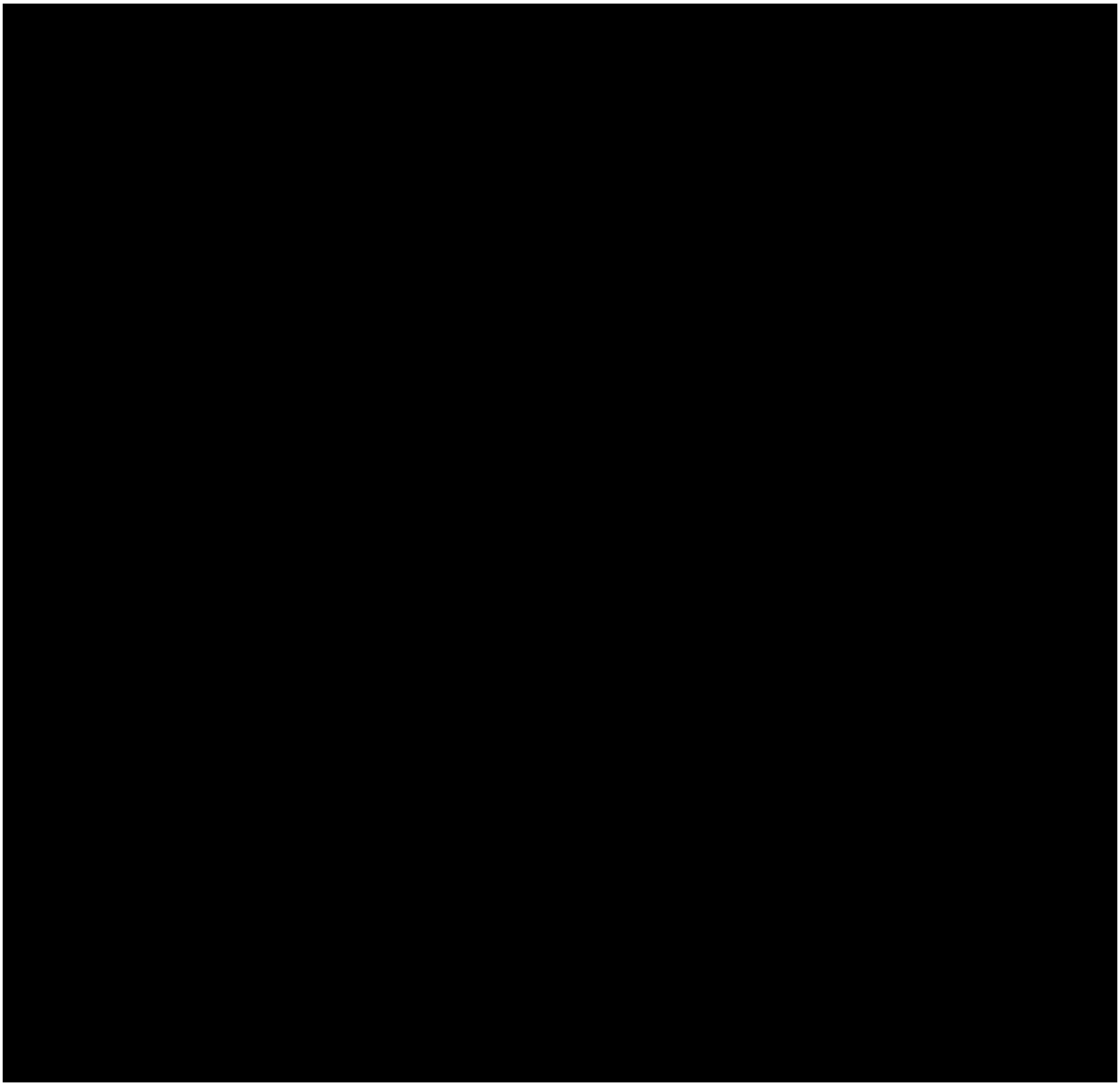


Appendix D. 5.5.3.1 Cardioversion

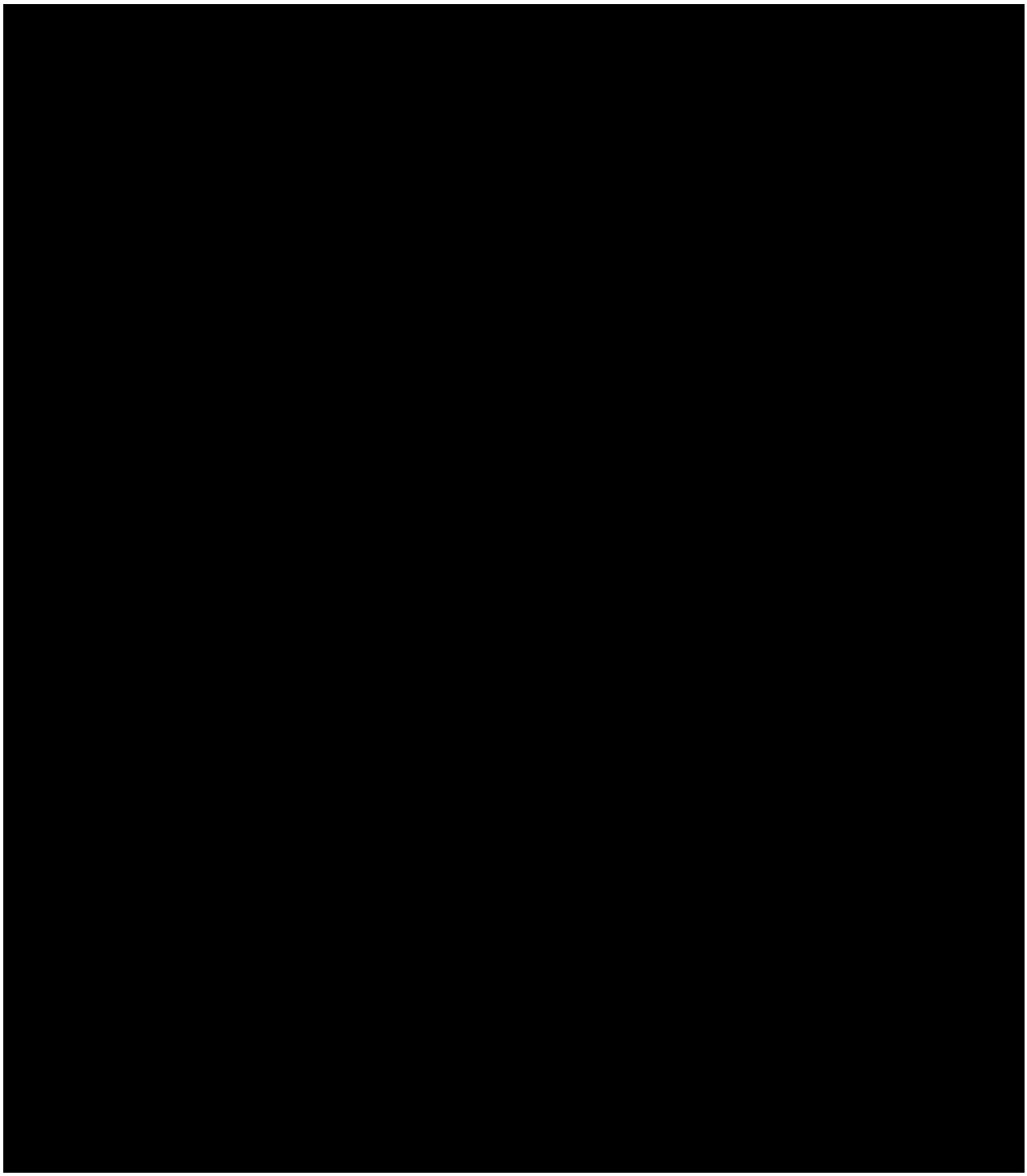
Appendix D. 5.5.3.2 Medications



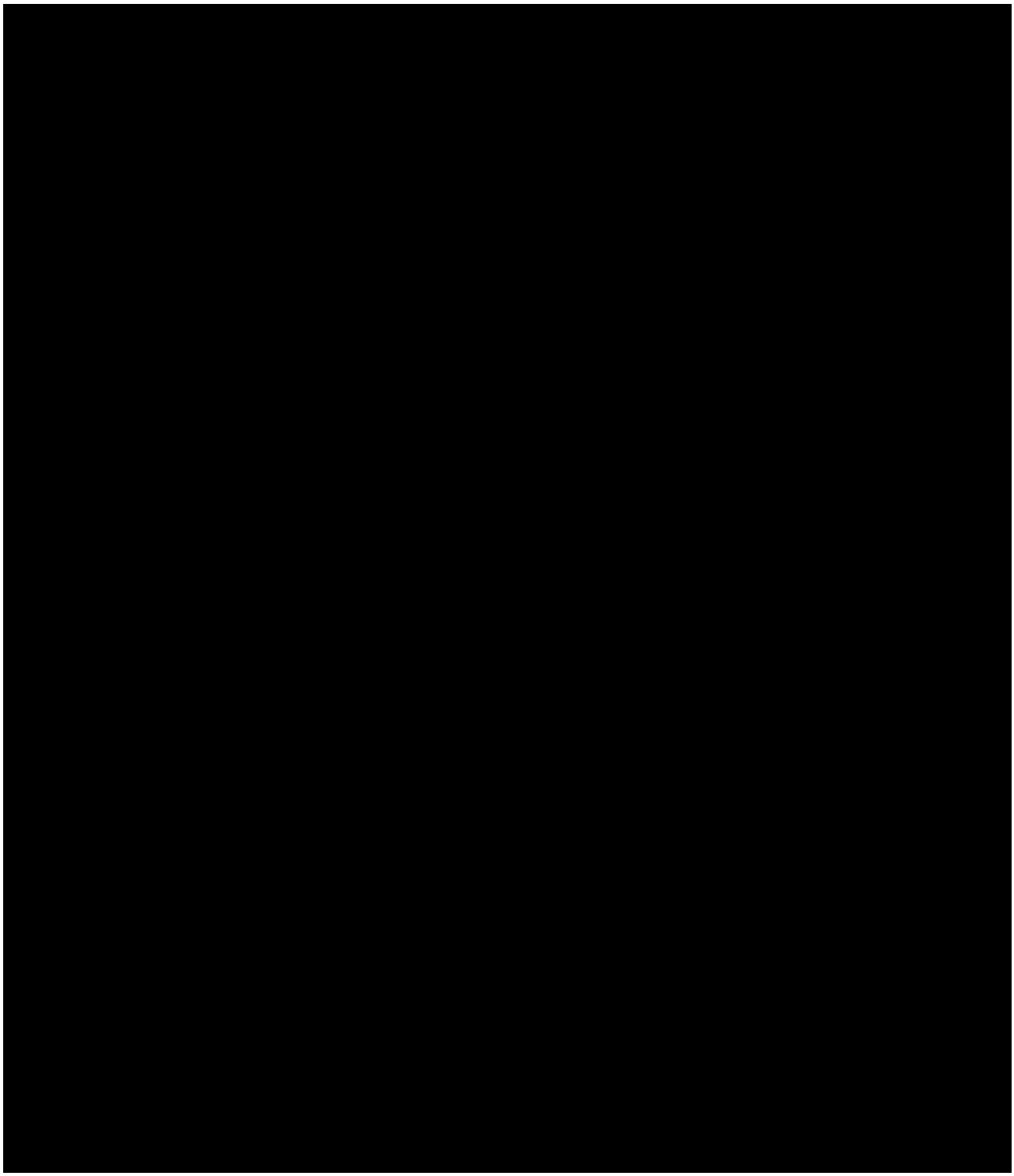
Appendix D. 5.5.3.3 Rate or rhythm control and side effects



