A study of the impact of substituting Warfarin with Direct Oral Anticoagulants (DOAC), in Atrial Fibrillation (AF) patients over 65 years old: The Patients' and Clinicians' Perspectives.

Richards, P.

UNIVERSITY OF WESTMINSTER

A study of the impact of substituting Warfarin with Direct Oral Anticoagulants (DOAC), in Atrial *Fibrillation (AF) patients over 65 years old: The Patients' and Clinicians' Perspectives.*

Patricia Richards BSc. MSc.

UNIVERSITY OF WESTMINSTER

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Abstract

The need for this research was identified during the researcher's daily practice in her Haematology clinic in London. The clinic specialises in anticoagulated patients, particularly those with the condition of Atrial Fibrillation. The researcher noted that while extensive research had been undertaken into the medical issues associated with the established oral anticoagulant Warfarin, the newer medication referred to as Direct Oral Anticoagulants (DOACs) was less broadly studied. Importantly, little was known about how patients coped on a daily basis with this new treatment. Furthermore, the practical and social impact of a switch from Warfarin to a DOAC for clinical reasons had rarely been studied from the patient's perspective.

An inductive, mixed-method research study was set up comprising two questionnaires and individual interviews. A sample of 56 patients, aged 65ys and over, grouped by age and sex, were selected from the clinic. The first questionnaire was a Perceived Stress Scale (PSS), which explored the participants' levels of stress at three time points: the switch over, then at 30 and 90 days. Concurrently a Medical Outcome Study (SF-36), a health survey was administered. Twenty of these patients were also interviewed by the researcher on two occasions, at the switch over then at 90 days. Thematic analysis was undertaken on the transcripts to identify themes across the patients' responses.

The findings showed that the switch to a DOAC had a positive impact on most of the respondents. They felt liberated from several of the constraints of taking Warfarin, for example, of not needing regular clinical monitoring so being able to travel further and more often, and eating a wider, healthier diet. The patients also reported feeling less stressed in general at the 30 day point, this was sustained over the remainder of the study period. There were some small differences between the ages, the older patients reported fewer benefits from the switch, although remaining positive about the experience. No significant difference was noted between the sexes. Patients highlighted the importance of personal resilience throughout, but that good GP support was also crucial in their continued wellbeing.

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Author's Declaration

I declare that all the information contained in this thesis is my own work.

Definitions

Anticoagulant – A drug or medicine that has the ability to help stop the blood from clotting (blood thinner).

Atrial fibrillation – An abnormal heart rhythm which presents as irregular and rapid heartbeats.

Bias – A prejudice shown from one person or group against another, especially in a way which may be considered unfair. In the context of this study, bias may be the author's own perspective that may be inadvertently introduced in the type of questions being asked, or the interpretation of answers given.

Bioavailability – The degree and rate at which an administered drug is absorbed by the body's circulatory system, the systemic circulation. Bioavailability is an essential measurement tool since it determines the correct dosage of drugs which are not administered via injections such e.g. oral therapy drugs such as Warfarin and direct oral anticoagulants.

Bridging – Therapy using short-acting anticoagulants such as Heparin or Low Molecular Weight Heparin (LMWH) for a period of time for patients whose Warfarin therapy is out of its prescribed therapeutic range and must be interrupted e.g. during surgery.

$CHADS_2$ score – Is a score acronym for **C**ongestive heart failure, **H**ypertension, **A**ge (≥ 65 = 1 point, ≥ 75 = 2 points), **D**iabetes, and **S**troke/TIA (2 points). Patients with high $CHADS_2$ scores (>2) are at significant risk for stroke.

CHA_2DS_2-VASc Score – This is an updated version (calculation) of the $CHADS_2$ score. It is a score acronym for **C**ongestive heart failure, **H**ypertension, **A**ge (≥ 65 = 1 point, ≥ 75 = 2 points), **D**iabetes, and **S**troke/TIA (2 points). **VASc** stands for **V**ascular disease (peripheral arterial disease, previous MI, aortic atheroma) and **S**ex **c**ategory. The female gender **is** also included in this **scoring** system.

Coagulation Pathway – The process by which blood changes from a liquid to a gel (clot), happens via several mechanisms or pathways.

Concomitant – Describes when several relevant factors exist concurrently e.g. taking multiple medications or having multiple medical conditions at the same time.

Direct oral anticoagulants – Anticoagulant medications which acts by directly targeting specific parts of the coagulation pathway.

Dyspepsia – Also known as indigestion, and the discomfort or pain felt in the upper abdomen.

European Society for Cardiology (ESC) – The (ESC) is an independent, non-profit organisation which aims to reduce the burden of cardiovascular disease by organising cardiac related discussion and generating medical guidelines on the treatment and prevention of heart diseases.

Heart rate – Also known as the pulse, which is the number of times a person's heart beats per minute. Normal heart rate varies from person to person, but a normal range for adults is 60 to 100 beats per minute.

Heparin – A fast acting anticoagulant (blood thinner) that prevents the formation of blood clots**.** Heparin is given to the patient as an injection and is therefore usually given in a hospital setting (e.g. during surgery).

International Sensitivity Index (ISI) – An internationally standardized number that is calculated and assigned to each batch of Warfarin testing reagent which is made from tissue factor.

International Normalised Ratio – INR –, The unit of measure for patients who are on Warfarin and is calculated using the ISI. For normal patients who are not on anticoagulation, the **INR** is usually 1.0 regardless of the **ISI** or the particular performing laboratory. Patients who are on anticoagulant therapy, the expected therapeutic **INR** range is between 2.0 to 3.0.

Intracranial haemorrhages (ICH) – A type of bleeding that occurs inside the skull (cranium). Bleeding around or within the brain itself is known as a cerebral haemorrhage (or intracerebral haemorrhage).

Metabolism – The process in which food is processed by the body and converted to energy. It is also the process used to describe the conversion of medicinal drugs into substances which can be more easily removed from the body.

Pharmacokinetics – The process by which the body processes the passage or movement of drugs through the body, including the time course of its absorption, bioavailability, distribution, metabolism, and excretion.

Pharmacology – The branch of biology concerned with the study of drug or medication action, where a drug can be broadly defined as any man-made, natural, or endogenous (from within the body) molecule which exerts a biochemical or physiological effect on the cell, tissue, organ, or organism.

Prothrombin – A clotting factor or protein which is integral to the clotting of blood.

Prothrombin time (PT) – A blood test that measures the time it takes for the liquid portion (plasma) of your blood to clot, the ISI calculation is then applied to covert to the INR which is a unit of measure of patients on Warfarin.

Rhythm control – Patients with Atrial Fibrillation require medical interventions to help return the heart to a normal rate. Rhythm control medications is one method of treatment to restore a normal heart rate and in order to reduce the risk of a stroke.

Stroke – A serious life-threatening medical condition that happens when the blood supply to part of the brain is cut off.

Vitamin K – A group of fat-soluble vitamins that, among other properties, plays a key role in the clotting of blood and so prevents excessive bleeding. The body needs vitamin K to produce prothrombin, a protein and clotting factor that is important in blood clotting and bone metabolism.

Chapter 1 - Introduction

1.0 Background

This chapter provides an introduction to the topic of Atrial Fibrillation (AF) in UK patients over 65 years, the current treatments for AF, and recent changes in treatment. Finally, it outlines the structure of the thesis. The researcher first became interested in knowing more about AF patients' broader perceptions of their treatment when at the Haematology clinic in west London where she was working. While extensive clinical research had been undertaken into the medical issues associated with these patients' treatments, little was known about their responses to the condition or treatment provided. Anecdotal evidence indicated that, while patients varied in their response to their long-term condition, some patterns emerged relating to individual coping styles with medication management and also with the personal and social impact of living with long term anti-coagulant medication. The researcher was not alone in her curiosity. The doctor, nurses, and pharmacists in the team were also keen to better understand their patients' perspectives of the treatment they were delivering, and whether their service could be improved. Given the lack of research in this area, it was clear to the researcher that a study was required which involved the patients directly so that their story could be heard. The researcher was working face to face with patients in clinic so would have no difficulty identifying and accessing a sample of participants. She did not have a research role at the hospital, therefore, in order to provide a sound academic basis for the study she applied for the University of Westminster's Professional Doctorate programme.

Since the government's call for more public and personal involvement (PPI) in all aspects of health care in the early 2000s, much work has been done to include patients in decision making. However, this has generally taken the form of patients joining committees for local health care planning and becoming lay members on hospital boards where: 'they can do little to challenge the prevailing clinical culture that affects the everyday experience of patients' (Binstock *et al*., 2011). Binstock goes on to say: 'People can contribute to their own health by, among other things, contributing to the understanding of coping with the effects of chronic illness and managing care'. Richards *et al*., (2015) also highlighted this problem, pointing to the rising number of people living with long term conditions of multimorbidity and frailty,

requiring services to be radically redesigned. Any revised service, they claim, must be: 'based on a better understanding of what people need from health and social service' (Wittenberg *et al*., 2019).

1.1 The Situation in the UK.

People in the UK are living longer. In 2010 there were 10 million people over the age of 65 years, with that number expected to rise to 19 million by 2050 (Davis *et al*., 2012). The growing number of patients using the NHS anti-coagulant services is having a huge impact on hospitals and General Practitioner (GP) surgeries, with state benefits and NHS treatments combined accounting for almost 50% of the total government expenditure in 2009/10 (Cracknell, 2010). Approximately 1.6% of the population suffers from Atrial Fibrillation (AF) (Scowcroft and Cowie, 2014). AF has an estimated prevalence in the United Kingdom of 15% of all patients over 75ys and is the most preventable cause of stroke. AF is the most common reason for taking Warfarin an anti-coagulant which was approved for use in 1954 (Pink *et al*., 2011). It is estimated that in the first year of a stroke, the cost of an AF patient to the NHS is £11,900 (Bauer, 2013; Folkerts *et al*., 2019).

Atrial Fibrillation requires lifelong treatment with oral anticoagulation therapy with many patients requiring surgical intervention for heart rate or rhythm control: pacemakers or mechanical heart valves, (OAT) (Worrall *et al*., 2018). Managing a patient on OAT is often multi-faceted as other medical conditions, such as diabetes mellitus, heart failure and hypertension are commonly present (Dagan *et al*., 2018, p1534). Concomitant drugs, age, mental capacity, diet and lifestyle also need to be taken into consideration (Patel *et al*., 2019, p912). Ongoing support, education and monitoring of OAT is usually conducted in a clinic setting, with the involvement of medical professionals such as anticoagulation nurses, doctors and medical scientists.

Usually when a patient is first prescribed Warfarin, a baseline measurement of the patient's Prothrombin Time (PT) and Internationalized Normalized Ratio (INR) is taken. The induction dose of 10mg daily for the first 2 days is then administered with

regular monitoring of the patient's Prothrombin Time (PT) and Internationalized Normalized Ratio (INR) conducted.

Primarily, these clinics focus on educating the patient in identifying and monitoring indicators of their disease. They provide information on how food, especially those rich in vitamin K such as green leafy vegetables, drugs (both prescribed and recreational) and lifestyle choices, such as excessive alcohol consumption, can affect Warfarin's very narrow therapeutic and prophylactic range (Kayyali *et al*., 2019, p425). Also, of major concern to clinicians is non-compliance which may increase or decrease the patient's INR. Very poorly managed INR patients may be seen as often as weekly in a hospital out-patient clinic setting. An effective clinic for testing the patient's INR usually requires laboratory staff, coagulation testing equipment with reagents and a specialist nurse. A specialist medical professional such as a consultant must also be on hand to make dosage amendments, to order further testing, reversal of Warfarin, or in some cases make hospital admissions. Figures released by the Department of Health in 2013 revealed that poor management of anticoagulation in AF patients has resulted in 7,000 preventable strokes and the preventable loss of 2,100 lives each year in England alone (Constitution, 2013). Therefore, finding an alternative to Warfarin which is easier to manage was deemed a priority. This was achieved in 2010 when three novel anticoagulants where approved for use. These anticoagulants are referred to collectively as Direct Oral Anticoagulants (DOACs) previously called Novel Oral Anticoagulants (NOACs) (Connolly and Spyropoulos, 2013).

1.2 Oral Alternatives to Warfarin

There are now 4 main Warfarin substitutes (DOACs) available on the market (Apixaban, Dabigatran, Endoxaban and Rivaroxaban). DOACs have a short half-life, a rapid onset of 2.5 to 4 hours (as opposed to Warfarin which requires 4 to 7 days for an optimal effect), have minimal drug and food interactions, and do not require bridging. Bridging is the use of short-term, interim anticoagulants such as heparin when an oral anticoagulant has to be stopped, for example in pre-surgical procedures. Bridging is commonly used as a Warfarin replacement during medical and surgical procedures, as even temporarily stopping Warfarin may result in the formation of blood clots which can lead to strokes. Dabigatran and other DOACs

have a predictable anti-coagulant effect and are pharmacokinetically stable, in contrast to Warfarin (Baglin *et al*., 2006; Chen *et al*., 2019).

1.3 The Structure of this Thesis

This study sought to ascertain the quality of life changes in patients with AF and over 65 years of age who had been asked to switch from Warfarin to DOACs. It comprises eight chapters including this introductory chapter.

Chapter 2 focuses on the current scientific research and highlights issues relating to Warfarin, direct oral anticoagulants and the rationale and decision making pathway for choosing one method of anticoagulant over the other. It also looks briefly at the role of patient responsibility and treatment.

Chapter 3 discusses the qualitative research approach employed, the sample size its composition and the data collection methods used. It justifies the data analysis methods and explains how the data was collected. Also explained are the scale instruments used to determine the patients' current health and perceived stress self-assessment.

Chapter 4 sets out the information governance and ethical approval process undertaken in order to fulfil the permissions and indemnity insurance requirements at the University of Westminster as well as the site of study – St Mary's Hospital, Paddington. Also included are the legal requirements for the storage and transportation of patient information.

Chapter 5 – Findings One – reports the qualitative findings of the first interviews with twenty patients at the time of the switch from Warfarin to a new anticoagulant. It explores their perceptions of their own health and stress levels before they switched, and their understanding of the need to change medication. Several themes emerged from the data that informed the subsequent data analysis.

Chapter 6 – Findings Two – reports on the material which emerged from the second interview with the same patients undertaken at 90 days after the switch of their medication regime. The original themes are elaborated on and findings clarified. The findings from the staff interviews are also described here.

Chapter 7 – Findings Three – reports on the findings emerging for the scale data administered to 56 patients at three points: at the time of the switch-over, and then at 30 and at 90 days afterwards. These findings support the themes emerging from the interviews.