Appendix D. 5.5.4 Support including healthcare professionals and online support



Appendix D 5.6 Extract from letter from participant following the focus group



Appendix E Chapter Six

Appendix E 6.1 Expert panel. Feedback form (blank)

AF PROM: Panel Group Meeting: Wednesday 1st July 2015

Domain/Area of Quality of Life: _____

1: How important is this domain of QoL for patients with:

a. Paroxysmal AF? (Please circle response)

Not Important				*Very Important*
1	*2*	*3*	*4*	*5*

b. Persistent AF? (Please circle response)

Not Important				*Very Important*
1	*2*	*3*	*4*	*5*

c. Asymptomatic AF? (Please circle response)

Not Important				*Very Important*
1	*2*	*3*	*4*	*5*

2: How closely do you feel the participant's quotations shown reflect this domain? (Please circle)

Not at all				*Very*
1	*2*	*3*	*4*	*5*

3: How well do you feel the domain name reflects this area of QoL? (Please circle)

Not at all				*Very*
1	*2*	*3*	*4*	*5*

4: How closely does this domain reflect the concerns of the patients that you work with? (Please circle)

Not at all				*Very*
1	*2*	*3*	*4*	*5*

5: In your setting how relevant do you feel this domain is in:

a. Paroxysmal AF? (Please circle response)

Not Important				*Very Important*
1	*2*	*3*	*4*	*5*

b. Persistent AF? (Please circle response)

Not Important				*Very Important*
1	*2*	*3*	*4*	*5*

c. Asymptomatic AF? (Please circle response)

Not Important				*Very Important*
1	*2*	*3*	*4*	*5*

Comments

_____
_____
_____
_____

Initials: ___

Appendix E 6.2 AF PROM: Version 1

AF PROMS: Draft Questionnaire v1.

Your Feelings	Not at all	A bit	Moderately	Quite a bit	Extremely
Feeling anxious or worried about the future					
Feeling anxious or worried about my treatments					
Feeling down or depressed					
Feeling 'I can't cope'					
'Not feeling like myself anymore'					
Not being able to do things I used to (like sports or hobbies)					
Not being able to eat or drink the things I used to (like drinking coffee, alcohol, particular foods)					

2. Over the past 4 weeks to what extent has your ability been affected in relation to:

Your Activities	How much has it affected you?				
	Not at all	A bit	Moderately	Quite a bit	Extremely
Your daily needs (such as washing and dressing)					
Your household chores (such as cooking and cleaning, shopping)					
Your usual leisure activities (gardening, sports)					
Your usual study or work					
Your sleep and rest					
Your day-to-day travel					
Going on longer journeys (like holiday)					
Getting about (at home and inside)					

Social/Relationships

3. **How much would you agree with the following statements,**

'I feel that since diagnosis AF has'

Statements	Not at all	A bit	Moderately	Quite a bit	Extremely
Since diagnosis AF has negatively affected my relationships with friends and family					
Since diagnosis AF has Negatively affected my sexual relationships					
Since diagnosis AF has Negatively affecting my social activities					

Appendix E 6.3.1 Theme 1: Physical: comparison to existing questionnaires

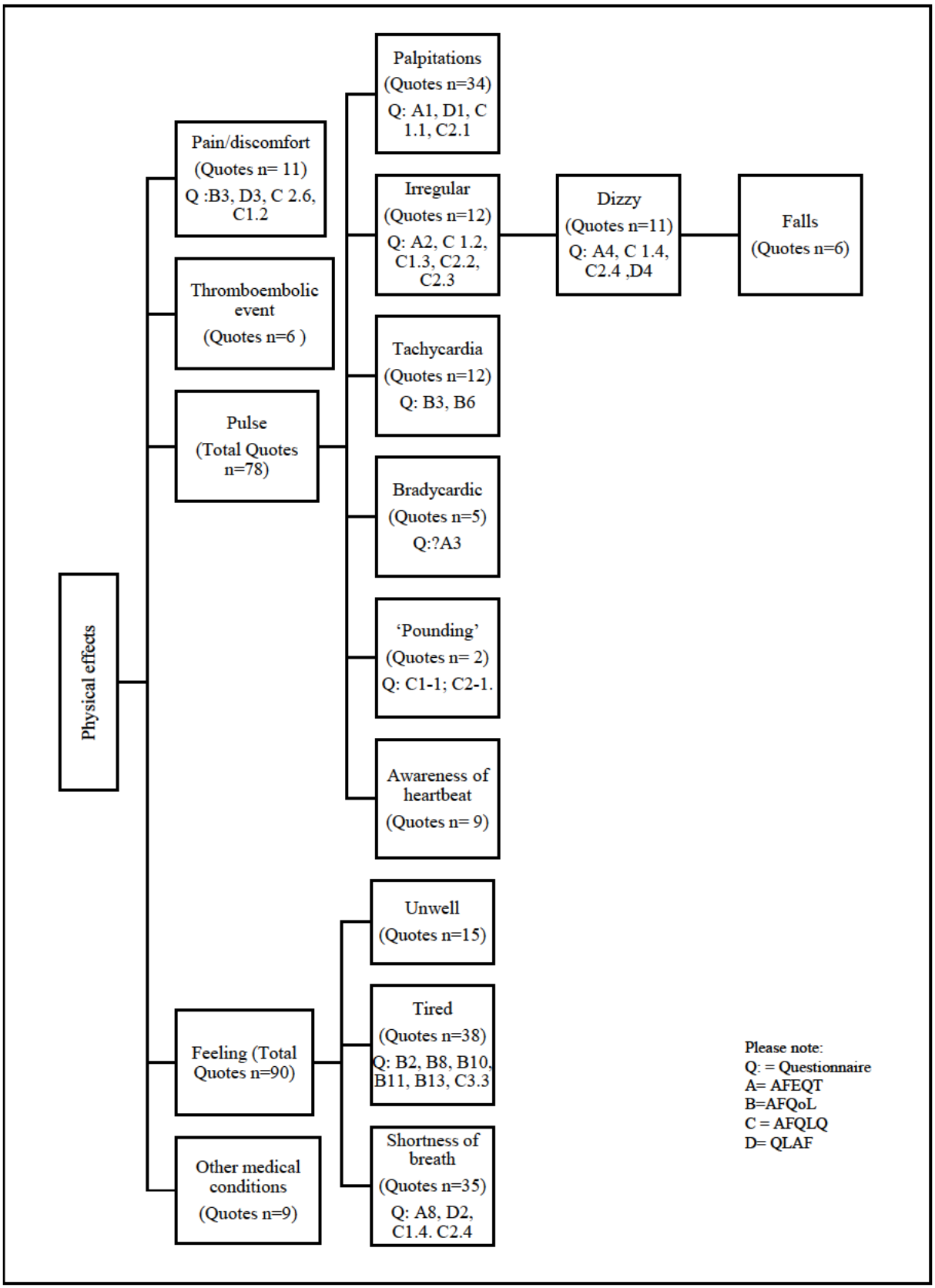


Figure 6.3.1 Overview diagram showing the physical themes and sub themes from the focus groups linked with other AF specific questionnaires.

Appendix E 6.3.2 Theme 2: Your Feelings: comparison to existing questionnaires.