Chapter 8 is the discussion and conclusions chapter which concludes the thesis with a summary of the findings as well as recommendation for the improvement of services for the elderly population. This includes, but is not limited to, patients who have Atrial Fibrillation.

Chapter 9 offers a self-reflection of the author's journey through this professional doctorate and summarises her personal learning.

Chapter 2 - Literature Review

2.0 Literature Review Introduction

During the 1920's, farmers in the town of Wisconsin noticed that local cows were sometimes bleeding to death, often due to minor or unexplained injuries. An investigation followed, and it was determined that the haemorrhaging was caused by the cows eating mouldy sweet clover plants (Attaya *et al*., 2012). Later in 1948, scientists showed that the haemorrhagic property of the plant was coumarin. This compound was then extracted, synthesised, and sold as rodenticide until 1954, when it was marketed for human use as the oral anticoagulant Warfarin (Pirmohamed, 2006). Warfarin quickly become the most commonly used oral anticoagulant and stroke prevention medication in the world (Scully, 2002). Warfarin remained the primary prescribed stroke prophylaxis for 56 years until 2010 when the first safe comparable alternative was found (Davis *et al*., 2012).

2.1 Atrial Fibrillation

The heart is made up of four chambers, two on each side of the heart (Figure 2.1 below). The two chambers on top are referred to as the atria (singular atrium), and the chambers below are referred to as ventricles (Steffel *et al*., 2018). Separating the left side and the right side of the heart is a thick wall of muscle referred to as a septum. The muscular walls of the atria relax to allow blood into the heart, then contract tightly to pump blood into the ventricles and from there out of the heart and around the body (Forslund *et al*., 2018).

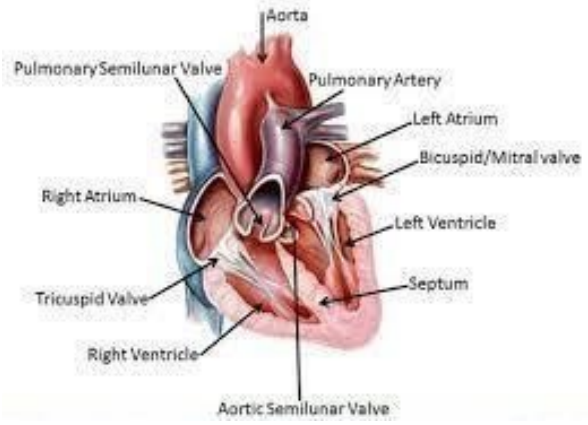


Figure 2.1
Diagram of the heart
(Hohnloser, et al., 2000)

The contracting of the ventricles allows for the relaxing of the atria, which then fill again with blood (Baglin *et al*., 2006). This pattern, referred to as the sinus rhythm or the heart rate, is repeated approximately 60 to 100 beats per minute when a normal, healthy person is at rest. The direction of the flow of blood is controlled by heart valves (mitral, tricuspid, aortic, and pulmonary). These valves open and close quickly to stop the blood from flowing backwards (Mitchell *et al*., 2019, p6-7).

Atrial Fibrillation (AF) in which the heart beats can be as much as can be as much as 200 to 600 beats per minute, is a very common heart condition which occurs when the natural pacemaker of the heart is interrupted by abnormal electrical impulses in the atria, see Figure 2.2 and 2.3 below.

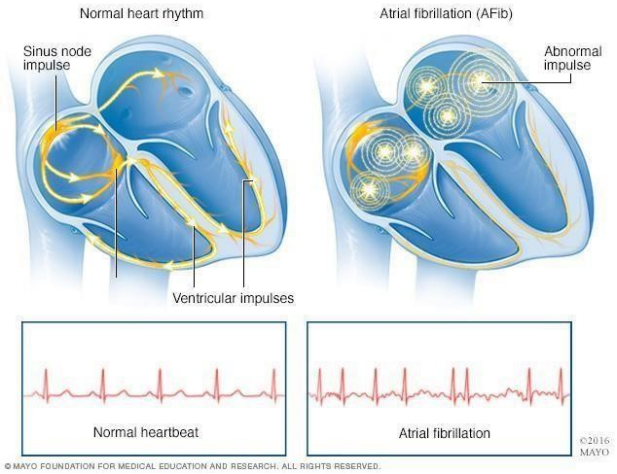


Figure 2.2
Atrial Fibrillation (Connolly et al., 2009)

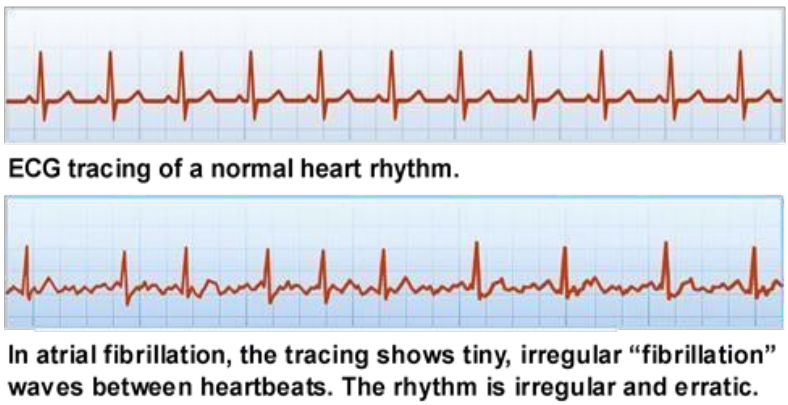


Figure 2.3
Atrial Fibrillation (Connolly et al., 2009)

AF symptoms are usually headaches, dizziness, tiredness, and shortness of breath. Some patients may be unaware of these symptoms which can last a few seconds or a few minutes (Fuster *et al*., 2006). The abnormal, irregular, and rapid heart rhythm often leads to the formation of blood clots inside the chambers of the heart, which is the leading cause of a stroke (see Figure 2.4). Untreated AF can lead to stasis of the blood (pooling) and clot formations in the heart, as blood is not completely pumped out of the heart chambers. If the resulting clot breaks away and travels to the blood vessels supplying the brain then there is a reduction in oxygen and nutrient supply which can lead to an ischemic stroke (Pirmohamed, 2006).

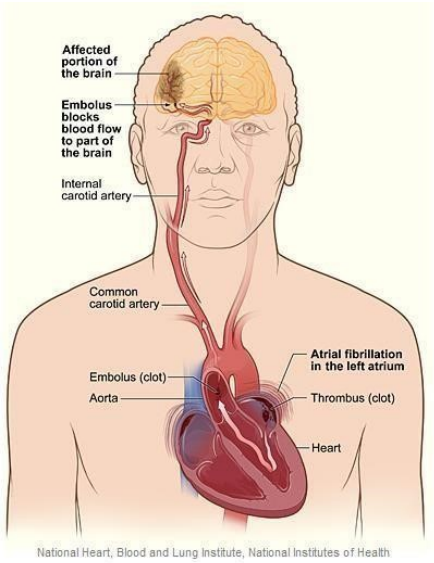


Figure 2.4
Image of the route of a stroke
(Healthjade.com, 2017)

Almost two-thirds of all stroke survivors have a life-changing disability because of their stroke. In Atrial Fibrillation patients, 20% are fatal and 60% are disabling. The social care costs and NHS costs associated with stroke treatment are approximately £1.7 billion. Therefore, investing in stoke prevention measures is important not just for reducing the number of stroke patients, but also the cost to the NHS (Camm *et al.,* 2012). Stroke is the fourth single leading cause of death in the UK (See Figure 2 below). The incidence of strokes in black people is double that in non-blacks (Mabley *et al*., 2019). Stroke is also the leading cause of disability in the UK (Ware, 2004).

The initial treatment for AF is focused on controlling the rate of the fibrillation. This is usually achieved with heart rate control medicines, such as Diltiazem (Cardizem) which is a calcium channel blocker, Metoprolol (Lopressor) which is a beta blocker, or Digoxin (Lanoxin). The second line of AF treatment is focused on prescribing lifelong anticoagulation (blood thinners) to prevent the formation of clots, and therefore minimise the patient's risk of suffering a stroke. The risk of stroke in AF patients is age dependent with the risk increasing with age (Lip and Halperin, 2010). Common causes of AF are excessive alcohol consumption, hypertension, physical inactivity, diabetes, smoking, thyrotoxicosis (over-active thyroid) and heart valve disease. (Connolly *et al*., 2009).

Warfarin has been the prescription of choice for stroke prevention since 1954, despite all its known drug and food interactions, and has been proven to reduce the risk of stroke by 65% (Baglin *et al*., 2006; Shamloo *et al*., 2019). A survey carried out in 2014 showed that there were 1.2 million people in the UK on Warfarin, resulting in 17 million out-patient appointments per year for Warfarin levels (INR) monitoring (Wenger, 2002; Patel *et al*., 2019). Warfarin monitoring is essential to ensure patient compliance in taking the medication. In the event of a major bleed there are effective, proven drugs for the reversal of Warfarin.

Negative characteristics of Warfarin include:

- High maintenance
- Affected by foods rich in vitamin K
- A very narrow therapeutic index
- Many drug interactions
- A slow/delayed pharmacodynamic onset

There is published evidence that describes the association between known modifiable risk factors, underlying conditions, and the development and progression of AF (Cutler *et al*., 2014) see Figure 2.5 below. Early management of underlying conditions to improve AF outcomes may provide perspective on the implementation of tailored AF management in daily clinical practice, as all these underlying issues as well as comorbidities have an impact on the patient's perception of their well-being.

Figure 2.5
Risk Factors and underlying Comorbidities of Atrial Fibrillation (Shamloo, et al., 2018)

Taking Warfarin has a significant impact on an individual's life as it requires complex organisation, which has both drawbacks and benefits, (Clemens *et al*., 2013). For example, the required regular monitoring may have an impact on planned activities such as holidays that last more than 3 or 4 days. The social impact of clinic attendance for the over 65s may also be significant as they often have transport arranged by the hospital for the day and may need to arrange other non-Warfarin related hospital appointments for the same day. On the positive side, the visit to the clinic has social benefits, often resulting in long conversations with other patients or with the health professional conducting the blood test (Camm *et al*., 2012).

2.2 Recent Publications

When this study began six years ago there were few publications examining the patient's perspective of life on Warfarin or the new anticoagulants. However, more recently, a few papers have appeared in the medical press. None, however, interviewed their respondents over time or enquired into daily life on their medication. Attaya *et al*., (2012) surveyed patients 18 years and over about their

willingness to switch from Warfarin to other anticoagulants. The research method was a 'one off' self-completion questionnaire with no face to face patient contact. Elewa *et al*., (2014) looked at patient satisfaction on Warfarin and Dabigatran using a short questionnaire administered in outpatients. No interviews were undertaken.

Pink *et al*., (2009) argued that the Quality of Life of AF patients is significantly lower than the general population or those with other types of coronary diseases. A review of Quality of Life studies conducted with elderly patients with AF in 2008 confirmed that there was a 'poorer Quality of Life among patients with AF compared to age matched population' (Lane and Lip, 2009, p243). Just over 26% of patients older than 65 may forget to take Warfarin, or accidentally take the dosage twice (Wang *et al*., 2014). This finding is also reflected in a patient compliance study carried out by Kumar *et al*., (2014), which showed that there are several socio-economic factors which influence compliance for taking long term medicines such as Warfarin. Such factors include diet, exercise, and alcohol consumption, as well as a network of support from friends and family.

Several other randomised control studies have explored Quality of Life (QoL) in AF patients, and appear to support the claim that the QoL of AF patients is significantly lower than that of the general population or of those with other types of coronary diseases. These surveys are as follows:

- The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study (Jenkins et al., 2005);
- Results from the Rate Control Versus Electrical Cardioversion (RACE) study (Hagens et al., 2004);
- Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomised trial (Hohnloser et al., 2000);
- The Strategies of Treatment of Atrial Fibrillation (STAF) study (Carlsson et al., 2003);
- How to Treat Chronic Atrial Fibrillation (HOT-CAFÉ) (Opolski et al., 2004).

However, these studies compare cardiac rhythm control methods, such as cardiac ablation (inserting a catheter into the heart to destroy small areas which may be causing the disruptive signals), cardioversion (using electrical shocks similar to a

defibrillator to re-introduce a synchronized heart rhythm) or rate control medicines such as Digoxin or Dronedarone (Camm *et al*., 2012). The long-term impact of the Quality of Life of patients who switch from Warfarin to DOAC has not been studied, most studies exploring short-term perceptions. A study conducted in Chicago by Attaya *et al.,* (2010) attempted to examine patients' attitudes towards the new DOAC in a survey entitled SWITCH. 180 patients were invited to take part in the patient survey; uptake was 86% with 155 patients participating. Of these 56% declined the use of the DOAC's due to various reasons including lack of information, as well as a lack of monitoring and effective reversal mechanism (Rottenstreich *et al.,* 2018). The patient survey also revealed that women were less likely to use the DOACs than men, but that the elderly patients (over 70 years old) were more likely to use the DOAC as a long term oral anticoagulant. Garcia *et al*., (2009) reported that the risk of haemorrhages and stoke in AF patients was greatly reduced when Warfarin was substituted for the DOAC. The creatinine clearance (CrCl) rate for the DOAC patients showed dramatic improvements as well, for example in the RECORD study the CrCl increased from 30 to 49ml/min clearance. This is significant as these DOACs rely on good renal functionality for effectiveness and excretion.

Since 2014, a series of patient-reported health survey studies have been conducted, involving AF patients who had switched from Warfarin to a direct oral anticoagulant (DOAC), each looking at a different perspective. One such study looked at the convenience of taking DOACs by asking a series of patient satisfaction questions via a survey (Choi *et al*., 2014). Several papers looked at the patience perception of adherence and how this impacts on their willingness to switch given a choice (Di Minno *et al*., 2014; Pandya and Bajorek, 2017; Auyeung *et al*., 2016). Other papers looked at the cost to the NHS including the Folkerts study, which used a Markov model to examine the impact of healthcare costs (Briere *et al*., 2019). A Canadian study conducted by Gomes *et al*., (2012) concluded that for Warfarin patients 66 years or older the rate of bleeding over a 13-year period was 3.8% per person per year. The study also showed that there was 1% rate of bleeding with Warfarin patients in the first 30 days of the Warfarin treatment. The study also found that 20% of all Warfarin patients who were admitted for a bleed died in hospital or very shortly after leaving hospital (Gomes

et al., 2013). Usually in elective surgical procedures, patients on Warfarin are advised to stop taking the prescribed dose at least 3 days before the surgery. In an emergency surgical situation, or in cases of Warfarin overdose, the bleeding related effects of Warfarin can be reversed with the administration of Prothrombin Complex Concentrate (PCC) in the first instance, Fresh Frozen Plasma (FFP) as a second option, and thirdly intravenous Vitamin K (Baglin *et al.,* 2012; Keeling *et al*., 2011; Millar and Laffan, 2017).

This recent interest in the patient's perspective of their treatment is to be welcomed and demonstrates that their views are increasingly valued and seen as contributing to the general knowledge base around this subject (Elewa *et al*., 2014). The current study would still appear to be unique in that it alone has combined qualitative (interviews) and quantitative (questionnaire / scales) data in its design. In addition, the patients were met at three points in time and focused on non-clinical factors.

2.3 Cost of Atrial Fibrillation to the NHS

For some time, Aspirin has been used as an alternative antiplatelet for patients with an adverse reaction to Warfarin, who cannot take Warfarin, or who have poor compliance with Warfarin (Sconce *et al*., 2005). In 2011 the British Society for Haematology (BSH) released guidelines which recommended stopping the routine use of aspirin as an anticoagulant for patients with atrial fibrillation (Bauer, 2011). Subsequently, a study into the cost of switching was commissioned (Cowie, 2014). The clinical experts involved in the study considered not only the stroke prevention rates as a result of switching, but also considered other factors such as the on-going difficulties some patients experience with adherence to the Warfarin dosage regime, especially as the dosage for some patients who do not cope well on Warfarin may require monitoring and dosage adjustments (NICE, 2012). In June 2014, The National Institute for health and Clinical Excellence (NICE) looked at the costing per year implications of patients in the United Kingdom who were on Warfarin and those who switched from Warfarin to DOACs. The estimated cost per patient for one year for a patient on Warfarin at the time was £283. This includes the cost of monitoring the patient (See table 2.1 & 2.2 below). It is estimated that 2.5% of people will continue to take aspirin against the BSH's recommendations.

Treatment	Percentage of population	Number of people (000s)
Warfarin	34.32%	305
Aspirin	22.49%	200
Dabigatran etexilate	4.73%	42
Rivaroxiban	4.73%	42
Apixaban	4.73%	42
No treatment	28.99%	258

Table 2.1
Current prescribing cost of anti-coagulation treatments in England http://www.preventaf-strokecrisis.org/report/chapter4

Treatment	Annual Cost of Treatment (£)
Warfarin (including monitoring)	283
Aspirin	32
Dabigatran etexilate	802
Rivaroxiban	767
Apixaban	802

Table 2.2
Annual cost of treatments for Atrial Fibrillation
http://www.preventaf-strokecrisis.org/report/chapter4

The increase in drug cost resulting from switching from Warfarin to DOACs is significant, especially when taking into consideration the size of the population involved. It is estimated by the panel of experts involved in the study on the cost implications of switching, that the change in anticoagulation treatment would result in a major bleed in 3 out of 100,000 people (Till and Cowie, 2014). This would result in an increased cost of £4,000 per 100,000 people to the NHS (Department of Health, 2013). The daily cost of Dabigatran, Apixaban and Rivaroxaban in the community is approximately £2.60 and in hospital £1.60. The daily cost of Warfarin (drugs + monitoring and dosing etc) is between £0.67 - £0.83 (Shah and Gage, 2011; Healthjade.com, 2017). It is also estimated that the cost of the newer drugs to the NHS will increase as more people are being offered them. However, the cost of the giving the newer anticoagulants may be offset by the reduction in cost due to fewer atrial fibrillation patients experiencing a stroke or AF-related hospital visit (Scowcroft and Cowie, 2014). In addition, savings will be gained from the reduced

anticoagulation clinic service, which would not be needed for DOAC patients. As a result the resources, financial and otherwise, that would have been spent on Warfarin, atrial fibrillation and the stroke related events (including secondary care providers and community nursing for these patients) can be reallocated to other areas of priory medical services such as cancer (Camm *et al*., 2012). According to the West Hampshire Clinical Commissioning Group, in January 2017 there were 106,000 patients in the West Hampshire area over 65 and 16,000 over 85. Of these it was estimated that 2,000 patients had undiagnosed AF, 12,000 had diagnosed AF and 10,500 patients with AF had a high risk of a stroke. Surprisingly 3,700 patients in this area were on no form of anticoagulation.

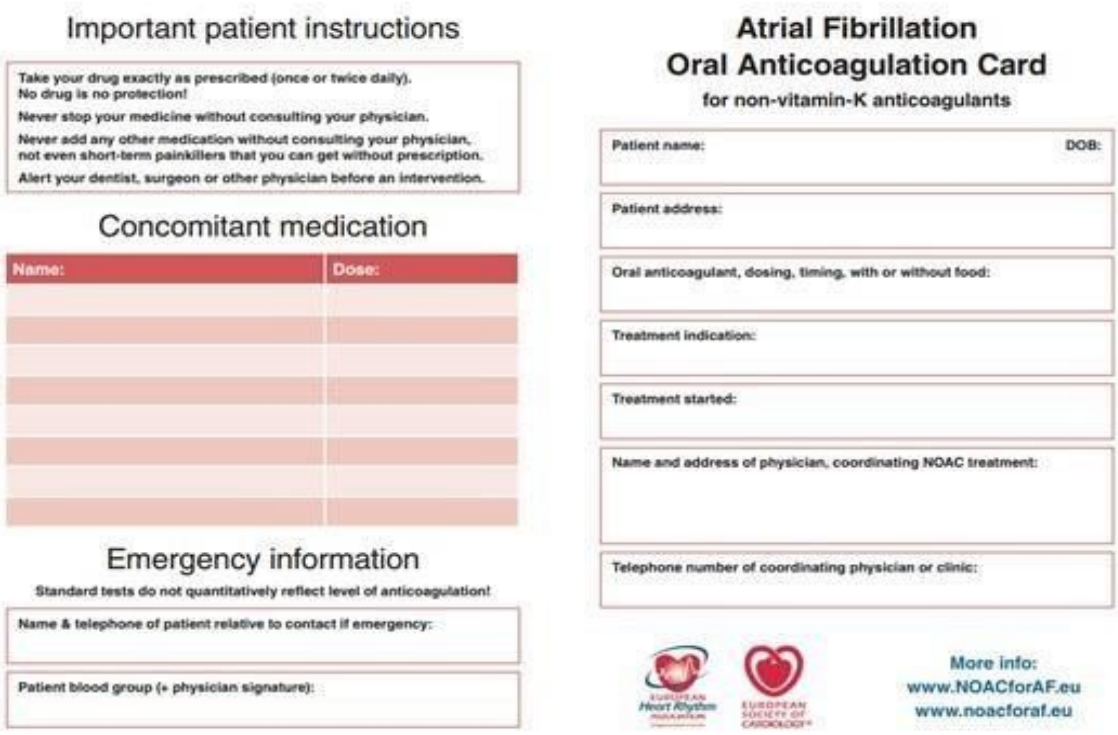
2.4 Pivotal Papers – Anticoagulation Policy Determinants

There are two key papers that directly influence this study as they were the principal safety and efficacy studies conducted comparing Warfarin with DOACs. The results of these two studies formed the basis of the decision from the National Institute for Health and Clinical Excellence (NICE) to introduce a new Warfarin alternative to the National Health Service for the treatment of AF patients. The first paper was on the RE-LY randomized control trial which compared Warfarin with Dabigatran in 18,113 patients with AF, using the two recommended doses of Dabigatran 110mg or 150mg twice daily (Connolly *et al*., 2009). The study found that Dabigatran performed as well as Warfarin at 110mg with a lower haemorrhagic rate of 2.71% for Dabigatran and 3.36% for Warfarin (Ganetsky *et al*., 2011). Conversely the 150mg dose of Dabigatran had a lower rate of stroke and embolus formation compared with Warfarin patients, but a similar rate of haemorrhage. The higher dose of Dabigatran was also linked to a series of intracranial haemorrhages (ICH). There is still limited information available relating to these bleeding events. 57% of the patients on Dabigatran continued with the Direct Oral medication after the bleeding event (Connolly *et al*., 2009)

The second paper was the ROCKET-AF study (Executive Steering Committee 2010), which looked at treatment of Non-Valvular Atrial Fibrillation. It involved 14,264 patients with non-valvular AF and compared Warfarin to Rivaroxaban. This was conducted using the two doses of 20mg daily and 15mg daily Executive Steering Committee 2010. The ROCKET study determined that in patients with AF,

Rivaroxaban was noninferior to Warfarin (i.e. performs as well as Warfarin) for stroke and embolism prevention. The study also showed no significant between group differences in the risk of major bleeding. The findings from the ROCKET study was later substantiated in 2014, by two research cardiologist looking at stroke identification and prevention in the International journal of cardiology (Scowcroft and Cowie, 2014). At about the same time, Camm *et al*., (2011) on behalf of the European Society for Cardiology (ESC) wrote guidelines on the safe use, dosage, long term management and contraindications for the use of DOACs. These guidelines brought together coagulation specialist representatives from eight European countries to decide how and when the new DOACs should be used, and in what circumstances Warfarin patients can be switched safely to DOACs. They also suggested a follow-up 90 days post DOAC substitution and suggested that this follow-up be performed by a clinician or medical professional in a locally arranged agreement.

As these DOACs currently have no routine mode of monitoring, testing or reversal, each NHS and primary care trust must use local arrangements to decide on the implementation of their own local anticoagulation arrangements according to the guidelines and their resources. The most practical and cost-effective solutions were considered. This resulted in a scoring system known as the CHA_2DS_2-VASc score (congestive heart failure, hypertension, age which has 3 age ranges (<65, 65-74 and ≥75), diabetes mellitus, stroke vascular disease history and sex (Ruff, 2011). This will be discussed in more detail later. Heidbuchel *et al.,* (2013) wrote a practical guide on behalf of the European Heart Rhythm Association (EHRA). A key suggestion from their work was the use of a patient card (see Figures 2.6a&b. below), to record the scheduled and unscheduled visits of the health professional or clinician to the patient during a follow-up. This card would then be used as clinical notes in the event of an adverse event such as a bleed or emergency surgical intervention to calculate information such as dosage, the most recent time the tablets were taken, etc., in order to assert the half-life and therefore the likelihood of a major bleed.



Important patient instructions

Take your drug exactly as prescribed (once or twice daily).
No drug is no protection!
Never stop your medicine without consulting your physician.
Never add any other medication without consulting your physician, not even short-term painkillers that you can get without prescription.
Alert your dentist, surgeon or other physician before an intervention.

Concomitant medication

Name:	Dose:

Emergency information

Standard tests do not quantitatively reflect level of anticoagulation!

Name & telephone of patient relative to contact if emergency:

Patient blood group (+ physician signature):

Atrial Fibrillation
Oral Anticoagulation Card
for non-vitamin-K anticoagulants

Patient name: DOB:

Patient address:

Oral anticoagulant, dosing, timing, with or without food:

Treatment indication:

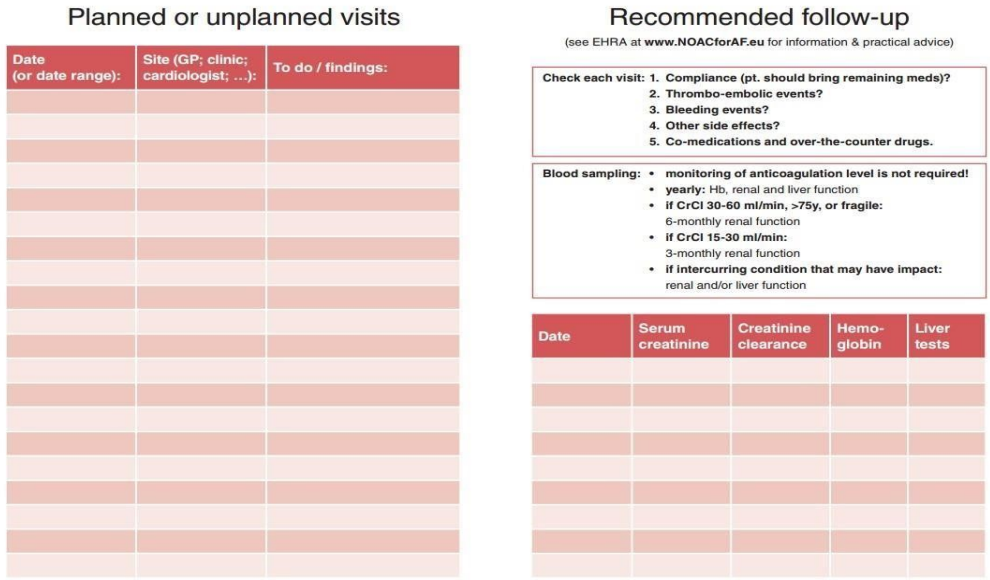
Treatment started:

Name and address of physician, coordinating NOAC treatment:

Telephone number of coordinating physician or clinic:

More info:
www.NOACforAF.eu
www.noacforaf.eu

Figure 2.6a (front)
Atrial Fibrillation Oral Anticoagulation Card (Camm, et al., 2011)



Planned or unplanned visits

Date (or date range):	Site (GP; clinic; cardiologist; ...):	To do / findings:

Recommended follow-up

(see EHRA at **www.NOACforAF.eu** for information & practical advice)

Check each visit:
1. Compliance (pt. should bring remaining meds)?
2. Thrombo-embolic events?
3. Bleeding events?
4. Other side effects?
5. Co-medications and over-the-counter drugs.