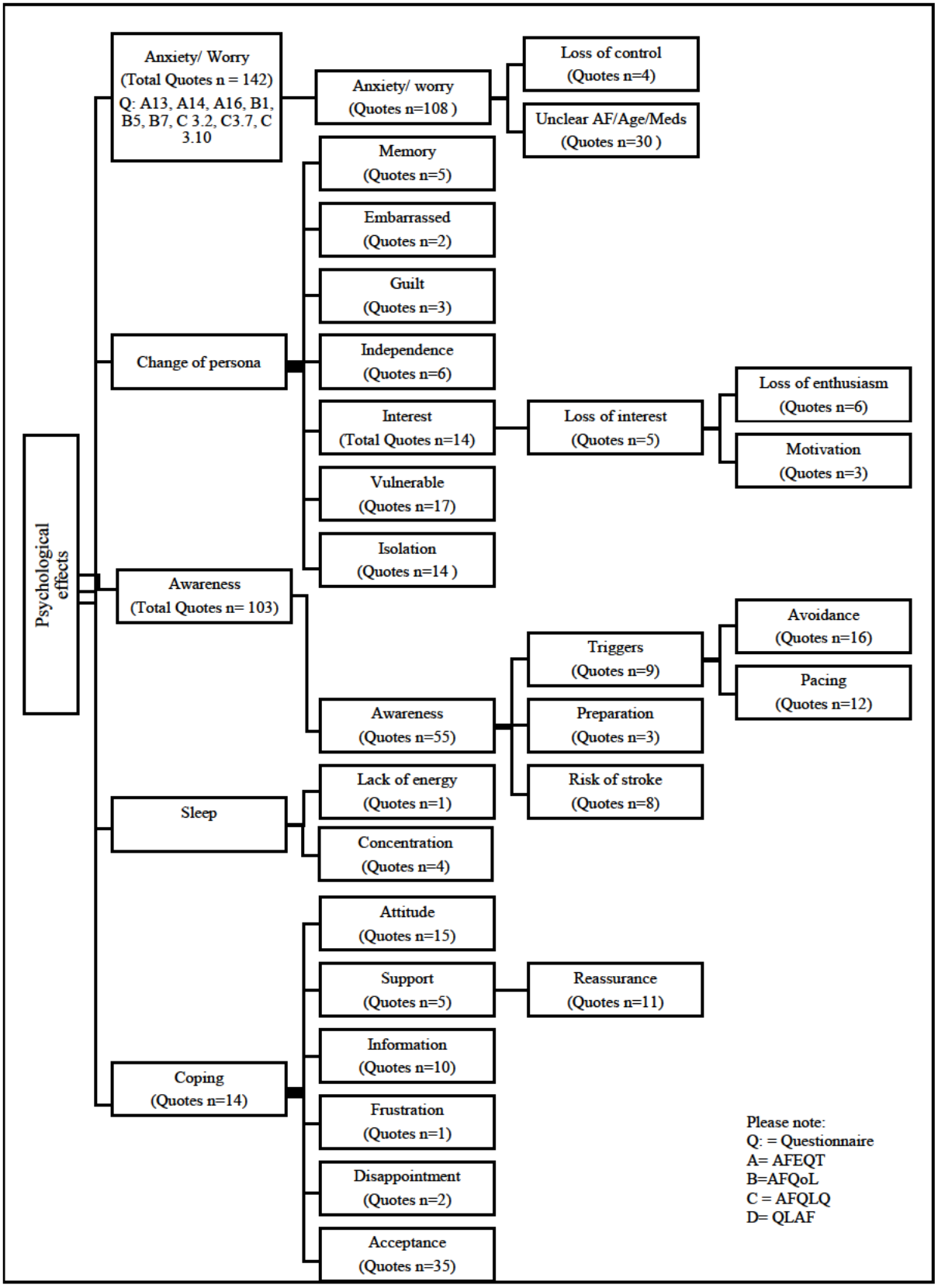


Figure: 6.3.2 Overview diagram showing the 'Your feelings' themes and sub themes from the focus groups inked with other AF specific questionnaires

Appendix E 6.3.3 Theme 3: Your Activities: comparison to existing questionnaires.

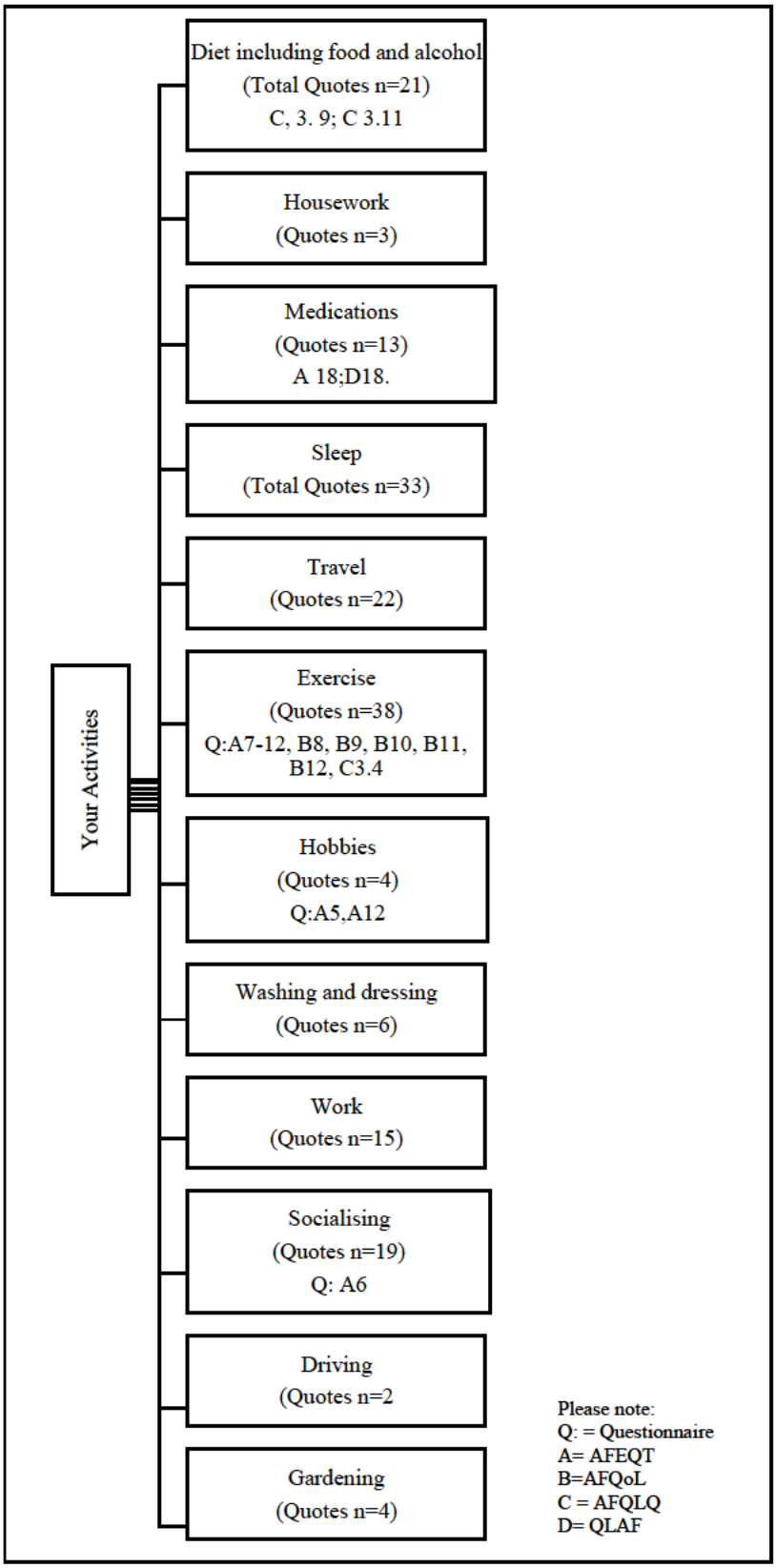


Figure: 6.3.3 Overview diagram showing 'Your Activities' themes and sub themes from the focus groups linked with other AF specific questionnaires

Appendix E 6.3.4 Theme 4: Relationships Comparison to existing questionnaires

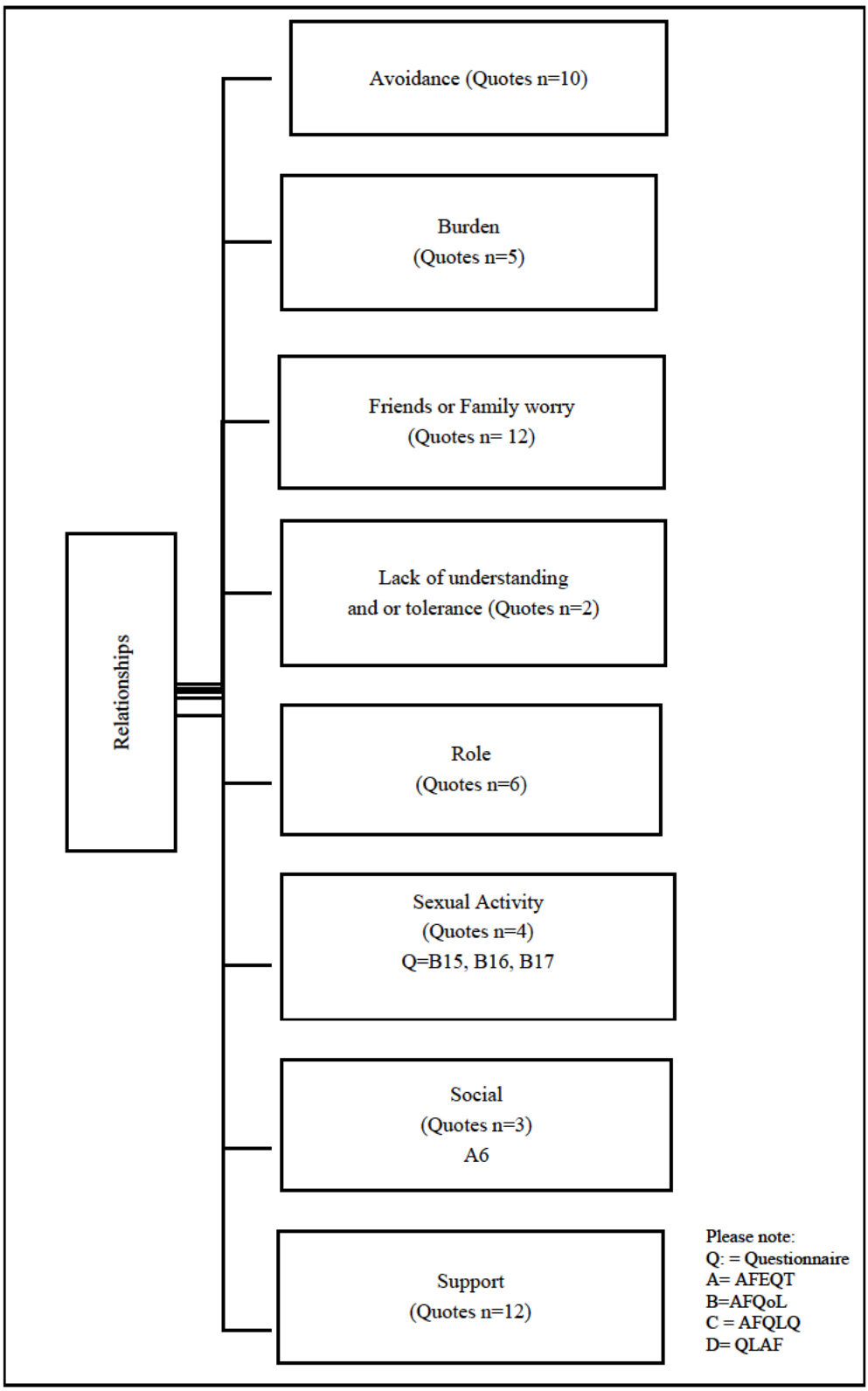


Figure: 6.3.4 Overview diagram showing the Relationship themes and sub themes from the focus groups linked with other AF specific questionnaires

Appendix E 6.3.5 Theme 5: Treatment: comparison to existing questionnaires

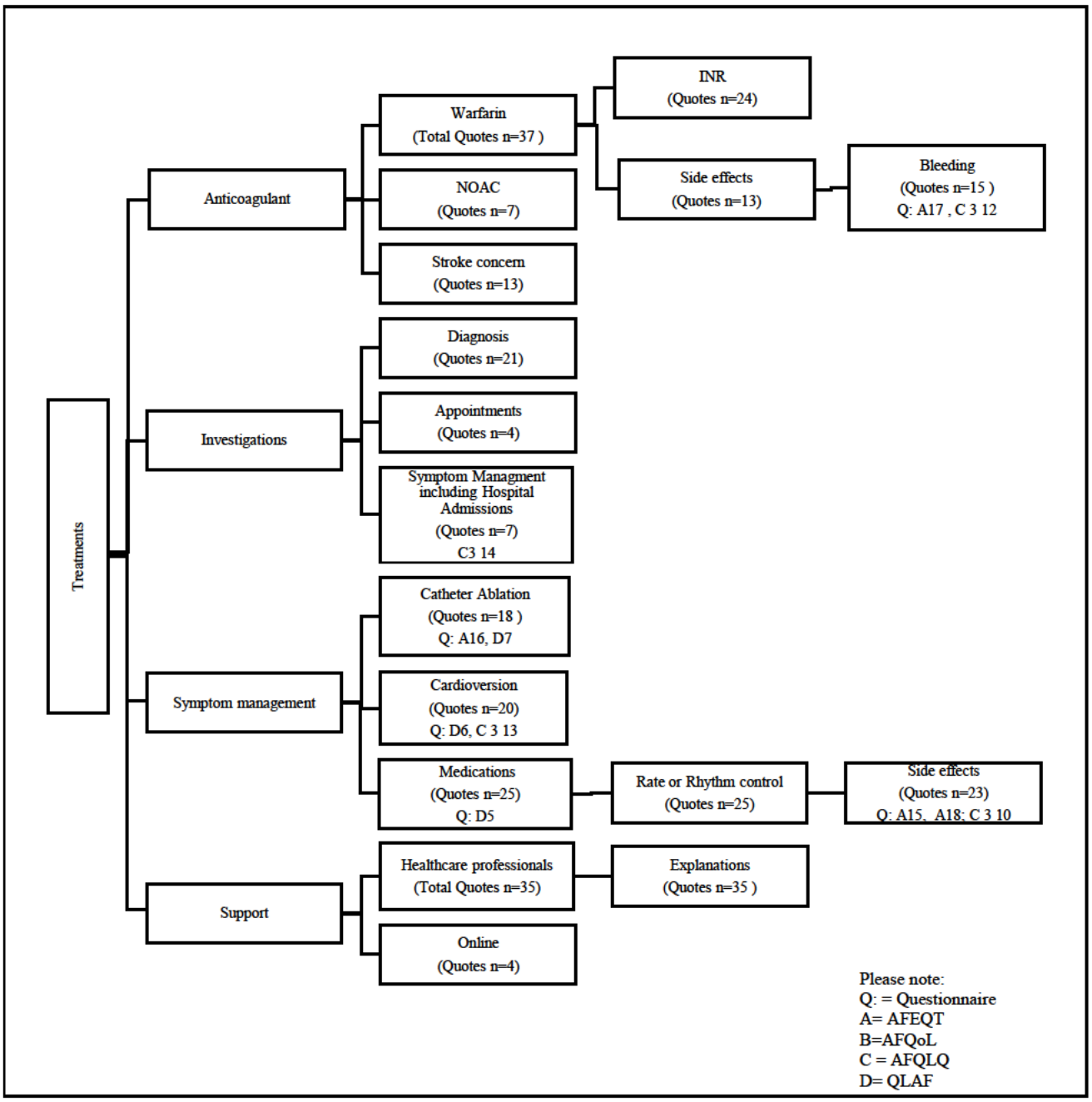


Figure: 6.3.5 Overview diagram showing the Treatment themes and sub themes from the focus groups linked with other AF specific questionnaires.

Appendix E 6.4.1 AF PROM version 8

Atrial Fibrillation Specific Patient Reported Outcome Measure: AF PROMS.

We would like to find out how atrial fibrillation has impacted on the quality of your life. Please answer each question honestly by **ticking the response option** that best describes your experience.

Over the past 4 weeks, how much have you been bothered by the following?

	Not at all	A bit	Moderately	Quite a bit	Extremely
1. Chest Pain					
2. Palpitations (being aware of my heart beating)					
3. My heart rate (fast or slow)					
4. Irregular heart beat (skipping, chaotic or missed beats)					
5. Feeling unwell due to my AF					
6. Feeling tired or fatigued due to my AF					
7. Feeling lightheaded or dizzy					
8. Shortness of breath					
9. Side effects of anticoagulants (blood thinners)					
10. Side effects of my other medications for AF					
11. Feeling anxious or worried about the future					
12. Feeling anxious or worried about my treatments					
13. Feeling down or depressed					
14. Feeling 'I can't cope'					
15. 'Not feeling like myself anymore'					
16. Not being able to do things I used to (such as sports or hobbies)					
17. Not being able to eat or drink the things I used to (such as coffee, alcohol, particular foods)					

Atrial Fibrillation Specific Patient Reported Outcome Measure: AF PROMS.

Over the past 4 weeks, how much have the following activities been affected?

	Not at all	A bit	Moderately	Quite a bit	Extremely
18. Taking care of my personal needs (such as washing and dressing)					
19. Taking care of my household chores (such as cooking and cleaning, shopping)					
20. Doing my usual leisure activities (such as gardening, sports)					
21. Doing my usual study or work					
22. Sleep and rest					
23. Getting about indoors					
24. Day-to-day travel (such as going to the shops)					
25. Going on longer journeys (such as holidays)					
26. My normal social activities					

Over the past 4 weeks, have the following been negatively affected?

	Not at all	A bit	Moderately	Quite a bit	Extremely
27. Relationships with friends and family					
28. Sexual relationships					

Thank you for taking the time to answer this questionnaire.

Appendix E 6.4.2 AF PROM version 9

CITY UNIVERSITY LONDON

Barts Health NHS
NHS Trust

Atrial Fibrillation Specific Patient Reported Outcome Measure:

AF PROMS

We would like to find out how atrial fibrillation has impacted on the quality of your life. Please answer each question honestly by **ticking the response option** that best describes your experience.

Over the past 4 weeks, how much have you been bothered by the following?

	Not at all	A bit	Moderately	Quite a bit	Extremely
1. Chest pain					
2. Palpitations (being aware of my heart beating)					
3. My heart rate (fast or slow)					
4. Irregular heart beat (skipping, chaotic or missed beats)					
5. Feeling unwell due to my AF					
6. Feeling tired or fatigued due to my AF					
7. Feeling lightheaded or dizzy					
8. Shortness of breath					
9. Side effects of anticoagulants (blood thinners)					
10. Side effects of my other medications for AF					
11. Feeling anxious or worried about the future					
12. Feeling anxious or worried about my treatments					
13. Feeling down or depressed					
14. Feeling 'I can't cope'					
15. 'Not feeling like myself anymore'					
16. Not being able to do things I used to (such as sports or hobbies)					
17. Not being able to eat or drink the things I used to (such as coffee, alcohol, particular foods)					

CITY UNIVERSITY LONDON

Barts Health NHS
NHS Trust

Over the past 4 weeks, how much have the following activities been affected?

	Not at all	A bit	Moderately	Quite a bit	Extremely
18. Taking care of my personal needs (such as washing and dressing)					
19. Taking care of my household chores (such as cooking and cleaning, shopping)					
20. Doing my usual leisure activities (such as gardening, sports)					
21. Doing my usual study or work					
22. Sleep and rest					
23. Getting about indoors					
24. Day-to-day travel (such as going to the shops)					
25. Going on longer journeys (such as holidays)					
26. My normal social activities					

Over the past 4 weeks, have the following been negatively affected?

	Not at all	A bit	Moderately	Quite a bit	Extremely
27. Relationships with friends and family					
28. Sexual relationships					

Thank you for taking the time to answer this questionnaire.

Appendix E 6.4.3 AF PROM version 10

CITY UNIVERSITY LONDON

Barts Health NHS
NHS Trust

Atrial Fibrillation Specific Patient Reported Outcome Measure: AF PROMS

Context

This draft questionnaire has been developed following 8 separate focus groups with patients who have atrial fibrillation (AF), relatives of those with AF and healthcare professionals involved in their care.

This questionnaire will be used on patients who have AF in an outpatient setting.

Aim

We are looking for feedback to enhance this questionnaire further.

We would be very grateful if you could rate each question on its usefulness and clarity and provide comments on each of the items. This should take no longer than 15 minutes.