Blood sampling:
- monitoring of anticoagulation level is not required!
- **yearly:** Hb, renal and liver function
- **if CrCl 30-60 ml/min, >75y, or fragile:** 6-monthly renal function
- **if CrCl 15-30 ml/min:** 3-monthly renal function
- **if intercurring condition that may have impact:** renal and/or liver function

Date	Serum creatinine	Creatinine clearance	Hemo-globin	Liver tests

Figure 2.6b (back)
Atrial Fibrillation Oral Anticoagulation Card (Camm, et al., 2011)

On a similar theme, a three month survey entitled Study of Warfarin Patients Investigating Attitudes Toward Therapy Change (SWITCH Survey) was conducted in Chicago (Attaya *et al*., 2012). It examined the attitudes of life-long Warfarin

patients towards the new DOACs, to assess whether patients would be interested in switching from Warfarin to the new drugs. One hundred and eighty patients were offered a place on their patient survey; the uptake was 86%, with 155 patients participating. Of these, 56% declined the use of the DOAC's for various reasons, including lack of information and cost, as well as monitoring and the absence of an effective reversal agent. The survey also revealed that women were less likely to use the DOACs than men, and that patients over 70 years old were more likely to use the DOAC as a long term oral anticoagulant (Attaya, *et al*., 2012). Patients on life-long Warfarin have commonly cited the negative social impacts on their Quality of Life. These include the regular need for clinic trips for blood testing, dietary and alcohol restrictions, increased stress, and anxiety from the increased risk of Warfarin-associated bleeds and drug interactions with concomitant drugs (Lip and Halperin, 2010). Their study, although valuable, showed that there are gaps in the literature regarding the impact of the medical, social, and personal implications to the QoL of patients who switch. The social and personal implications of any treatment are important (Frendl and Ware Jr, 2014), but are virtually unexplored for the over 65s. Research has already demonstrated the vital role of patient information provision to compliance and other areas of treatment, as well as in treatment outcomes (McNaughton and Shucksmith, 2015; Horne *et al*., 2005; Horne, Robert and Weinman, 1999).

One such example is an article from the Journal of Public Health in which the paper determined that '*sustained compliance was due, in part, to a number of individuals being afforded the opportunity to reconFigure their medications*' and '*indicates that patients experiencing side effects…. are more likely to remain adherent if GPs are willing to listen to their concerns and review medication*' (McNaughton and Shucksmith, 2015, p124). Therefore, the more that is known about the challenges of switching treatment for the over 65s, the better able healthcare providers and clinicians will be to help patients achieve effective treatment. In addition, it is known that the written information (supplied by the pharmaceutical company) given to the patient may vary in amount and quality. Patients often enquire about information regarding their personal medical situation (Bauer, 2011), therefore, it is important to investigate the patient's perception of the information source or information given to them as well as any other factors that might raise. Garcia *et al*., (2009) looked at

bleeding outcomes and reported that the risk of haemorrhages and stoke in atrial fibrillation patients was greatly reduced when Warfarin was substituted for the DOAC. He also looked at co-morbidities such as renal function and noted that the creatinine clearance (CrCl) rate for the DOAC patients showed dramatic improvements as well. For example, in the RECORD study the CrCl increased from 30 to 49ml/min clearance. This is significant, as these DOACs rely on the renal functionality for effectiveness and excretion.

The existing literature explores the many complexities and challenges faced by the elderly on lifelong medications such as Warfarin. These include concomitant therapies, clinic visits for monitoring and adjustments of the medication, and logistical challenges such as transportation of the patient to and from hospital. The literature, however, does not explore the patients' perceptions of being on Warfarin or of switching from Warfarin to the Direct Oral Anticoagulants (DOACs).

2.5 Direct Oral Anticoagulant Patient's Review.

The assessment criterion when selecting patients for initiating or substituting prescription medication involves the balancing of risk versus benefit (Connolly and Spyropoulos, 2013). Currently there are no routine monitoring tests for DOACs, and routine coagulation parameters such as the prothrombin time (PT) which is used to measure Warfarin, thrombin time (TT), and activated partial thrombin time (APTT), have limited diagnostic value in measure the DOACs (Connolly and Spyropoulos, 2013; Ganetsky *et al.,* 2011). There are also variations in sensitivities of different laboratory reagents to the DOACs (Ganetsky *et al*., 2011). At the start of this study, there were also no key policies governing testing, reversal, monitoring, or reference ranges of DOACs (Baglin *et al*., 2006). A select number of specialised laboratories now offer testing of DOACs (Patel *et al*., 2019), but testing is still not universally or routinely offered. Baglin *et al*., (2012) suggested that the use of a reference range should consider the dose-dependent reactions of DOAC to laboratory routine clotting tests. The absence of a test or reference range can complicate medical decisions for patients, especially pre-operatively for DOAC patients or in emergency situations, such as in the event of a major bleed (Martin and Moll, 2016).

There is a concern within the scientific community with the lack of data which addresses what happens with non-compliance. As with Warfarin, sometimes

patients for a variety of reasons, such as simply forgetting or feeling unwell, do not take their medication. Having conducted a database search on the safety and efficacy of DOAC administration at extremes of patient body weight, no such literature could be found. There are, however, several articles which address the cost to the National Health Service as well as the implications of renal impairment (Baglin *et al*., 2012).

According to a review on the DOACs by Connelly *et al*., (2013), the predictability of the new drugs' pharmacokinetics as well as their rapid onset makes the DOACs very appealing to both patients and clinicians. As stated above, the unpredictability of Warfarin as well as the variability of the doses and the many interactions with food, alcohol and other medications has been a considerable problem for patients and clinicians over the years (Lip and Halperin, 2010).

The variation in modes of action for each of these new drugs is the main focus of a paper by Schulman *et al*., (2011). Potentially it will become very expensive if hospitals stock all three new agents as well as the currently used anti-coagulation agents such as Fondaparinux, Enoxaparin and the various forms of Heparin (as low molecular weight heparin, LMWH, and unfractionated heparin, UFH) which all have different modes of actions (Mani, 2014). Warfarin stops the formation of clots by interfering with a set of vitamin K dependent blood clotting factors in the body. However, the new DOACs work by targeting and blocking a single coagulation factor within the coagulation pathway. For example, Apixaban, Rivaroxaban (Xarelto®) and Edoxaban all work on activated Factor 10 (FXa) to prevent coagulation from progressing past this point in the pathway (cascade), as shown in Figure 2.7 below.

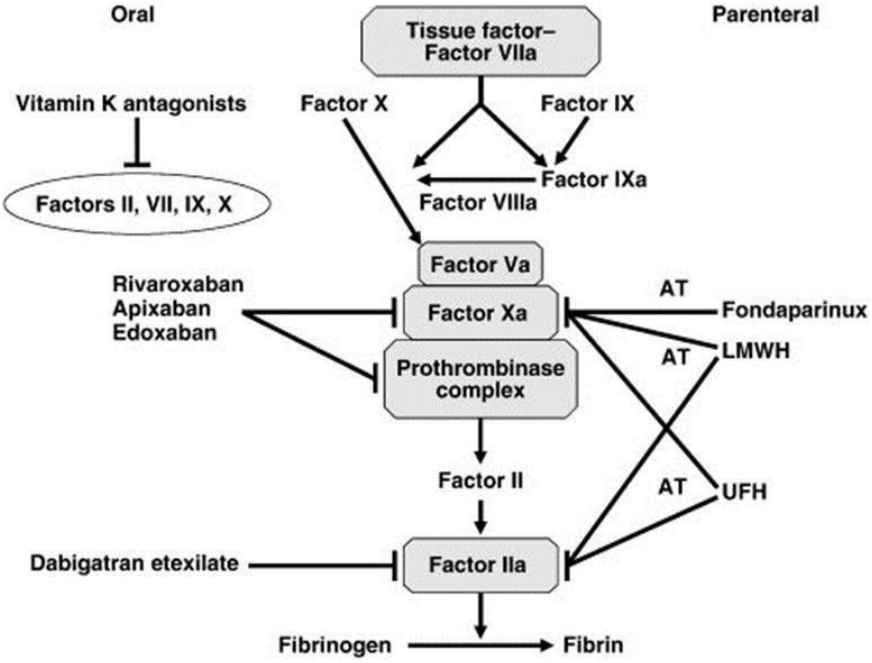


Figure 2.7
Mode of action of Anticoagulation Drugs
(Asselin, 2003)

There are still no approved reversal agents for use in the UK, nor is there a requirement for regular medication compliance checking in the form of finger pricking or attending clinics. However, the assessment of renal function must be regularly checked as the mode of elimination from the body is the kidney. The age, sex, weight, other medical conditions of the patient such as diabetes and other medications that the patient is on, should also be considered.

The principle benefits of DOACs are:

- They are not impacted by dietary vitamin K.
- They have more consistent pharmacokinetics.
- There are fewer drug interactions.
- There is a relatively quick onset of action; and
- They do not require Heparin administration at the start (bridging).

DOACs are pharmacokinetically stable and have a short half-life, which is the time taken to lose half its effective biological and pharmacological concentration in the blood plasma, and this negates the need for routine monitoring (Bauer, 2013). They also have a rapid onset of two and a half to four hours as opposed to Warfarin which requires four to seven days for optimal effect. This means that DOACs work faster

at thinning the blood and leave the blood faster, some within a few hours. Warfarin on the other hand, could take at least two to three days to leave the circulation. As DOACs leave the circulation so quickly, it is therefore imperative that the patient adheres to their daily dose of DOAC. Not taking the daily dose of DOAC may result in the patient being prothrombotic, forming clots and thereby increasing the risk of a stroke (Mesko, 2014). A full comparison list of Warfarin and DOACs is listed in Appendix 12.

There are several factors which determine whether a patient can take DOACs. These include the health condition of the patient, such as atrial fibrillation (but only in the absence of heart valve disease), or deep vein thrombosis (DVT) or pulmonary embolisms (PE). The ability for the kidney to metabolise and process these medications is also considered, and generally would not be offered to patients who have poor renal function. If the kidneys are unable to clear these DOACs from the bloodstream, they build up in the blood and lead to an increased risk of bleeding. In these situations, Warfarin may be a better alternative to DOAC, since Warfarin does not require the use of the kidney for metabolism, using the liver instead. Patients on DOACs do not require regular prothrombin time and INR monitoring, but will require regular monitoring of their kidney function (Pink *et al.,* 2011). The kidneys are required for the elimination and excretion of DOACs, therefore periodic assessment of the kidney's ability to function is carried out in the lab. The metric is usually the measurement of the rate at which creatine is cleared by the kidneys. This creatinine clearance (CrCl) should be >30ml/min. A CrCl of 30-50 ml/min requires close monitoring of the patient and the dose of DOACs should be adjusted or halted depending on the result of the CrCl.

2.5.1 Dabigatran (Pradaxa®)

Dabigatran is a direct inhibitor of thrombin (the final intermediate of coagulation), has a rapid onset, a predictable anti-coagulant effect and very few drug interactions, with the main exception of p-glycoprotein inducers such as Rifampicin which reduces the efficacy of Dabigatran through p-glycoprotein induction (Camm *et al.,* 2012; Folkerts *et al*., 2019). Dabigatran capsules are made from tartaric acid which induces an acidic environment aiding in the rapid intestinal tract absorption of the

drug. This often results in the most common side effect of Dabigatran which is dyspepsia (Heidbuchel *et al*., 2013). These capsules are sensitive to moisture and therefore need to be kept in their original blister pack and should not be decanted into another container such as a Dosette box (shown in Figure 2.8 below). Dosette boxes are usually used by older patients to help keep track of multiple daily medications.

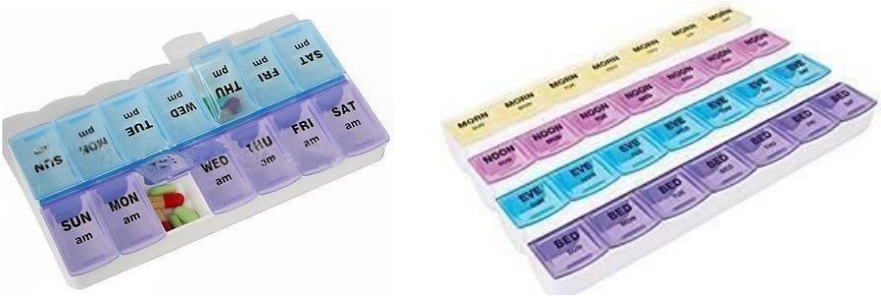


Figure 2.8
Dosette boxes (Amazon.co.uk, 2018)

Dabigatran is prescribed as either a 100mg or 150mg dose. The larger dose has been shown to cause more GI bleeds than Warfarin as previously mentioned in the RELY study. The 110mg dose has been shown to be non-inferior to Warfarin but causes fewer intracranial haemorrhages (ICH) (Eikelboom *et al*., 2011).

2.5.2 Rivaroxaban (Xarelto®)

Rivaroxaban has 3 doses: 10mg, 15mg and 20mg and is taken once daily, advisably at the same time each day, and is typically the 20mg dose taken with the evening meal. Patients wishing to switch or who have been cleared to switch to Rivaroxaban must discontinue Warfarin and their prothrombin time and INR monitored. The patient may only switch to Rivaroxaban once the INR falls below 3. Other anticoagulants such as heparin (often given peri-operatively or post operatively), must be discontinued before the commencement of Rivaroxaban. To date there are no clinical trial data available for switching from Rivaroxaban to Warfarin. For patients who need to be switched from Rivaroxaban to Warfarin, one approach is to stop the Rivaroxaban, then give the first dose of Warfarin at the time that the next dose that the next dose of Rivaroxaban would have been given, along with a parenteral anticoagulant such as heparin or a heparinoid. There are very few

interactions with other medications. However, patients who are prescribed concomitant drugs which also influence coagulation, such as aspirin and antiplatelet medications (e.g. clopidogrel), must be closely monitored.

There is documented evidence that compared with Warfarin there may be an increased incidence of bleeding in patients taking Rivaroxaban. Below are some possible side effects of Rivaroxaban:

- bloody, black, or tarry stools (an indicator of an overdose)
- pink, or brown urine (an indicator of an overdose)
- coughing up or vomiting blood or material that looks like coffee grounds (an indicator of an overdose)
- frequent nosebleeds
- bleeding from the gums
- heavy menstrual bleeding
- weakness
- tiredness
- headache
- dizziness or fainting
- blurred vision
- pain in arm or leg
- rash
- itching
- difficulty breathing or swallowing
- hives
- pain or swelling at wound sites

2.5.3 Apixaban (Eliquis®),

This medication needs to be taken twice daily. Apixaban has a short duration of action. Therefore, if a dose is missed, the patient is at an increased risk of thrombosis (clot formations) and stroke. Inversely, for patients who accidentally take more than the required dose, they are at an increased risk of bleeding. There is no specific reversal or antidote for Apixaban. It is not uncommon for patients on Apixaban to experience joint pain, headaches, and bleeds. Since Apixaban is a new medication, interactions with the patient's other medications, as well as side effects are being still being discovered as new studies are conducted (Mabley *et al*., 2019).