This draft version is for viewing the questionnaire and you will be unable to edit it. Please see the other attachment which will allow you to provide feedback.

Thank you for agreeing to complete this questionnaire.

CITY UNIVERSITY LONDON

Barts Health NHS
NHS Trust

Atrial Fibrillation Specific Patient Reported Outcome Measure:

AF PROMS

We would like to find out how atrial fibrillation has impacted on the quality of your life. Please answer each question honestly by **ticking the response option** that best describes your experience.

Over the past 4 weeks, how much have you been bothered by the following?

	Not at all	A bit	Moderately	Quite a bit	Extremely
1. Chest pain					
2. Palpitations (being aware of my heart beating)					
3. My heart rate (fast or slow)					
4. Irregular heart beat (skipping, chaotic or missed beats)					
5. Feeling unwell due to my AF					
6. Feeling tired or fatigued due to my AF					
7. Feeling lightheaded or dizzy					
8. Shortness of breath					
9. Side effects of anticoagulants (blood thinners)					
10. Side effects of my other medications for AF					
11. Feeling anxious or worried about how my AF will progress in the future					
12. Feeling anxious or worried about my AF treatments					
13. Feeling down or depressed because of my AF					
14. Feeling that 'I can't cope' because of my AF					
15. 'Not feeling like myself anymore'					
16. Not being able to do things I used to (such as sports or hobbies)					
17. Not being able to eat or drink the things I used to (such as coffee, alcohol, particular foods)					

Appendix E 6.4.4 AF PROM version 11

Atrial Fibrillation Specific Patient Reported Outcome Measure: AF PROMS

Context

This draft questionnaire has been developed following 8 separate focus groups with patients who have atrial fibrillation (AF), relatives of those with AF and healthcare professionals involved in their care.

This questionnaire will be used on patients who have AF in an outpatient setting.

Aim

We are looking for feedback to enhance this questionnaire further.

We would be very grateful if you could complete and review this questionnaire. A member of staff will ask whether the questions make sense and what the questions actually mean to you. The interview will be recorded to allow the researcher to go back and review your answers. The research team member will also takes notes during the interview. This should take no longer than 15 minutes.

Thank you for agreeing to complete this questionnaire.

CITY UNIVERSITY LONDON

Barts Health NHS
NHS Trust

Atrial Fibrillation Specific Patient Reported Outcome Measure:

AF PROMS

We would like to find out how atrial fibrillation has impacted on the quality of your life. Please answer each question honestly by **ticking the response option** that best describes your experience.

Over the past 4 weeks, how much have you been bothered by the following?

	Not at all	A bit	Moderately	Quite a bit	Extremely
1. Chest pain					
2. Palpitations (being aware of my heart beating)					
3. My heart rate (fast or slow)					
4. Irregular heart beat (skipping, chaotic or missed beats)					
5. Feeling unwell due to my AF					
6. Feeling tired or fatigued due to my AF					
7. Feeling lightheaded or dizzy					
8. Shortness of breath					
9. Side effects of anticoagulants (blood thinners)					
10. Side effects of my other medications for AF					
11. Feeling anxious or worried about how my AF will progress in the future					
12. Feeling anxious or worried about my AF treatments					
13. Feeling down or depressed because of my AF					
14. Feeling that 'I can't cope' because of my AF					
15. 'Not feeling like myself anymore'					
16. Not being able to do things I used to (such as sports or hobbies)					
17. Not being able to eat or drink the things I used to (such as coffee, alcohol, particular foods)					

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Over the past 4 weeks, how much have the following activities been negatively affected by your AF?

	Not at all	A bit	Moderately	Quite a bit	Extremely
18. Taking care of my personal needs (such as washing and dressing)					
19. Taking care of my household chores (such as cooking and cleaning, shopping)					
20. Doing my usual leisure activities (such as gardening, sports)					
21. Doing my usual study or work					
22. Sleep and rest					
23. Getting about indoors					
24. Day-to-day travel (such as going to the shops)					
25. Going on longer journeys (such as holidays)					
26. My normal social activities					

Over the past 4 weeks, have the following been negatively affected?

	Not at all	A bit	Moderately	Quite a bit	Extremely
27. Relationships with friends and family					
28. Sexual relationships					

Thank you for taking the time to answer this questionnaire.

Appendix E 6.5.1 Expert Panel: Comments version 7

Table showing the expert feedback comments from version 7 of AF PROM (total n=3)

Items in AF PROM version 7	Comments from expert panel: Items in AF PROM version 7
1	**'Perhaps should be month… or indicate chest pain' (3)**
2	**'Strictly palpitations are simply an awareness of the heart beating. Fluttering is often ascribed to ectopics. Many people with AF may describe racing of the heart. I would just put "palpitations (an awareness of your heart beating)"'. (4) 'I wonder if some patients may get confused with questions 2, 3, & 4 as they are similar (especially 2&3). Also do you just want them to comment on symptoms of fluttering or all episodes of palpitations.' (5)**
3	**'Overlap with previous question?' (3)**
4	**'Or heavy heart beat' (3)**
5	**'This could cover anything.' (4)**
6	**'Unexpected tiredness perhaps? I am tired for instance!' (3) 'I would make it fatigue as this has a slightly different connotation.' (4)**
7	
8	**'Not really a common symptom of AF. You can have slow AF, but you can have any rhythm slow.' (4)**
9	
10	
11	**'Blood thinners/ anticoagulants? clear to me but perhaps not to all patients' (3)**
12	**'Does this include INR checks?' (4)**
13	**'Perhaps the stem for this question should be different from that asking if they have been bothered by…?' (3)**
14	
15	
16	
17	**People often say they feel like they have aged quickly with this. ' (4)**
18	
19	**'Sports, hobbies, recreations, enjoyable pursuits' (3)**
20	**'I would use 'such as' rather than like.' (3)**
21	
22	
23	
24	**'Usual work – well now that might be different because of AF. I don't think this is very clear what the meaning of this question. ' (3)**
25	
26	
27	
28	
29	**'Hmm, what might be a normal social activity for me might not be for you, so there is perhaps an assumption in this question' (3) 'Could do with examples. Sports, dancing, boles, probably yes, coffee mornings probably no' (4)**
30	
31	

Appendix E 6.5.2 Expert Panel: Comments version 8

Table showing the expert feedback comments from version 8 of AF PROM (total n=1)

Items AF PROM version 8	Comments from expert panel: Items in AF PROM version 8
1	**'On the left side of my chest only when I had it at night time!'**
2	
3	
4	
5	
6	
7	
8	
9	**'a little headache at the beginning of the treatment (not now)'**
10	**'not anymore'**
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	**'Could ask are you doing as much DIY gardening as before?'**
24	
25	
26	
27	
28	
Comments	**'a very good questionnaire'**

Appendix E 6.5.3 Expert Panel: Comments version 9

Table showing the expert feedback comments from version 9 of AF PROM (total n=2)

Items inv.9	Comments from expert panel: Items in AF PROM version 9
1	'Very Good'(6)
2	The brackets: comments most helpful'(6) 'Are you expecting them to take own pulse' (7)
3	'Its relevant of course but there should be a question 'yes or no' then a section on: - all the time/some of the time/more than once/ etc. '(6) 'could say the 'sensation of, is this the reported feeling of' irregularity or are they expected to palpate own pulse?' (7)
4	'Very good! Again tho (in brackets) is very clear explanation as to what info you want to know'(6)
5	'How can they know what the cause of any fatigue is? Could take out 'due to my AF' (7)
6	'Very good'(6)
7	'Do you not need to know if it's a one off? Or how often?'(6)
8	'I am never sure whether this means I am puffing/ labouring or whether as at times I find myself conscious that need to breath deeper'(6)
9	'Very relevant! I had a bleed when the warfarin went haywire but how does one know other than having a bleed if a side effects are just the AF and not the anticoagulant? (maybe another bracket example please). '(6) ' Only clear if they know what are side effects of their medication' (7)
10	'Again with AF symptoms / anticoagulant possible side effects of medications for AF. How do you know what is making you tired (bracket example). '(6)
11	'Very good! Yes as AF becomes more longer / frequent it can and does make you anxious sometimes. '(6)
12	'Good! I have no worries at moment but there is one medication I do not want to progress to as it has a recorded side effect as maybe causing blindness – that's not a pill I would take. '(6)
13	'Good. '(6)
14	'Good.'(6)
15	'Good!'(6)
16	'Good like the (in brackets explanation) '(6)
17	'V. Good! Yes again (in brackets good) '(6)
18	'Good '(6)
19	'V. Good. '(6)
20	'V Good! Love the in brackets explanations again). '(6)
21	'Good'(6)
22	'Important question but is this generally or only when or because A.F? How often? An odd night or more frequent?'(6)
23	'Is this when in AF? Or overall heath? Not clear.'(6)
24	'As above? When in AF? etc. '(6)
25	'As before. Also is this anticipation of a problem effecting decision on how a long journey needs to be planned or actual problems occurring on holiday taken etc? '(6)
26	'Is this 'have you found problems when' or is it do you anticipate or expect? '(6)
27	'Very good!'(6)
28	'V. Good. '(6)
Comments	'Overall a very good form / feedback questionnaire Love the (in brackets) comments! Really helps!! I know it is difficult because designing a form that suits someone like me who has paroxysmal events and someone who has more frequent or continual AF overall – well done! '(6) 'A couple of comments, but overall good' (7)

Appendix F Chapter Seven

Appendix F 7.1 Questionnaire Battery

Questionnaire Battery included:

- Demographic cover page
- AF PROM
- WHOQOL-BREF
- AFSymp

WHOQOL-BREF:

Reference: World Health Organization, 1996. WHOQOL-BREF: introduction, administration, scoring and generic version of the assessment: field trial version, December 1996. Available online: http://apps.who.int/iris/bitstream/10665/63529/1/WHOQOL-BREF.pdf accessed 01/10/2017

(Please Note: Although licence agreement allows the use of WHO QOL BREF for this study, permission to include a copy of the questionnaire in appendix was not received in time for submission, however a sample is available online)

AFSymp:

Medin, J., Arbuckle, R., Abetz, L., Halling, K., Kulich, K., Edvardsson, N. and Coyne, K.S., 2014. Development and Validation of the AFSymp™: An Atrial Fibrillation-Specific Measure of Patient-Reported Symptoms. *The Patient-Patient-Centered Outcomes Research*, *7*(3), pp.319-327.