2.5.4 Edoxaban (Savaysa ®)

Edoxaban works directly on Factor Xa inhibitors and prevents the triggering of the normal clot formations portion (thrombin) of the coagulation pathway. Thrombin is the protein portion of the blood needed for the formation of clots and does so by trapping platelets and red cells in a mesh, which is referred to as a thrombus (clot). By blocking the thrombin formation, this enables the blood to remain fluid and Edoxaban is therefore referred to as an oral blood thinner. This drug has a black box warning from the Food and Drug Administration (FDA). A black box warning is the most serious warning that can be issued by the FDA about a product. This alerts clinicians and patients to the side effects of a medicine that can be very dangerous. These effects include increased risk of a potentially fatal bleed, increased incidents of unexpected bleeding, poor efficacy in AF patients who have good kidney function, and an increased risk of stroke or thrombosis if a dose is missed or if the drug is stopped. There is no specific reversal for Edoxaban, and there are several non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, naproxen, and diclofenac, which interact with Edoxaban to increase the risk of bleeding.

2.6 Review of Aanticoagulation Guidelines

A systematic review of 36 published consensus guidelines, original and review journal articles was sourced from the online databases: PubMed, Cochrane Library, SCIENCE DIRECT, MEDLINE, and GOOGLE SCHOLAR. The search was limited to the English language and to publications between 2008 and 2017. The online critical appraisal skills programme (CASP), was then used to determine the usefulness and validity of the papers (Appendix 17). Based on the CASP criteria 31 articles were included. Five papers were excluded for the following reasons: they were not related to the area of atrial fibrillation or did not directly address the questions related to the topic of interest. Eight key papers were then selected from the 31 for detailed critical appraisal and data analysis. In addition to published articles, pharmaceutical package inserts and patient information leaflets were reviewed to evaluate information available to the patients about their medications.

Key search phrases used for the searches were as follows:

1. Direct Oral anti-coagulants + patient survey

2. New oral anti-coagulants + patient survey
3. Direct Oral anticoagulants guidelines
4. Apixaban + Rivaroxiban + Dabigatran clinical trials
5. Quality of life of oral anti-coagulated patients.
6. Apixaban + Rivaroxiban + Dabigatran laboratory testing

The same search string was used across each database, initially resulting in thousands of searches relating to oral anti-coagulation in post hip replacement surgery and hip-revision, pre-dental extraction or background information related to Warfarin. Once the filter of 'atrial fibrillation' was added then this dramatically cut the search outputs to just a few hundred. After this the various databases were compared and any duplication of publications was omitted, resulting in 42 papers.

Five of these papers were reviewed which overlapped in the references cited and were omitted. Of the remaining 36 papers (selected based on reading the abstract only) five were excluded as they did not meet the CASP criteria. As well as the CASP criteria. An example of the CASP criteria can be seen in Appendix 17.

2.7 Review of Quality of life in AF patients

'The quality of life is determined by its activities'. - Aristotle

The well-being of patients over 65 is recognized by the World Health Organization as determinant to overall health and Quality of Life (Peterson *et al*., 2006). The WHO defined health as '*a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity*' (Lip and Halperin, 2010, p127). The Quality of Life of the AF patient is therefore impacted by the increased risk of stroke and morbidity by these conditions as well as the constant need for physiological assessment (Pink *et al*., 2011; Pirmohamed, 2006; Rottenstreich *et al*., 2018). Hughes *et al*., (2009) argued that the quality of life of AF patients is significantly less than the general population or those with other types of coronary

diseases. Several other randomised control studies have been conducted on the quality of life (QoL) with AF patients, and appear to support this claim.

A search of EMBASE, Cochrane Library, SCIENCE DIRECT, MEDLINE, CINAHL, and GOOGLE SCHOLAR revealed that there are currently no studies or patient surveys undertaken to assess the QoL of AF patients currently receiving DOACs apart from the SWITCH survey by Attaya *et al*., (2010) as outlined above. The patient survey also revealed that women were less likely to use the DOACs than men, and that the elderly patients (over 70 years old) were more likely to use the DOAC as a long-term oral anticoagulant.

2.8 Safety and Efficacy of DOAC

As with most medicines, there is patient exclusion for the DOACs based primarily on their mode of removal, which is via renal excretion (Bauer, 2011). Therefore, patients who currently have poor renal function are not allowed to switch from Warfarin by the clinical team.

While no papers relating to allergies and DOACs have been found, there are however several sources of information highlighting Dyspepsia (indigestion) as a major side effect. These sources include Garcia *et al*., (2013); Camm *et al*., (2010) and Connelly (2009), as well as the Dabigatran (Pradaxa©) and Rivaroxaban patient information leaflet and medication insert. Camm *et al*., (2009) also highlighted other issues surrounding laboratory monitoring such as detecting DOAC levels in a suspected overdose, as the current coagulation panel of tests is insensitive to the DOACs. The concern is that by the time the level is detected the patient may be several times over the therapeutic dose and at risk of a major bleed or intracranial haemorrhage.

2.9 Pharmacology of DOACS

According to a review on the DOACs by Connelly *et al*., (2013), the predictability of the new drugs' pharmacokinetics as well as their rapid onset, makes the DOACs very appealing to both patients and clinicians. Unpredictability of Warfarin as well as the variability of the doses and the many interactions with food, alcohol and other

medications has been a considerable problem for patients and clinicians over the years. Direct Oral anticoagulants for stroke prevention in non-valvular AF has been greeted with excitement by the scientific and medical community. They offer several benefits such as the rapid onset of action, broad therapeutic window, renal excretion, fixed dose administration, minimal monitoring (generally 2 follow ups), before a life-long prescription is issued to the patient. The ease of use by the patient, and the stability of the drugs pharmacokinetics are all also significant bonuses. DOACs also have a short half-life and have minimal known interactions with food and concomitant medications as does its predecessor Warfarin. However, there is limited knowledge of long term use of these drugs due to their novelty, and several issues exist regarding a lack of effective antidote, as well as a routine diagnostic test to be used in the case of a bleeding event or unplanned surgical intervention. My thesis will attempt to address some of these issues as well to gain a unique patient perspective on the medium-term use of these drugs.

2.10 Literature Review of Stroke

A stroke is a serious life-threatening condition and occurs due to the disruption of the blood supply to the brain. The blood supply the brain provides oxygen and nutrients to the brain as well as removing the waste materials produced by the brain's activity. A reduction of blood or disruption to the supply of blood to the brain therefore leads to loss of brain cells and tissues which relies on the blood supply. There are two types of strokes, ischemic and haemorrhagic (Figure 2.9). Ischaemic stokes occurs when the blood vessels are blocked. This blockage may result from the narrowing of blood vessels caused by: (a) increased plaque formation from cholesterol (lipids) or calcium or nicotine in the blood vessels, a condition known as atherosclerosis; (b) clots (thrombus) in the blood vessel, a condition known as thrombosis; or (c) narrowed blood vessels due to disease.

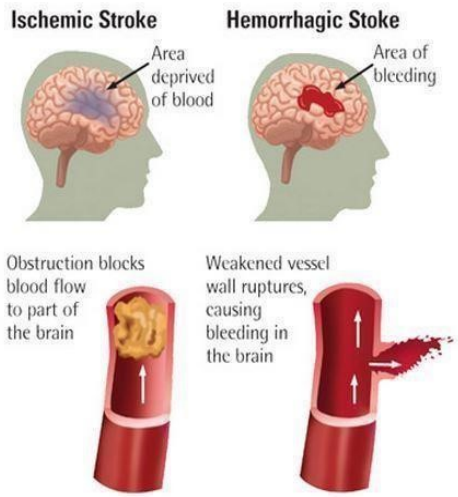


Figure 2.9
Types of strokes
(Lip & Halperin, 2010)

There are two types of Haemorrhagic stroke: intracerebral and subarachnoid. Intracerebral haemorrhages occur when there is leakage of blood from the circulatory system into the brain. This leakage usually results from ruptured blood vessels, or a brain aneurysm burst. This collection of blood around the brain results in swelling and increased pressure, which damages the cells and tissues of the brain. Subarachnoid haemorrhagic stroke is the term used to describe when the bleed occurs between the brain and the tissue covering the brain, known as the subarachnoid space. Haemorrhagic stroke is less common than ischaemic strokes as only 15% of all strokes are haemorrhagic. However, 40% of all stroke deaths are related to haemorrhagic strokes.

Risk factors which increase the likelihood of a stroke occurring include diet (high cholesterol and fat), obesity, illnesses, drug use (nicotine and cocaine) and some birth control medication. The risk of a stroke increases 5- to 7-fold following AF (Ganetsky *et al*., 2011), and this risk is further increased by compounding factors which are scored and used as a predicative index of stroke - the CHA_2DS_2-VASc score as mentioned above (based on congestive heart failure, three age ranges, sex and co-morbidities (Ruff, 2011), see Figure 2.10.

Risk Factors	Score	CHA2DS2-VASc score	Stroke Risk per Year
Congestive Heart Failure/LV dysfunction	1	0	0%
Hypertension	1	1	1.3%
Age ≥ 75 years	2	2	2.2%
Diabetes Mellitus	1	3	3.2%
Stroke/TIA/Thromboembolism	2	4	4.0%
Vascular Disease	1	5	6.7%
Age 65 – 74	1	6	9.8%
Female	1	7	9.6%
Total	**9**	8	6.7%
		9	15.2%

Figure 2.10
Stroke Risk Factors – CHA2DS2-VASc Score
(Pisters, et al., 2010)

The CHA_2DS_2-VASc score is used in conjunction with the HAS-BLED score (hypertension, abnormal renal and liver function, stroke, bleeding history, labile INR (the measurement unit of Warfarin), elderly >65, and drugs and alcohol concomitantly (see Appendix 10). The HAS-BLED score is essentially an estimate of the risk of a major bleeding occurrence in patients who have AF. This is done by assigning a score to each risk factor, then adding them together to get a predictive risk value. The higher the value, the higher the risk of a stroke event. See Figure 2.11.

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

Figure 2.11
Bleeding Risk Factors -HASBLED Score
(Pisters, et al., 2010)

2.11 Ischaemic Stroke and morbidity

In 2013 Public Health England determined that ischaemic stroke is the third largest cause of mortality in the country (National Audit Office, 2013). Results from a meta-

analysis of 33 studies showed that Warfarin-related complications are the third most common cause of all hospital admissions in the UK (Pink *et al*., 2011; Pirmohamed, 2006; Mitchell *et al*., 2019). This is partially due to its narrow therapeutic window and multiple interactions with concomitant drugs and food, as well as its well documented side effects. The study, which analysed 6554 patients, also discovered that AF patients' INR was outside their target range for almost 50% of the time. Being above the INR range results in a threefold increased risk of a haemorrhage and being below the INR range results in an increased risk of clot formation (thrombotic event) (Pirmohamed, 2006 and Mabley *et al*., 2019).

2.12 Warfarin

Clotting or blood thickening is a particularly complex process that involves many proteins or substances called clotting factors. These clotting factors are primarily produced by the liver. When a cut or bleeding occurs, clotting factors are activated by platelets. A domino effect of these clotting factor proteins is then initiated which results in the formation of a stable clot, therefore stopping the bleed. The liver needs a healthy supply of vitamin K rich foods to produce these clotting factors.

Warfarin works by inhibiting vitamin K dependent coagulation factors (F) such as FII, FVII, FIX & FX. Warfarin also inhibits two co-factor anticoagulant proteins known as Protein C and Protein S. See Figure 2.7. As mentioned above, in the normal clotting process vitamin K in its reduced form is required for clotting; Warfarin prevents vitamin K from being reduced therefore preventing the clotting process. Warfarin does not, however, reverse the effects of already synthesized and circulating clotting factors.

As Warfarin also reduces the activity of the anticoagulant proteins C and S, the patient may become hypercoagulable and prone to the formation of clots shortly after the initiation of Warfarin. Therefore, in some situations, such as following an emergency surgical intervention, the initiation of Warfarin should be given with heparin (Baglin *et al*., 2012). This is known as 'bridging'. As concomitant heparin can affect the laboratory tests for Warfarin, the use of heparin is usually discontinued at least six hours before monitoring of Warfarin is conducted.

Vitamin K rich foods tend to be green fruits and vegetables such as those shown in Figure 2.12. Patients who are prescribed Warfarin are advised to monitor their intake of these sources of vitamin K as they interact with Warfarin to produce an increased anti-coagulant (thinning) effect.

Figure 2.12
Vitamin K rich foods
(Healthjade.com, 2017)

Most often Warfarin is prescribed as prophylaxis for the primary prevention of stroke or following a stroke as secondary prevention. It is also prescribed following surgical intervention to prevent the formation of clots, to correct cardiac arrhythmias or irregular heart rhythms such as atrial fibrillation (Davis *et al*., 2012). Warfarin is also used to prevent the formation of clots in patients who have had a heart attack, deep vein thrombosis (DVT) or pulmonary embolism (PE). Warfarin can also be used to help treat a group of congenital or acquired blood clotting disorders known as thrombophilia.

Warfarin oral tablets (Figure 2.13) are available in a range of dosages and are colour coded to assist the patients in taking the correct dose. This is particularly useful for

the elderly who often have several other medications to take or may require Warfarin dosage adjustments.

Figure 2.13
Warfarin tablet doses (CanadianPharmacy.com,2018)

Usually when a patient is first prescribed Warfarin, a baseline measurement of the patient's Prothrombin Time (PT) and Internationalized Normalized Ratio (INR) is taken. The induction dose of 10mg daily for the first 2 days is then administered, with regular monitoring of the patient's PT and INR conducted.

The patient's Warfarin dose therapeutic range (INR range), is determined by whether the drug being given as a preventative measure (prophylaxis), which is 2.0-3.0 or therapeutically 2.5-3.5**.** It is also influenced by the recommended dose for each patient's medical condition, the prothrombin time and their INR. Some patients may require other coagulation tests to be done. The daily maintenance dose for Warfarin patients is usually 3 to 9mg, and it is recommended that that this dose is taken at the same time every day (Baglin *et al*., 2012). This dose may be changed or stopped if the prothrombin time and INR are excessively prolonged. Once the maintenance dose is stabilised within the required therapeutic range, then there is no need to make dosage adjustments. Patients not optimally coagulated with Warfarin for reasons such as concomitant drugs interactions, bleeding risk, lifestyle issues, poor compliance, allergy (or other reactions to Warfarin e.g. alopecia), or if the time within their therapeutic INR range (TTR) on Warfarin falls below ≥65%, are considered suitable for scoring for DOACs (Clemens *et al*., 2013).

Warfarinised patients are offered regular blood tests on a finger prick or venous sample to calculate the time it takes for the blood to clot, and the subsequent Warfarin maintenance dose is further adjusted according to these results (as in Figure 2.14). The effect after a single dose of Warfarin can last for as long as 5-7 days (Keeling *et al.,* 2011). Lack of familiarity with the interactions between Warfarin

and other drugs may lead to clinically relevant and avoidable increases or decreases in prothrombin time (PT).