(Please Note: Although licence agreement allows the use of AFSymp for this study, permission to include a copy of the questionnaire in appendix was not received in time for submission, however a sample is available online, available at: https://www.astrazeneca.com/content/dam/az/orphan-page-files/Patient%20Reported%20Outcomes/Atrial%20Fibrillation%20Symptoms%20Questionnaire.pdf)

AF PROMS: Demographic Information: Version 1. 14th/October/2015

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AF PROMS: Demographic Information

Please tick the box that applies to you best.

I have Atrial Fibrillation and currently **I am** receiving treatment for this condition ☐

I have Atrial Fibrillation but **I am not** currently receiving treatment for this condition ☐

I am a carer or relative for someone with Atrial Fibrillation ☐

Age: .....

I am:

Please tick one box.

Male ☐ Female ☐

I currently am:

Please tick the box that applies to you best.

Unemployed ☐ Employed ☐

Retired ☐

Ethnic Group:

Please tick the box that applies best.

White ☐
English/Welsh/Scottish/Northern Irish/British
Irish ☐
Gypsy or Irish Traveller ☐
Other White background,
Please describe

.....

Mixed/Multiple ethnic group's ☐

White and Black Caribbean ☐
White and Black African ☐
White and Asian ☐
Other Mixed/Multiple ethnic background,
Please describe

.....

Asian/Asian British ☐

Indian ☐
Pakistani ☐
Bangladeshi ☐
Chinese ☐
Other Asian background,
Please describe

.....

Black/ African/Caribbean/Black British ☐

African ☐
Caribbean ☐
Other Black/African/Caribbean backgrounc
Please describe

.....

Other ethnic group ☐

Arab ☐
Other ethnic group,
Please describe

Barts Heart Centre

POSITIVE ABOUT DISABLED PEOPLE

Barts Health NHS Trust: Mile End Hospital, Newham University Hospital, The Royal London Hospital, St Bartholomew's Hospital and Whipps Cross University Hospital.

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Atrial Fibrillation Specific Patient Reported Outcome Measure: AF PROMS

Context

This draft questionnaire has been developed following 8 separate focus groups with patients who have atrial fibrillation (AF), relatives of those with AF and healthcare professionals involved in their care.

This questionnaire will be used on patients who have AF in an outpatient setting.

Aim

We are looking for feedback to enhance this questionnaire further.

We would be very grateful if you could complete and review this questionnaire. A member of staff will ask whether the questions make sense and what the questions actually mean to you. The interview will be recorded to allow the researcher to go back and review your answers. The research team member will also takes notes during the interview. This should take no longer than 15 minutes.

Thank you for agreeing to complete this questionnaire.

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Atrial Fibrillation Specific Patient Reported Outcome Measure:

AF PROMS

We would like to find out how atrial fibrillation has impacted on the quality of your life. Please answer each question honestly by **ticking the response option** that best describes your experience.

Over the past 4 weeks, how much have you been bothered by the following?

	Not at all	A bit	Moderately	Quite a bit	Extremely
1. Chest pain					
2. Palpitations (being aware of my heart beating)					
3. My heart rate (fast or slow)					
4. Irregular heart beat (skipping, chaotic or missed beats)					
5. Feeling unwell due to my AF					
6. Feeling tired or fatigued due to my AF					
7. Feeling lightheaded or dizzy					
8. Shortness of breath					
9. Side effects of anticoagulants (blood thinners)					
10. Side effects of my other medications for AF					
11. Feeling anxious or worried about how my AF will progress in the future					
12. Feeling anxious or worried about my AF treatments					
13. Feeling down or depressed because of my AF					
14. Feeling that 'I can't cope' because of my AF					
15. 'Not feeling like myself anymore'					
16. Not being able to do things I used to (such as sports or hobbies)					
17. Not being able to eat or drink the things I used to (such as coffee, alcohol, particular foods)					

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Over the past 4 weeks, how much have the following activities been negatively affected by your AF?

	Not at all	A bit	Moderately	Quite a bit	Extremely
18. Taking care of my personal needs (such as washing and dressing)					
19. Taking care of my household chores (such as cooking and cleaning, shopping)					
20. Doing my usual leisure activities (such as gardening, sports)					
21. Doing my usual study or work					
22. Sleep and rest					
23. Getting about indoors					
24. Day-to-day travel (such as going to the shops)					
25. Going on longer journeys (such as holidays)					
26. My normal social activities					

Over the past 4 weeks, have the following been negatively affected?

	Not at all	A bit	Moderately	Quite a bit	Extremely
27. Relationships with friends and family					
28. Sexual relationships					

Thank you for taking the time to answer this questionnaire.

Appendix F 7.2 Correlation matrix (AF PROM) (28items)

Correlation Matrix[a]																														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Correlation	1	1.000																											
	2	.583	1.000																										
	3	.461	.725	1.000																									
	4	.566	.738	.735	1.000																								
	5	.510	.537	.680	.697	1.000																							
	6	.394	.443	.641	.558	.786	1.000																						
	7	.382	.454	.593	.507	.741	.531	1.000																					
	8	.396	.456	.599	.532	.667	.774	.460	1.000																				
	9	.137	.197	.210	.127	.063	.096	.180	.148	1.000																			
	10	.198	.166	.227	.100	.111	.198	.129	.268	.409	1.000																		
	11	.371	.627	.552	.529	.450	.397	.521	.380	.407	.301	1.000																	
	12	.347	.550	.440	.412	.385	.359	.365	.256	.398	.380	.852	1.000																
	13	.592	.409	.489	.488	.498	.416	.442	.333	.361	.403	.650	.585	1.000															
	14	.287	.239	.351	.151	.160	.257	.218	.208	.483	.565	.518	.558	.698	1.000														
	15	.299	.278	.461	.325	.381	.500	.238	.499	.331	.521	.545	.591	.598	.652	1.000													

Appendix F 7.2 Correlation matrix (AF PROM) (28items) continued (1)

	16	.272	.262	.468	.328	.396	.475	.265	.462	.246	.468	.478	.542	.595	.632	.782	1.000												
	17	.562	.515	.411	.445	.348	.302	.351	.321	.364	.378	.610	.609	.668	.492	.535	.437	1.000											
	18	.233	.298	.374	.257	.272	.354	.206	.391	.168	.457	.271	.306	.455	.578	.623	.512	.304	1.000										
	19	.177	.284	.491	.258	.423	.484	.377	.370	.213	.363	.422	.526	.391	.372	.520	.515	.306	.603	1.000									
	20	.296	.320	.583	.378	.544	.569	.359	.488	.150	.420	.471	.518	.542	.466	.656	.809	.379	.480	.665	1.000								
	21	.320	.233	.336	.167	.327	.382	.254	.173	.167	.200	.535	.639	.570	.499	.499	.601	.433	.349	.663	.716	1.000							
	22	.267	.279	.375	.301	.440	.485	.310	.501	.176	.344	.468	.556	.398	.375	.712	.592	.490	.583	.651	.700	.578	1.000						
	23	.527	.382	.472	.423	.518	.524	.325	.559	.098	.171	.305	.246	.412	.263	.493	.379	.440	.509	.542	.462	.370	.484	1.000					
	24	.471	.379	.629	.444	.591	.619	.449	.552	.188	.291	.473	.389	.562	.380	.540	.593	.365	.510	.752	.733	.571	.550	.764	1.000				
	25	.244	.300	.613	.401	.582	.573	.448	.472	.169	.448	.419	.400	.466	.415	.648	.694	.289	.492	.635	.838	.476	.587	.530	.743	1.000			
	26	.333	.338	.534	.420	.596	.589	.402	.490	.115	.425	.439	.475	.541	.468	.726	.768	.253	.639	.700	.815	.577	.706	.473	.730	.835	1.000		
	27	.241	.411	.533	.325	.319	.386	.301	.308	.340	.332	.398	.508	.454	.465	.607	.477	.535	.662	.651	.532	.458	.633	.444	.483	.476	.486	1.000	
	28	.357	.344	.421	.356	.333	.241	.309	.222	.368	.232	.436	.472	.319	.177	.306	.278	.295	.254	.537	.444	.431	.514	.241	.343	.357	.387	.517	1.000

Appendix F 7.2 Correlation matrix (AF PROM) (28items) continued (2)

Sig. (1-tailed)	1																												
	2	.000																											
	3	.000	.000																										
	4	.000	.000	.000																									
	5	.000	.000	.000	.000																								
	6	.001	.000	.000	.000	.000																							
	7	.002	.000	.000	.000	.000	.000																						
	8	.001	.000	.000	.000	.000	.000	.000																					
	9	**.152**	**.070**	**.057**	**.171**	**.318**	**.237**	**.088**	**.134**																				
	10	**.069**	**.106**	.043	**.226**	**.203**	**.068**	**.168**	.021	.001																			
	11	.002	.000	.000	.000	.000	.001	.000	.002	.001	.011																		
	12	.004	.000	.000	.001	.001	.003	.002	.026	.001	.002	.000																	
	13	.000	.001	.000	.000	.000	.001	.000	.005	.003	.001	.000	.000																
	14	.015	.035	.003	**.128**	**.115**	.026	.050	**.059**	.000	.000	.000	.000	.000															
	15	.011	.017	.000	.006	.002	.000	.036	.000	.006	.000	.000	.000	.000	.000														
	16	.019	.024	.000	.006	.001	.000	.022	.000	.031	.000	.000	.000	.000	.000	.000													
	17	.000	.000	.001	.000	.004	.011	.003	.007	.002	.002	.000	.000	.000	.000	.000	.000												

Appendix F 7.2 Correlation matrix (AF PROM) (28items) continued (3)

	18	.039	.011	.002	.026	.020	.003	**.061**	.001	**.103**	.000	.020	.010	.000	.000	.000	.000	.010										
	19	**.092**	.015	.000	.025	.000	.000	.002	.002	**.054**	.003	.000	.000	.001	.002	.000	.000	.010	.000									
	20	.012	.007	.000	.002	.000	.000	.003	.000	**.131**	.001	.000	.000	.000	.000	.000	.000	.002	.000	.000								
	21	.007	.039	.005	**.105**	.006	.002	.027	**.097**	**.105**	**.066**	.000	.000	.000	.000	.000	.000	.000	.004	.000	.000							
	22	.021	.017	.002	.011	.000	.000	.009	.000	**.093**	.004	.000	.000	.001	.002	.000	.000	.000	.000	.000	.000	.000						
	23	.000	.002	.000	.000	.000	.000	.006	.000	**.232**	**.099**	.010	.031	.001	.023	.000	.002	.000	.000	.000	.000	.002	.000					
	24	.000	.002	.000	.000	.000	.000	.000	.000	**.079**	.013	.000	.001	.000	.002	.000	.000	.002	.000	.000	.000	.000	.000	.000				
	25	.032	.011	.000	.001	.000	.000	.000	.000	**.102**	.000	.001	.001	.000	.001	.000	.000	.014	.000	.000	.000	.000	.000	.000	.000			
	26	.005	.005	.000	.001	.000	.000	.001	.000	**.195**	.000	.000	.000	.000	.000	.000	.000	.028	.000	.000	.000	.000	.000	.000	.000	.000		
	27	.034	.001	.000	**.006**	.007	.001	.011	.009	.005	.005	.001	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	
	28	.003	.004	.001	.003	.005	.034	.009	.047	.002	.040	.000	.000	.007	.092	.010	.017	.012	.027	.000	.000	.000	.000	.034	.004	.003	.001	.000

Code: Yellow = not significant
Grey= significant

Appendix F 7.3 AF PROM: PCA 28 item: Five Fixed factor solution

list wise n = 58. (Oblique rotation)

Items (Variables)	Pattern Matrix					Structure Matrix					Communalities
	1	2	3	4	5	1	2	3	4	5	
1	-.205	**.703**	.234	.007	.031	.073	**.709**	.391	-.301	.039	.573
2	-.268	**.776**	.107	-.191	-.081	.039	**.796**	.350	**-.454**	-.083	.738
3	.107	**.725**	.014	-.162	.043	.392	**.827**	.326	**-.484**	.112	.729
4	-.090	**.888**	-.010	-.025	-.038	.180	**.865**	.242	-.338	-.004	.758
5	.305	**.836**	-.181	.021	-.021	**.507**	**.866**	.134	-.322	.086	.846
6	.379	**.666**	-.073	.050	.152	**.582**	**.751**	.204	-.299	.267	.732
7	.158	**.690**	-.083	-.046	-.181	.326	**.721**	.175	-.325	-.109	.569
8	.176	**.686**	.035	.115	.337	**.431**	**.726**	.247	-.227	**.414**	.696
9	-.250	-.020	**.598**	-.222	-.074	-.055	.164	**.621**	-.386	-.101	.476
10	.129	-.095	**.718**	.052	.210	.305	.151	**.707**	-.254	.257	.573
11	.131	**.404**	.388	-.212	**-.444**	.323	**.616**	**.614**	-.564	-.374	.816
12	.185	.167	**.420**	-.378	**-.435**	.365	**.470**	**.658**	**-.667**	-.364	.833
13	.191	.372	**.621**	.060	-.162	**.406**	**.583**	**.748**	-.400	-.078	.748
14	.215	-.056	**.874**	.074	-.014	.387	.241	**.878**	-.335	.059	.811
15	.392	.070	**.570**	-.092	.187	**.621**	**.408**	**.733**	**-.482**	.296	.790
16	**.652**	.061	**.470**	.035	-.001	**.775**	.389	**.635**	-.387	.155	.814
17	-.194	.371	**.586**	-.165	-.081	.099	**.545**	**.715**	**-.493**	-.074	.690
18	.116	.002	.376	-.301	**.569**	**.421**	.301	**.552**	**-.505**	**.613**	.758
19	**.400**	-.011	-.058	**-.692**	.178	**.633**	.375	.333	**-.790**	.271	.825
20	**.719**	.133	.120	-.233	-.007	**.860**	**.480**	**.434**	**-.557**	.160	.863
21	**.561**	-.078	.150	**-.444**	-.305	**.647**	.294	**.439**	**-.644**	-.178	.746
22	.367	.031	.106	**-.539**	.173	**.605**	.395	**.437**	**-.712**	.265	.710
23	.055	**.465**	.029	-.217	**.487**	.374	**.604**	.290	**-.436**	**.531**	.663
24	**.440**	.382	.022	-.232	.226	**.682**	**.627**	.349	**-.530**	.346	.748
25	**.659**	.227	.091	-.115	.144	**.817**	**.510**	.374	**-.447**	.301	.783
26	**.689**	.178	.126	-.164	.139	**.854**	**.500**	**.423**	**-.501**	.302	.855
27	-.046	.043	.230	**-.696**	.295	.300	.386	**.533**	**-.800**	.309	.774
28	-.047	.093	-.117	**-.849**	-.111	.192	.367	.250	**-.820**	-.104	.704

Appendix F 7.4 Justification for the removal of items from domains

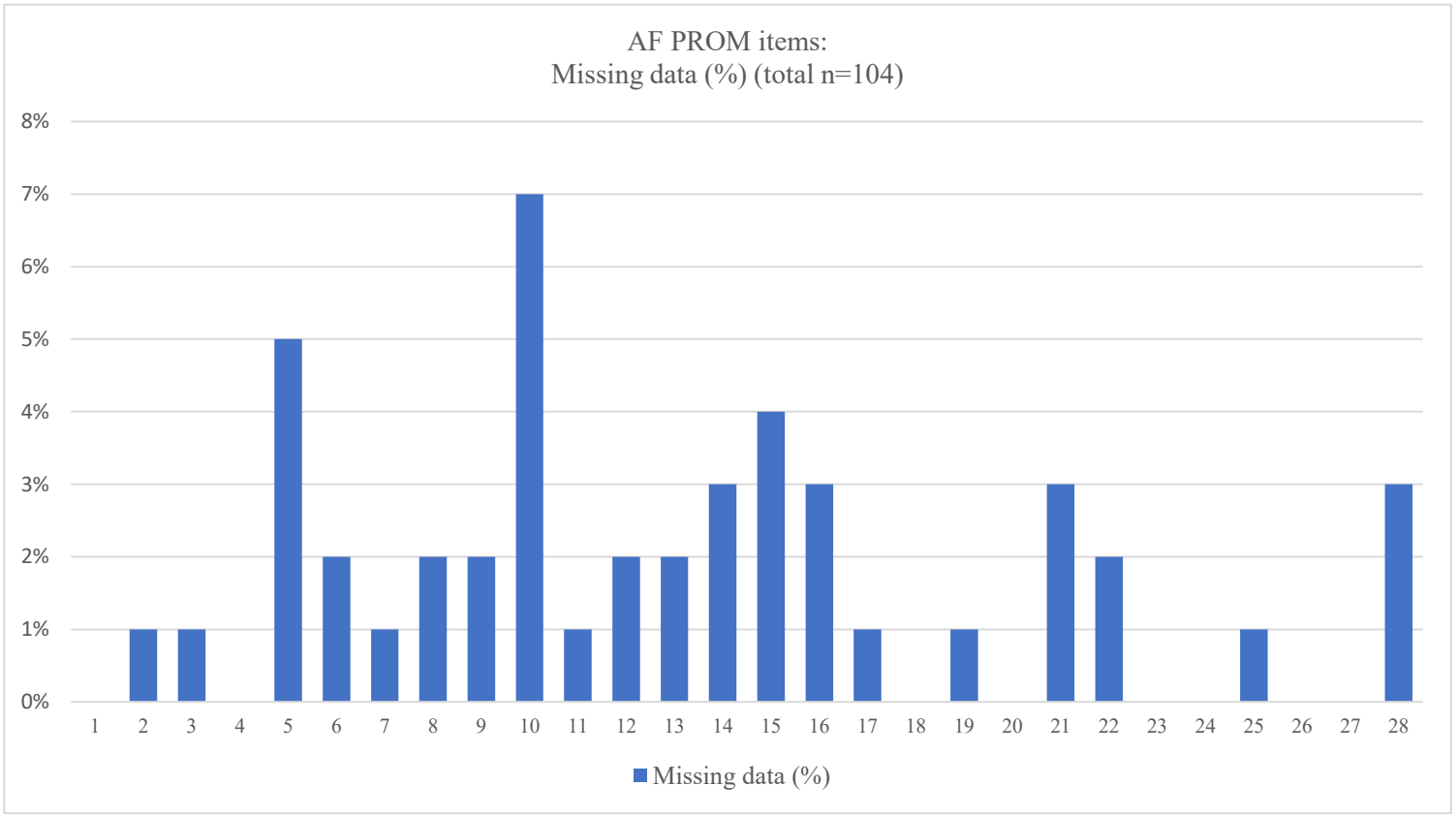
In the five fixed factor PCA analysis item 11 (*Feeling anxious or worried about how my AF will progress in the future*) and item 23 (*Getting about indoors*) both loaded into component two (*'My physical symptoms'*) and component five (*'ability and future concerns'*). The loading of these items in both components may suggest these may be related. A reason for this may be that anxiety or worry about the progress of AF is not only because of fear of symptoms, but also the potential impact on ability. This is supported by one participant in the focus groups (PA005) who described current anxiety about future symptoms of AF as '*still waiting for that next time*' and in addition, expressed the fear of the potential impact of stroke, stating '*I don't want to be suddenly disabled to the point where you're … having family having to look after you.' (PA005).* One possible reasons for item 23 loading into both components may be because the *'physical symptoms'* are restricting or affecting the patient's ability to mobilise *'indoors'* as well as leading to concern about how this may be impacted in the future because of associated risks.