Figure 2.14
Warfarin Clinic-Monitoring Machines
(http://www.elitmedical.com/images/technoclone/thrombotrack_duo.jpg, n.d.)

The following circumstances have an exaggerative effect on Warfarin and may indicate the requirement of a reduction of Warfarin dosage:

- Loss of weight
- Acute illness
- Cessation of smoking
- Excessive alcohol consumption

The following circumstances have a reducing effect on Warfarin and may indicate the requirement of an increase of Warfarin dosage:

- Weight gain
- Diarrhoea
- Vomiting
- Antibiotics

2.13 Contraindications for Warfarin

According to Connelly *et al*., (2013) Warfarin is haemo-dynamically unstable and has a wide spectrum of interactivity with foods, alcohol, nutrients, other drugs (e.g. antibiotics) and herbs. Warfarin is also affected by the following:

- Alteration of intestinal flora (increased INR)

- Fever (increased INR)
- Hepatic failure (increased INR)
- Thyroid function (hypo decrease INR, hyper increase INR)
- Stress (increase INR)
- Smoking (decrease INR)
- Non-compliance (may increase or decrease INR)

Therefore, Warfarin must be constantly monitored closely and tested routinely.

Additionally, Warfarin is contraindicated in the following situations and should not be administered:

- Allergy or hypersensitivity to any of the active ingredients in Warfarin.
- Following or during and haemorrhagic stroke episode.
- Following or during any significant bleeding episodes.
- Within 72 hours of any major surgery which carries the risk of severe bleeding.
- Within 72 hours post-partum.
- During pregnancy, especially the first and third trimesters); and during labour.
- With concomitant drugs which are known to be increase the risk of bleeding, e.g. anti-platelet medication and aspirin etc. See list below in Figure 2.15.

Figure 2.15
Drugs that interact with Warfarin
Patel, 1999 & Scowcroft & Cowie 2014

It is widely accepted and published that Warfarin is a particularly effective drug for oral anticoagulation. However, due to its narrow therapeutic range, the margin between Warfarin efficiency and Warfarin toxicity is also very narrow. Added to this is the fact that the patient's response to Warfarin varies widely between patients. This means that there is no 'one size fits all' or fixed dose for all patients. The measurement of Warfarin (the INR) is used to maintain the haemostatic balance between risk of thrombosis, stroke, or venous thrombosis (thrombophilia) and the risk of bleeding (haemophilia).

Other common food and drugs that interact with Warfarin are shown below in Figure 2.16.

Warfarin: Food and drug interactions

	Increase anticoagulation		Decrease anticoagulation
Foods	St. John's Wort Ginseng Garlic		Gingko biloba Avocado Spinach Brocolli
Drugs	Acetaminophen Amiodarone Androgens Allopurinol Aspirin (high dose) Cimetidine Clofibrate Chloramphenicol Disulfiram Dipyridamole Erythromycin Fluconazole Fluoxetine HCl Glucagon	Indomethacin Liquid paraffin Metronidazole Phenylbutazone Phenytoin Probenecid Phenformin Quinidine Sulfinpyrazone Tamoxifen Tolbutamide Thyroid hormone Trimethoprim-sulfamethoxazole	Antithyroid drugs Barbiturates Carbamazepine Cholestyramine Gluthimide Griseofulvin Oral contraceptive Rifampicin Sucralfate

Gogna A, Arun S. Oral Anticoagulation in Clinical Practice. JIACM 2005;6(1):53-66

Figure 2.16
Warfarin Food and Drug Interactions (Gogna & Arun,2005)

The benefits of Warfarin can be summeries as:

- Is extensively studied
- Clearance is not affected by renal function
- Inexpensive
- Poor adherence is rectifiable.
- Can be used for many indications
- Antidote available for effect reversal
- There is much clinical experience
- Efficacy is well established

Warfarin is also not without adverse effects. These can include:

- Nausea and vomiting
- Haemorrhage
- Alopecia
- Rash

- Diarrhoea
- Skin and soft tissue necrosis
- Priapism
- Hypersensitivity/Allergy

2.14 Cytochrome P450 CYP2C9

Cytochrome P450 is a group of more than 50 enzymes which are responsible for the metabolism of many medications including Warfarin. It is also essential in assisting the liver to detoxify. Some genetic variations of the cytochrome P450 genes can result in a varied metabolic response of the patient to medications such a Warfarin. Commonly Warfarin patients who have cytochrome P450 variants may have responses to Warfarin which vary from reduced activity in metabolising the drug to complete inhibition of Warfarin. This may lead to increased toxicity in the liver and peripheral circulation, haemorrhages, or death. Fifty-five percent of Warfarin patients who have poor control of the drug have been found to have a genetic polymorphism of their CYP2C9 gene, which is responsible for the metabolism of Warfarin (Sconce *et al*., 2005). Therefore, the AF patient's benefit-risk ratio for DOAC and Warfarin is paramount in determining the clinician's decision to switch (Camm *et al*., 2010).

2.15 Warfarin Self-Testing

NICE in 2012 ran a small pilot study in which Warfarin patients self-monitored at home and digitally transmitted the results back their GP or local anti-coagulation centre. The trial had some successes in the younger age groups (under 50 years), who were on Warfarin and only a marginal uptake in the older population of Warfarin patients (NICE, 2014a). Self-monitoring of OATs involves the use of a small hand-held device. See Figure 2.17. The patient pricks their finger to acquire a single drop of blood, which is then dropped onto the machine to measure Warfarin level and generate an INR result. The patient can then seek Warfarin dosage adjustment advice from a medical professional if the INR is outside of their own reference range. Often patients may adjust their own Warfarin dose based on their own experience of taking Warfarin long-term.

Figure 2.17
Warfarin Self-Monitoring Device
https://heartveinvascular.com/heart/advanced-lipid-and-inr-monitoring/

Self-monitoring encourages self-care and can promote a positive approach to managing long-term condition and is a key NHS initiative. Self–monitoring is a convenient way to check INR at any time and avoids the need for Warfarin patients to attend clinics and the waiting time for their results.

2.16 The Patient Experience.

Much has been written in the last ten years about the value of engaging patients in their own treatment. This arose from a recognition of the absence of the patient's voice in previous decades. Coulter (2011, p3) quotes the Secretary of State for Health 2010:8.

'The NHS scores relatively poorly on being responsive to the patients it serves. It lacks a genuinely patient-centred approach in which services are designed around individual needs'.

(Richards *et al*., 2015) concur with this statement, reporting that patients should be led away from dependency on professionals to be confident self-managers, particularly the frail with long-term, multiple conditions. Coulter lists four areas that

particularly lend themselves to improvement with more patient input: patient's knowledge; patient's experiences; services utilization; and health behaviour status. Each relates to the study presented in this thesis in varying degrees. In the first area of focus the patients experience, (knowledge of condition and long-term complications, self-care knowledge, comprehension of information, and recall of information) are pertinent here. In the second area, the patient's experience (doctor-patient communication, confidence to manage health problems; self-care activities) is also key. Coulter's third area, service provision (quality of life, psychological well-being, treatment adherence, system control and functional ability) is, in varying degrees, at the core of this study's aim and objectives. Finally, Coulter's discussion on the education of healthcare professionals is also regarded as key to improved patient care; just knowing what patients want and need is not enough, staff education must follow newly found knowledge about patient's needs. This study aims to contribute to staff education.

2.17 Study Background and Originality

Research into the long-term use of Direct Oral Anticoagulants (DOACs) is still relatively limited, as the first was only introduced in the United Kingdom in 2010 and validated for use in 2012 (Patel *et al*., 2019). As such, there are no key policies regarding their long-term use or associated quality of life changes in patients over 65. In fact, each NHS trust or primary care facility uses their own local set of guidelines on the use of these new drugs and has their own set of rules that govern how and when patients currently on Warfarin are switched to the new drugs. Whilst the pharmacokinetics of these drugs may be well researched, the speed with which these medicines and technologies are being introduced has meant that little is known about the long-term effects of these drugs, particularly in the over 65s.

Testing Warfarin in an anti-coagulation clinic for over 8 years has resulted in the author having a clear understanding of some of the challenges faced by the Warfarin patients, who often have other commitments such as jobs, children, grandchildren, partners, the care of elderly relatives and social activities to attend. From brief conversations with patients in the clinic, it was noted that having to attend the clinic

once or twice a week for monitoring also had an impact on planned activities which may last more than 3 or 4 days, such a holiday. The social impact of clinic attendance for the over 65s can therefore be complex. They often have transportation arranged by the hospital, and so try to arrange other non-Warfarin related hospital appointments for the same day. The visit to the clinic may also give opportunities for long conversations with other patients or the scientist conducting the blood test, as frequently these elderly patients are housebound, widowed or may be lonely. Often their Warfarin may be poorly controlled due to a variety of reasons such as alcohol consumption, interaction with concomitant drugs, or food interactions particularly with foods rich in vitamin K. Also, the over 65s may forget to take Warfarin, or accidentally take the dosage twice. Over-Warfarinisation has an increased risk of an intracranial haemorrhage, and therefore requires immediate quantitation in the laboratory and reversal. Patients may also require hospitalisation and monitoring during the reversal process.

The number of patients living past 65 is increasing, and the number of patients living with AF is expected to double by the year 2040 (Ganetsky *et al*., 2011). Anticoagulation clinics are already struggling to meet the increasing demands of testing oral anticoagulated patients. Patients may not therefore receive the best quality of service due to recent national cuts in NHS finances, with consequent time constraints and staffing shortages. However, the success of using these Direct Oral anticoagulants may result in a standardised level of care as well as an improvement to the services currently offered to patients on long term anticoagulant therapy. Nevertheless, the social impact on the removal of these clinics for the over 65s needs to be explored. The financial implications of the implementation of these Direct Oral drugs are also discussed though are not the focus of this study.

From a laboratory perspective, there is no linear value associated with the DOACs, coagulation assays values and drug dosage. The international normalised ratio (INR) currently used for testing Warfarin is not sensitive enough for DOACs. With so little in-depth knowledge known about the Direct Oral drugs and with such limited resources in the NHS, particularly in small district general hospitals, there is a need to examine whether these new drugs will provide a better quality of life for patients. What impact will the lack of testing or monitoring have on patients' health and social

well-being? Would the investment made in introducing costly Direct Oral drugs be better spent improving clinic services? It is therefore the author's intention to ascertain whether this key change in the way oral anti-coagulants are monitored has significant impact on the quality of life of patients who are over 65 years.

There is undoubtedly a cost/quality of life equation to be addressed. Somerset NHS trust estimates that Dabigatran will cost £9.5 million per year as opposed to the current cost of £1 million for Warfarin patients - including prescription and clinic services (*NOAC innovation in anticoagulation report.* 2014). So, it is important that we know more about the positive impact on the new medications and identify what are the main concerns of the patients and clinicians regarding these Direct Oral drugs. For example, should there be a rapid laboratory diagnostic test available as standard procedure for emergency situations? Would this reduce anxiety or save lives? There is no published research worldwide which looks at the long term quality of life of patients receiving anticoagulation drugs who have switched from Warfarin to the new DOACs. This gap in the literature demonstrates the originality of this paper. The quality of life as well as social and personal implications of any treatment are important, as research outlined above has already demonstrated the vital role of compliance and patient information provision in other areas of treatment as well as in treatment outcomes. One such example is an article from the Journal of Public Health in which the authors determined that '*sustained compliance was due, in part, to a number of individuals being afforded the opportunity to reconFigure their medications*' and '*indicates that patients experiencing side effects…. are more likely to remain adherent if GPs are willing to listen to their concerns and review medication*' (McNaughton and Shucksmith, 2015).

The exploration of the patient's experience with regards to compliance and long term use of this treatment in patients over 65 is explored here for the first time. By 'experience' it is meant the patient's sense of life quality issues such as well-being, side effects of the medication, and the challenges they face with self-monitoring and compliance. This research provides information for clinicians responsible for the management of the oral anticoagulation service at the London NHS Trust where the study was conducted, and elsewhere with the aim of improving the patient

experience of this demanding medication regime. The research has explored, from both the patients' and clinicians' perspective, the patients' quality of life after switching to DOACs with respect to the clinical, personal, and social issues that may arise. It has also looked at the impact on the patient's overall perception of their health and wellbeing, and the issues which relate to taking a lifelong medication such as Warfarin or DOAC, as well as the impact of the switch-over on their compliance with treatment.

2.18 Research Aim and Objectives

The principal aim of the study was to explore the patient's perspective of switching from a life-long medication on Warfarin to one of three Direct Oral Anticoagulants (Apixaban, Rivaroxiban or Dabigatran), none of which required monitoring and have fewer side effects than Warfarin as well as fewer drug and food interactions. Of primary focus was the impact from the patients' perspective of the substitution on the daily life. Additionally, the clinicians' knowledge of the impact of the switch on their patients' lives was also explored with the aim of developing a more patient focused anticoagulant service.

Objectives:

1. To describe a sample of 20 patients' perceptions and understanding of their treatment using individual interviews at the time of the switch and at 90 days afterwards.
2. To explore the Consultant's, nurses' and pharmacists' level of knowledge relating to issues faced by the patients with regards to safety and compliance, as well as their awareness of the social implications of switching to DOACs through the use of interviews.
3. To ascertain the impact of switching on a sample of 50 patients by assessing their perceived quality of life and stress levels at three points: at the switch, then at 30 and 90 days into the new treatment regime, through the use of standardised questionnaires.

4. To explore the effects sex and age may have on the participants' quality of life and perceived stress level.
5. To produce recommendations to provide a more effective and personalised patient-involved treatment programme for older AF patients.

The following chapter sets out how the research was achieved: the research approach, sampling strategy and methods used.

Chapter 3 - Research Approach and Methods

3.0 Introduction – the research approach and methods

When this research was in the design stage a purely qualitative study was the approach decided upon. This was because the author had noted that nearly all the literature on this subject was clinical or quantitative in nature and there had been few opportunities for the patient's voice to be heard in its natural form. This study would, therefore, adopt an 'inductive' reasoning approach - drawing meaning from specific observations (the interviews) as opposed to 'deductive' reasoning - testing an established theory, Robson (2011). This study attempts to fill the gap in the literature discussed in chapter two. Green and Thorogood (2005) call this the 'deficit model' and state that 'the value of qualitative methods to public health lies in their ability to answer important questions that cannot be answered from a quantitative perspective' (p22). The 'usefulness of this approach is to sensitize professionals to the patient's point of view' (p23).