Item 12 (feeling anxious or worried about my AF treatments) loaded into component three (treatment and psychological concerns) and component five (ability and future concerns). This item may have loaded into both as the feelings of anxiety may be related to both domains, treatment and future concerns.

Item 16 (not being able to do things I used to [such as sports or hobbies]) loaded into component one ('my physical ability to carry out activities') and component three (treatment and psychological concerns). Although this loaded stronger to component one and perhaps makes stronger conceptual sense initially to load into component one as sports or hobbies are related to ability to carry out activities. However, when considering the focus group data, it could be suggested that it makes theoretical sense to load into both factors. For example, participants' activities may be affected because of treatments or therapies with associated medications. For example, one participant described how taking anticoagulants caused concern when carrying out activities such as snowboarding (AS020) (Chapter 5).

Appendix F 7.5 AF PROM: Missing data all participants (n=104)

Graph in appendix 7.5 showing the percentage of missing data for each of AF PROM item with all participants (n=104)
NB: x-axis= item numbers of AF PROM



Appendix F 7.6 Pearsons Correlation Matrix

Pearsons Correlation Matrix: AF PROMs, WHO QOL BREF and AFSympt questionnaire																
		AF P1	AFP2	AFP3	AFP4	AFP5	AFPROM (total)	W1	W2	W.3	W4	WQ	AFS1	AFS2	AFS3	AFS (total)
AFP 1	Pearson Correlation	1														
	Sig. (2-tailed)															
AFP 2	Pearson Correlation	.635**	1													
	Sig. (2-tailed)	<.001														
AFP 3	Pearson Correlation	.681**	.560**	1												
	Sig. (2-tailed)	<.001	<.001													
AFP 4	Pearson Correlation	.716**	.478**	.528**	1											
	Sig. (2-tailed)	<.001	<.001	<.001												
AFP 5	Pearson Correlation	.731**	.700**	.810**	.671**	1										
	Sig. (2-tailed)	<.001	<.001	<.001	<.001											
AFP (total)	Pearson Correlation	.894**	.846**	.830**	.749**	.898**	1									
	Sig. (2-tailed)	<.001	<.001	<.001	<.001	<.001										
W1	Pearson Correlation	**.688****	**.665****	**.567****	**.543****	**.555****	.734**	1								
	Sig. (2-tailed)	<.001	<.001	<.001	<.001	<.001	<.001									
W2	Pearson Correlation	.401**	.385**	**.476****	.393**	**.375****	.479**	.701**	1							
	Sig. (2-tailed)	<.001	<.001	<.001	<.001	<.001	<.001	<.001								

Pearsons Correlation Matrix continued (1)

W3	Pearson Correlation	.186	.155	.267**	**.361****	.234*	.259**	.339**	.623**	1						
	Sig. (2-tailed)	.064	.123	.007	.000	.019	.009	.001	<.001							
W4	Pearson Correlation	.364**	.313**	.344**	.393**	.360**	.409**	.606**	.754**	.540**	1					
	Sig. (2-tailed)	<.001	.002	<.001	<.001	<.001	<.001	<.001	<.001	<.001						
WQ	Pearson Correlation	.582**	.531**	.533**	.450**	.497**	**.624****	.800**	.620**	.330**	.609**	1				
	Sig. (2-tailed)	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	.001	<.001					
AFS1	Pearson Correlation	-.528**	-.649**	-.519**	-.375**	-.594**	-.650**	-.467**	-.367**	-.237*	-.346**	-.458**	1			
	Sig. (2-tailed)	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	.017	<.001	<.001				
AFS2	Pearson Correlation	-.666**	-.645**	-.579**	-.550**	-.595**	-.729**	-.705**	-.466**	-.268**	-.422**	-.632**	.742**	1		
	Sig. (2-tailed)	<.001	<.001	<.001	<.001	<.001	<.001	<.001	**<.001**	<.001	<.001	<.001	<.001	<.001		
AFS3	Pearson Correlation	-.365**	-.526**	-.411**	-.296**	-.445**	-.499**	-.317**	-.328**	-.207*	-.349**	-.367**	.717**	.587**	1	
	Sig. (2-tailed)	<.001	<.001	<.001	.003	<.001	<.001	.001	.001	.039	<.001	<.001	<.001	<.001		
AFS (total)	Pearson Correlation	-.634**	-.693**	-.582**	-.489**	-.632**	**-.734****	-.621**	-.443**	-.267**	-.408**	-.576**	.941**	.925**	.701**	1
	Sig. (2-tailed)	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	.007	<.001	<.001	<.001	<.001	<.001	
****. Correlation is significant at the 0.01 level (2-tailed).**																
***. Correlation is significant at the 0.05 level (2-tailed).**																
c. Listwise N=100																

NB: AF PROMS: AFP1 = AF PROMS Component 1: My physical ability to carry out activities; AFP2= AF PROMS Component 2: My physical symptoms; AFP3= AF PROMS Component 3: My Treatment and psychological concerns; AFP4: PROMS Component 4: Impact on my Social Relationships; AFP5: AF PROMS Component 5: Ability and future concerns; AFPROM (total): AFPROMS total scores reversed (higher score indicates better QoL) **WHO QOL BREF:** W1 WHO QoL BREF: Domain 1: Physical; W2: WHO QoL BREF: Domain 2: Psychological; W3: WHO QoL BREF: Domain 3: Social Relationships; W4: WHO QoL BREF: Domain 4: Environment; Self-rating QoL scores as measured by WHO QoL BREF item 1 **AFSymptom Questionnaire**: AFS1: AFSymp: Subscale score of heart symptoms; AFS2AFSymp: Subscale score of tiredness; AFS3AFSymp: Subscale score of chest discomfort; AFS (total)Summary score of AFSymp questionnaire Relationship Strength (as suggested by Evans, 1996): 00-.19 = Very weak (grey); 0.2 -.39= weak (blue); .40- .59 = moderate (orange); .60-.79 = strong (yellow); .80-1.0 = very strong (red)

Appendix F 7.7 AF PROM: Group Validity

Table 1. showing the results of a ANOVA of the mean differences between overall summary scores of groups			
	Mean difference (between groups)	**Std. Error**	**Sig.**
Pair One PAF and Persistent AF	1.0079	4.87807	.997
Pair Two PAF and Asymptomatic	18.7850*	6.85907	**.036**
Pair Three PAF and Healthy control Group	28.3776	4.56231	**.000**
Group Four Persistent and Asymptomatic	19.7929*	7.44615	.045
Group Five Persistent and Healthy control group	29.3855*	5.40491	**.000**
Group Six Asymptomatic and Healthy control group	9.5926	7.24322	.550

Table 2. showing the results of a ANOVA of the mean differences between summary scores of Factor 1.			
	Mean difference (between groups)	**Std. Error**	**Sig.**
Pair One PAF and Persistent AF	1.0158	1.56154	.915
Pair Two PAF and Asymptomatic	5.5700	2.19569	.060
Pair Three PAF and Healthy control Group	6.4219*	1.46046	**.000**
Group Four Persistent and Asymptomatic	6.5859*	2.38362	.034
Group Five Persistent and Healthy control group	7.4377*	1.73019	**.000**
Group Six Asymptomatic and Healthy control group	.8519	2.31866	.983

Table 3. showing the results of a ANOVA of the mean differences between summary scores of Factor 2.			
	Mean difference (between groups)	**Std. Error**	**Sig.**
Pair One PAF and Persistent AF	.7312	1.65178	.971
Pair Two PAF and Asymptomatic	4.9686	2.32257	.148
Pair Three PAF and Healthy control Group	10.7834*	1.54485	**.000**
Group Four Persistent and Asymptomatic	4.2374	2.52136	.339
Group Five Persistent and Healthy control group	10.0522*	1.83017	**.000**
Group Six Asymptomatic and Healthy control group	5.8148	2.45265	.089

Table 4. showing the results of a ANOVA of the mean differences between summary scores of Factor 3.			
	Mean difference (between groups)	**Std. Error**	**Sig.**
Pair One PAF and Persistent AF	.5566	1.20188	.967
Pair Two PAF and Asymptomatic	2.9333	1.68698	.309
Pair Three PAF and Healthy control Group	5.0444*	1.12465	**.000**
Group Four Persistent and Asymptomatic	3.4899	1.82806	.231
Group Five Persistent and Healthy control group	5.6010*	1.32692	**.000**
Group Six Asymptomatic and Healthy control group	2.1111	1.77824	.636

Table 5. showing the results of a ANOVA of the mean differences between summary scores of Factor 4.			
	Mean difference (between groups)	**Std. Error**	**Sig.**
Pair One PAF and Persistent AF	.0593	.81878	1.000
Pair Two PAF and Asymptomatic	2.4155	1.15129	.161
Pair Three PAF and Healthy control Group	2.3043*	.76578	.017
Group Four Persistent and Asymptomatic	2.4747	1.24983	.202
Group Five Persistent and Healthy control group	2.3636	.90721	.051
Group Six Asymptomatic and Healthy control group	.1111	1.21577	1.000

Table 6. showing the results of a ANOVA of the mean differences between summary scores of Factor 5.			
	Mean difference (between groups)	**Std. Error**	**Sig.**
Pair One PAF and Persistent AF	.5099	.73335	.899
Pair Two PAF and Asymptomatic	2.4952	1.03116	.080
Pair Three PAF and Healthy control Group	3.4211	.68588	**.000**
Group Four Persistent and Asymptomatic	3.0051*	1.11942	**.042**
Group Five Persistent and Healthy control group	3.9310*	.81255	**.000**
Group Six Asymptomatic and Healthy control group	.9259	1.08892	.830

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