However, this position changed as a result of discussions with Dr Abdul Shlebak, the haemostasis and thrombosis consultant in charge of the clinic at St Mary's where the patients were located. His concern was that a purely qualitative study would not gather all the potential data from the patients and that it would be seen, in the medical world at least, as less valuable research than a study which included some quantitative data and statistical analysis as evidence of change. This view is in line with commentators' observations that research in healthcare has been traditionally quantitative or 'positive' in nature with a bias towards measurable data (Doyle *et al.,* 2009). Given that the author of the current study hoped to influence practice in the clinical field of haematology, producing results that were considered to be 'credible' in that field was important. On reflection, the author and supervision team agreed that that producing a standardised, quantifiable data set would indeed support the primary method of individual interviews. It would also allow the sample size to be larger for part of the study: 50+ patients not 20 which was the interview sample size. A mixed-method study was, therefore, undertaken.

Pragmatism is the paradigm underpinning this research. Robson (2011) cites Onwuegbuzie and Leech (2005) who hold that 'pragmatic researchers' are simply those who learn to utilize and to appreciate both quantitative and qualitative research'

p171. Doyle *et al*., (2016) support this view arguing that it 'offers health researchers the freedom to choose the best methods to answer the research question to hand (Bishop, 2015a), advocating for a balance between subjectivity and objectivity throughout the research' p625. But Robson (2011) cautions researchers employing mixed-methods not to be encouraged down the 'anything goes' route that he fears pragmatism may seem to allow' (p29). 'There is a danger of being open to the criticism of carrying out incoherent projects lacking a rationale and of dubious validity' (p171). The research reported here although mixed-method is a relatively small study using only two methods both of which address the same issues but from a different perspective.

Doyle *et al*., (2016) offers a clear definition of mixed-methods research given by Creswell (2015). 'An approach in which the researcher collects, analyses and interprets both quantitative and qualitative data, integrates the two approaches in various ways and frames the study within a specific design' p624. The secondary method used in this study were two health-based questionnaires: The Perceived Stress Scale (PSS) and the Short Form 36 Health Survey, (SF36) which are discussed in full below. The interviews were semi-structured and would generate qualitative material on the general experiences of the respondent's life on anticoagulants. The questionnaires, on the other hand, allowed for the collection and measurement of group and subgroup data focused on the patient's feelings about their health in general and, more specifically, their stress levels at three time points during and after the switch of medication. Any change in perception over the three-month research period would be captured.

Mixed-method research is now common in healthcare, but this was not always the case. Doyle *et al*., (2009) outline the struggle mixed-methods research has had to find acceptance. The days of a strict demarcation between the traditional positive (quantitative data) paradigm and the emerging naturalistic (qualitative material) approach softened during the 1980s and mixed-methods were increasingly found to be useful in a wide range of social science settings. Its popularity grew, in part, due to the encouragement of interdisciplinary research. Doyle *et al*., (2016) offer a list of rationales for a mixed-method approach. To summarise:

Triangulation: different methods may be mutually corroborated. (Convergence)

Expansion: a qualitative method may offer an explanation of the quantitative data.

Exploration: an initial qualitative phase is required to develop secondary quantitative tools.

Completeness: it provides a more detailed and comprehensive picture of the phenomena under study.

Offsetting weaknesses: the limitations of each method can, to some extent, be neutralised by the strengths of the other.

Different research questions can be asked: both quantitative and qualitative questions can be asked.

Illustration of findings: using a qualitative approach to illustrate quantitative findings (p624).

Several of these factors can be applied to this study. A more complete picture of the patient's perspective was sought than could be produced with interviews alone. The questionnaires would offset the limitations of the individual interview method by providing a group analysis of standardised data to support the personal stories. The questionnaires would also answer different research questions, one focused on the participant's self-reported general health and the second had a particular focus on stress. To complete the picture, the qualitative data would, it was hoped, both explain and illustrate the quantitative findings.

Creswell (2015) offers three mixed-method designs: convergent, explanatory sequential and exploratory sequential (Doyle *et al*., 2016, p625). The mixed-method design used here is a *convergent design* (concurrent). 'It is used to address one overarching research question but employs more than one method when looking for convergence affording a more complete understanding of the phenomena' (Doyle *et al*., 2016, p626). Findings from the qualitative data (interviews) and quantitative data (questionnaires/scales) were compared and contrasted during the interpretive stage of this design.

3.1 Mixed-method health related studies are now numerous and reach across the whole field of healthcare, being particularly popular when exploring patient's perceptions of their quality of life. They are now also increasingly used within the field of anticoagulant research. For example, Barns *et al*., (2017) employed semi-structured interviews and a survey to study the personal barriers to integrating direct oral anticoagulants into outpatient clinic care. Bhat *et al*., (2019) used retrospective and prospective medical records, and a prospective patient survey, to evaluate the real-world use of anticoagulants with ischaemic stroke patients. A study that also included clinic staff was undertaken by Barns *et al*., (2019). They used patient interviews and staff computer assisted surveys to explore the potential of reducing the frequency of INR test clinic visits among patients who were stable on Warfarin. A study which is close in focus to the study reported here is by Bajorek *et al.,* (2018). Their aim was to explore and compare the level of patient satisfaction with Warfarin and the new anticoagulants; a vignette-based questionnaire and patient interviews were used.

Despite its popularity, mixed-method research is not without its problems. Bressan *et al.,* (2017) provides a critical review of mixed-methods research in nursing. They found it to be increasingly popular but that, at times, training in mixed-methods was limited and inconsistent and that methods may be applied in a less than rigorous way. Concerns were also expressed about a novice researcher's potentially poor choice of tool and weak administration of the chosen instruments. To ensure the correct choice of quantitative data collection instrument here expert help was sought from Dr Trudy Edginton (Westminster University) for the selection of the health questionnaires. She also provided training in their administration and data analysis Therefore, in the author's view, the charge of having no underpinning rational is not a risk here.

3.2 Research Methodology

The outline of the data gathering process is shown in Figure 3.1.

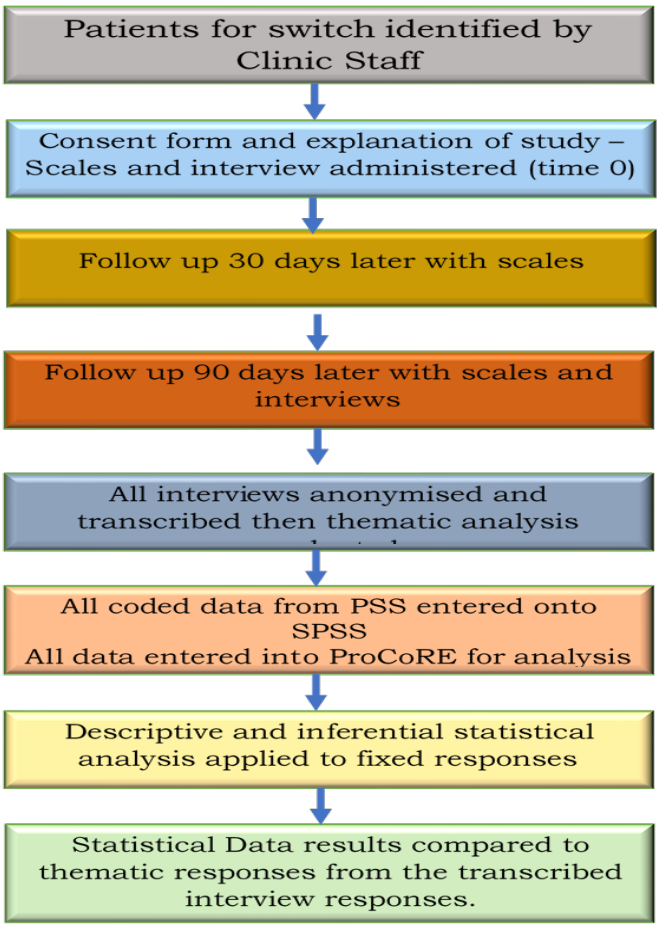


Figure 3.1
Research Process outline

The population from which the sample was drawn are the current AF patients within the Imperial Hospital Trust. The AF population accounts for approximately 85% of the total 1394 orally anti-coagulated patients (St Charles site 262, St Mary's site 820, Queens Park site 112 and Hammersmith site 200). Of these more than 70% are over the age of 65 (829 patients). The numbers are approximate, as patient numbers change due to being discharged from the anti-coagulation monitoring centres for reasons such as clinical requirement for the patients to be switched to DOACs or else moved to other forms of anti-coagulation.

The target group is therefore, the over 65s attending the clinic and the range of problems that they can encounter related to their treatment. The inclusion criteria were 1) being on Warfarin for more than 6 months (established long term use) and 2) needing to switch from Warfarin to any of the 3 DOACs: Dabigatran, Apixaban or Rivaroxaban for clinical resaons. The exclusion criteria were patients who were not switching medication, those under 65ys and those covered by the Mental Capacity Act. As this last group of patients are generally treated at home, they are unlikely to appear in clinic. In addition, patients who speak English as a second language and require an interpreter were excluded. Although a relative or carer could assist with this task eliminating bias can be an issue. Within the current funding constraints, it was not possible to translate the questionnaire and supporting material into other languages. After this research is completed, there may well be a case for further research focused on these excluded groups of patients.

3.3 Recruitment and the sample frame

Imperial Trust anti-coagulated patients on Warfarin attend a designated outpatient centre at Queens Park Health Centre (QPCH), Hammersmith Hospital (HH), St Mary's Hospital (SMH) or St Charles Health Centre (SCHC). This is weekly, biweekly, or monthly, depending on the stability of their results as well as changes to their medical condition or concomitant medical regimen (e.g. taking antibiotics which interfere with Warfarin). The patients are then subjected to a finger prick blood test to monitor Warfarin levels, which are then recorded into the electronic database DAWN® or INRstar®. This session is where the researcher recruited the research sample. The database not only records the patient's results, but trends changes in these results and calculates the next Warfarin dose adjustment for the patient. This is plotted on a graph and helps determine the time in therapeutic range (TTR). Patients outside the TTR for ≥65% over the last 12 months are referred to the clinician for a switch by the anti-coagulation nurse, who can then inform the researcher of patients who have been invited to attend for switching from Warfarin to DOACS. Surprisingly, there is no national database of patients who have been switched from Warfarin to DOACs; this may because DOACs do not require regular monitoring and testing.

It is difficult to establish a precise projection of how many patients would be switching to DOACs, as patients are switched when they are not coping on Warfarin. Switching is not uncommon, but is also not easy to predict. Difficulties arising with Warfarin control are usually due to changes in patient's health circumstances which can cause interference with the Warfarin from concomitant medications or from the physiological condition itself.

According to the chief coagulation scientist in the Imperial Trust, since December 2012 there have been 148 recorded requests for DOAC testing by clinicians within the laboratory for reasons such as DOAC associated bleeding events, or that the DOAC plasma level is required for unrelated surgical interventions, representing almost 18% (17.85%) of the total imperial DOAC patients. Patients who are deemed to be too frequently outside their therapeutic range for Warfarin, and therefore suitable for switching, are assessed over a period of 6 months and are therefore commonly known to the anti-coagulation team. I looked at the number of patients in the trust who had been switched over the past 4 years and estimated that 50 could be recruited within 12 months or sooner.

Condition	$CHADS_2$ score	Points	CHA_2DS_2-VASc score	Points
Congestive heart failure (or Left ventricular systolic dysfunction)	C	1	C	1
Hypertension: blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	H	1	H	1
Age ≥75 years	A	1	A_2	2
Diabetes Mellitus	D	1	D	1
Stroke or TIA or thromboembolism in history	S_2	2	S_2	2
Vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque)			V	1
Age 65–74 years			A	1
Sex category (i.e. female gender)			Sc	1

This table shows the components of the $CHADS_2$ (Gage et al., JAMA 2001 [36]) and CHA_2DS_2-VASc scores (Lip et al., Chest 2010 [41]) tools to assess stroke risk in patients with AF. These risk assessment tools help to determine who should and who should not receive anticoagulation. CHA_2DS_2-VASc improves risk stratification in patients with $CHADS_2$=0 or 1, and allows for identification of patients at truly low risk.

Table 3.1
$CHADS_2$/CHA_2DS_2-VASc Score Chart Lip et al 2010 page 41

3.4 Interviewing older people

Research shows that interviewing older people presents several challenges for all concerned. These include physiological changes such as memory loss, deteriorating health, loss of vision, and hearing impairment The interviewer(s) need to prepare for these, allowing plenty of time for interview, and ensuring written material is clear with large print when necessary (Connolly and Spyropoulos, 2013; Lane and Lip, 2009; Davis *et al*., 2012). In this study the interviews were conducted over a relatively short period of time, so memory loss, deterioration of hearing, sight or medical condition were not an issue. Each patient was assessed by their medical consultant who deemed them fit for interview. The researcher was aware of the possibility of tiredness and checked from time to time with the patient that they were happy to continue.

The patients were approached by the researcher or named clinic nurse as they arrived for their regular appointment until a sample of 50 was achieved. Only one person declined to participate. Indeed, six additional patients volunteered to participate and were interviewed bringing the total up to 56. They were recruited according to the *convenience* method of arriving the quotas required (Neuman and Robson, 2012; McNaughton and Shucksmith, 2015). This included choosing the nearest and most convenient persons to act as respondents (Neuman and Robson, 2012). The research aims and the terms of their involvement were explained to them, and they were interviewed after their next appointment or as soon afterwards as possible depending on the researcher's availability.

The patients attending this clinic do so by appointment made by the anti-coagulation team to monitor their Warfarin, therefore assistance in identifying potential patients was required from a member of the anticoagulation team. The patient was given time to consider and was approached again at the next appointment for a decision. If, however, they responded positively right away, a time was made for the interview there and then. They were assured that participation was voluntary and that there would be no difference to their treatment if they participated or not, and that they could withdraw from the study as any point if they wished. Permission was asked to maintain further contact for later interviews. The approach was made easier by the

familiarity of the team nurse and researcher with the patient; however, the questionnaires and interviews were conducted only by the researcher. The consent form would be signed at the start of the interview.

The second interview, 90 days after the switch, reflected and built on the information gathered at interview one in the light of new experiences, and recorded any changes to the patient's wellbeing after switching medication. It should be noted that these interviewees had also completed the scales at the 30-day point. Only two of the patient interviews were completed by telephone, the rest were face-to-face. Respondents were given the opportunity to remain anonymous and were assured of the confidentiality of their responses. The study invitation letter, study information sheet and reminder letter can be found in Appendix Six.

3.5 The Sample - interviews and questionaires

Twenty patients, 10 men and 10 woman were interviewed. About half lived alone, others had a partner who required care. They were a diverse group with regards to occupation counting among them retired teachers, a vet, baker, barrister, van driver and architect as well as a still working solicitor and publican. For the interview, semi-structured questions were used as a conversation starting point, and the patients were encouraged to talk freely. Exemplar transcripts of these conversations can be found in Appendix 15. Of note is that information pertinent to the study (such as age and reason for switching to DOAC) was provided by the anti-coagulation nurse rather than the patient. Therefore, some of the questions had to be rephrased or skipped in order to have a naturally flowing conversation.

The sample size of 56 was dictated in part by the need for the minimum of 50 cases required for the questionnaires to be scientifically valid for analysis, but six additional patients asked to be included; all 56 patients completed scales at 3 time points. A minimum sample of 50 patients is based on the validation data for the SF36 instrument; according to Ware et al 2004, between 24 and 50 patients are needed as a sample size for the study findings to be statistically robust (Ware, 2004). As further validation, a review over a period of 10 years and based on over 9,800 publications, shows that 50 is the most common respondent sample size with this instrument (Turner-Bowker *et al*., 2002).

The patients' perception of Quality of Life changes (QoL) were assessed using 3 data points and two questionnaires as outlined in Table 3.2.

Patient	Questionnaires/sales: SF 36 and the PSS.	Face-to-face Interview
DOAC (switched Patients) Former Warfarin patients before switching, which is at the point of referral for switching. *	56 patients subdivided by age group and sex. The scales were to be administered by the researcher.	20 of these 56 patients, subdivided by age group and sex, were also interviewed by the researcher (selected according to the availability of patients).
Follow up (30 days)	Same 56 patients	
Follow up (90 days)	Same 56 patients	20 re-interviewed

Table 3.2
Research Sample outline

The Perceived Stress Scale (PSS) and the Short Form 36 questionnaire were used at the baseline data collection point (before switch), and feeling of stress measured post switching, at 30 days, and 90 days later. After 90 days the patient's prescription would be passed to the GP, and at this point the final scales were administered. This was not only to ascertain the patient's views on the new medication but also to reveal whether they had had any adverse (e.g. bleeding) events associated with the new drugs. After the first administration of the scales the volunteers were given the option of completing the scales by face-to-face contact or by telephone/skype, though all preferred a clinical setting.

3.6 Piloting the instruments

The scales used in this study are established validated questionnaires that have been used in many studies worldwide, so it was not necessary to pilot them with

regards to content. However, the instruments were piloted for the purpose of establishing an estimated time-frame in which the patients would be able to comfortably complete the scales. They were piloted on colleagues in the clinic and with my two supervisors. Feedback about the ease of completing the questionnaires was also encouraged, no major changes were required. Recent examples of SF-36 studies include:

1. 'Satisfaction, quality of life and therapy adherence assessment in real life patients transitioning from vitamin K antagonists to direct oral anticoagulants' (Serrao *et al*., 2020).
2. Knowledge, Adherence, and Quality of Life among Warfarin Therapy Users (Matalqah *et al*., 2019).
3. 'Comparing quality of life and treatment satisfaction between patients on Warfarin and direct oral anticoagulants: a cross-sectional study', (Ng *et al*., 2019).

3.7 Description of the Perceived Stress Scale (PSS)

The Perceived Stress Scale (PSS) is an established psychological test used to measure an individual's perception of stress in his or her life. The instrument was originally developed in 1983 by Sheldon Cohen and is used to determine how different situations affect feelings, an individual's overall stress levels, stress triggers and the perceived stress in a person's life. It is a one-page scale and takes less than two minutes to complete. There are 10 questions enquiring about the feelings and thoughts of the person during the last month. Some of the questions are very similar to each other but with subtle differences. In such an elderly population there are likely to be psychological age related changes such as bereavement and loss, living alone, depression and loneliness (Bowling and Gabriel, 2004; Lane and Lip, 2009; Wenger, 2002). These life factors may impact on the patient's perception of their level of coping with medication. An example of the PSS questionnaire in use in this field is the work of Fumagalli *et al*., (2014) who explored the psychological effects of treatment with new oral anticoagulants in elderly patients with atrial fibrillation using the PSS scale to measure the level of stress.

Each scale item is rated on a 5-point range from 'never' (0) to 'almost always' (4). PSS-10 scores are obtained by reversing the scores on the four positive items, for example, 0=4, 1=3, 2=2, etc., and then summing across all 10 items. Items 4, 5, 7, and 8 are the positively stated items. The choices for the perceived stress scale questions include never, almost never, sometimes, fairly often, and very often. The PSS scale is shown in Appendix 11. Higher scores indicate greater perceived stress. Research has found that high stress groups usually have a stress score of around 20 points or greater. High psychological stress is associated with high blood pressure, higher BMI, larger waist to hip ratio, shorter telomere length, higher cortisol levels, suppressed immune function, decreased sleep, and increased alcohol consumption. These are all important risk factors for cardiovascular disease. Although scores on the 14-item PSS tend to exhibit good reliability estimates across literature, four of the items tend to perform poorly when evaluated using factor analysis. As a result, the PSS is usually implemented using the 10-item version. Cohen *et al*., (1988) further reduced the PSS to a four item form for quick measurements; however, scores on the 4-item PSS tend to exhibit lower reliability estimates than researcher would like.

Potentially stressful life events are thought to increase risk for disease since the demands these events impose tax or exceed a person's adaptive capacity (Lazarus & Folkman, 1984). In turn, the perception of stress may influence the pathogenesis of physical disease by causing negative affective states (e.g., feelings of anxiety and depression), which then exert direct effects on physiological processes or behavioural patterns that influence disease risk (Cohen *et al*., 1983; Cohen *et al*., 2007). The Perceived Stress Scale (PSS) measures psychological stress associated with sex, age, education, income, employment status, and a number of other demographics. Before the development of the PSS, assessment of stress tended to focus on objective indicators (e.g., frequencies) of specific stressors (e.g., chronic illness, family loss, new family members). This tendency subsequently overlooks the influence an individual's subjective interpretation of a stressor might have upon the experience of a stressor. Cohen *et al*., (1983) viewed the void of the subjective component in assessing stress as an unwanted quality and developed the PSS in response. Specifically, the PSS is based upon Lazarus's original

transactional model of stress, which argues that the experience of a stressor is influenced by evaluations on the part of the person as to how well they can manage a stressor given their coping resources. The 14 items of the original PSS are purported to form a uni-dimensional scale of global perceived stress (Lazarus, 2000).

Data from the returned questionnaires were coded and entered into SPSS 25.0, which was then used to generate statistical analyses. The coding process and subsequent statistical analyses will now be described. The perceived stress scale and the Short Form 36 Medical Outcomes questionnaire were both structured and pre-coded for ease of analysis, it also included several questions with a binary or categorical response format. This involved pooling of data from UK quality of life studies which had used the SF-36. A non-probability sample was drawn which was considered appropriate because the research aims to explore the perceptions of the patients in this hospital 'not to make statistical generalizations to any population beyond the sample'. (Neuman and Robson, 2012, p274). A quota sampling was used 'with the aim of including representatives of the various elements of a population, usually in the relative proportions in which they occur in the population'. (Robson and McCartan, 2016) p274. In other words, people who were typical of the clinic population at the point of being 'switched'.

Age and sex are the categories, so patients fall into two groups: male (n=29) and female (n=27) each with three age subgroups: 65-74ys (n=19), 75-84ys (n=21), and >85 years, (n=16). The mean age was 79.5. All patients who were identified as meeting the inclusion criteria were invited to participate and continued to be approached until the quota – 12 or 13 cases in each group - was achieved. The age division is to explore whether over 75-year olds experience the treatment regime in a different way – more or different personal problems from those who are slightly younger. Likewise, male/female subgroups were identified to see if any difference in perception or experience exists between the sexes. See Appendix 15 table 16 for the SPSS calculations.

3.8 Perceived Stress Scale Scoring and analysis

PSS scores are obtained by reversing the scores on the four positive items as described above, and then summing across all 10 items. Scores around 13 are considered average. Individual scores on the PSS can range from 0 to 40, with higher scores indicating higher perceived stress.

- Scores ranging from 0-13 are considered low stress.
- Scores ranging from 14-26 are considered moderate stress.
- Scores ranging from 27-40 are considered high perceived stress.

Scoring the Perceived Stress Scale requires a simple calculation where a number value is assigned to each possible choice a respondent could choose. The numbers for the possible responses coincide with how much that particular response correlates to stress for the question. For example, an answer of 'never' would be assigned a score of four for the question 'In the last month, how often have you felt confident about your ability to handle your personal problems'? However, for the question 'In the last month, how often have you felt that things were going your way'? the 'never' response would be assigned a value of zero. By totalling the scores, researchers, psychiatrists, and other health care providers can get a relative idea of how stressed the individual feels in his daily life. This can help with diagnosis of physical and mental problems, since high levels of stress can contribute to high blood pressure, heart problems, appetite changes, depression, and many other mental and physical conditions. If an individual is highly stressed, treatment may include therapy or relaxation techniques to help lower the perception of stress and allow the body and brain to heal. Data from the returned PSS questionnaires was coded and entered into SPSS 25.0, which was then used to generate statistical analyses. The coding process and subsequent statistical analyses will now be described. The impact of the patient's age and sex on the patient's overall self-perception of their health was assessed using one way ANOVA.

3.9 Description of the Short Form 36 Scale (SF-36), scoring and analysis.

The SF-36 is an indicator of overall health status and is also well validated. This instrument addresses health concepts from the patient's perspective. It is a structured, self-report questionnaire that a patient can complete with little or no counselling from an interviewer. SF-36, as provided by Ware *et al*., (2004) exists in various revised forms. Quality of Life studies, using the short form 36 (SF-36) instrument, have been published in over 41,000 surveys worldwide (Ware and Sherbourne, 1992; Dixon *et al*., 2019). The SF-36 questionnaire contains 36 items that assess patient's health status and its impact on their lives:

Physical Functioning (**PF**) 10 items; Physical Role limitations (**RP**) four items; Bodily Pain (**BP**), two items; General Health perceptions (**GH**) five items; Energy/Vitality (**VT**) four items; Social Functioning (**SF**) two items; Emotional Role limitations (**RE**) three items; and Mental Health (**MH**) five items. See Figure 2.

Each scale is graded from 0–100 with 0 being the maximum disability, or in this case the least improvement of Quality of Life, with 100 being the best outcome. Therefore, higher scores indicate higher HRQoL. A scoring algorithm is used to convert the raw scores into the eight dimensions listed above. The scores are transformed to range from zero, where the respondent has the worst possible health, to 100 where the respondent is in the best possible health. All scales contribute in different proportions to the scoring of both PCS and MCS measures, which are composite QoL scores of mental and physical health. The correct calculation of SF-36 summary measures of PCS and MCS requires the use of special algorithms, which are strictly controlled by a private company (QualityMetric - OPTUM).

The two summary scores are derived from the Physical Component Summary (PCS) score and the Mental Component Summary (MCS) score. PCS and MCS scores are an aggregation of individual scores. The eight scaled scores are weighted sums of the questions in each section. Scores range from 0 - 100

Lower scores = more disability, higher scores = less disability

Sections:

- Physical functioning
- Physical role functioning
- Bodily pain
- General health perceptions
- Vitality
- Social role functioning
- Emotional role functioning
- Mental health

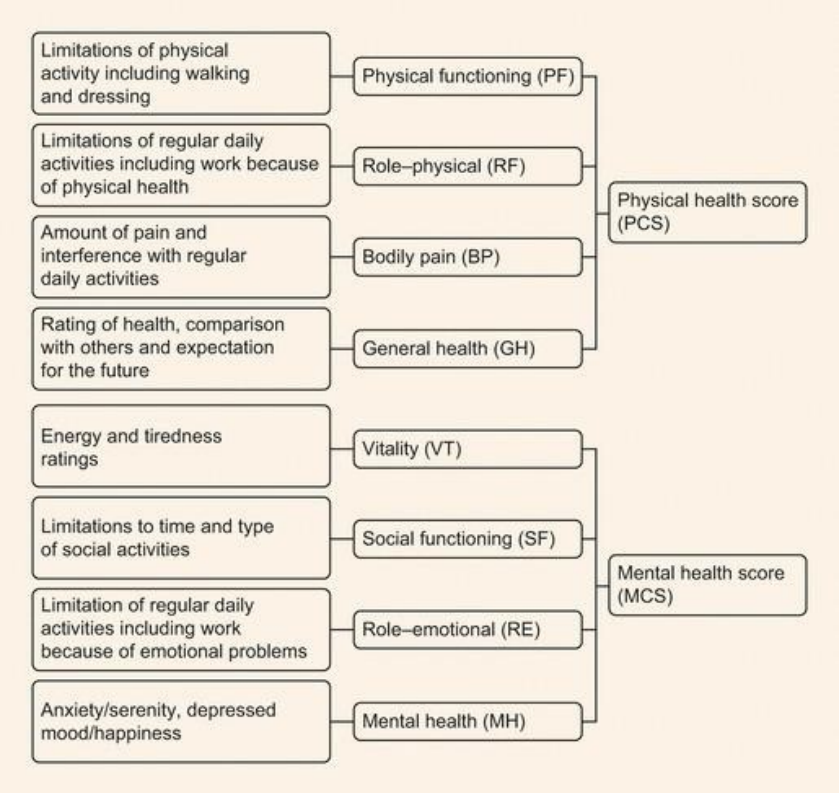


Figure 3.2
Short Form 36 (SF-36) summary components

As scores from the SF-36 are used to measure clinical outcomes, it is imperative that applicable normative data are used to judge effectiveness. In the last decade (2000–2010), 40 articles published in the *BMJ* have used SF-36 as an outcome measure, and of these papers 23% have potentially used inappropriate norms for calculating SF-36 scores, as samples were selected that extended beyond the boundaries of England (i.e. stated as UK wide), or encompassed England and Wales, or were located solely within Wales. The analysis for the Short-form 36 followed the process outlined by the authors of the scale. Different aspects of the patient's well-being were scored for the patients who have switched, with a comparison of overall scores for SF-36 calculated at the three separate intervals (pre-switch, 30 days, and 90 days post switch). Then an individual comparison of each interval score was interpreted and trended to determine if the level of Quality of Life for patients who have switched has improved or decreased. The QoL model used is shown in Figure 3.3.

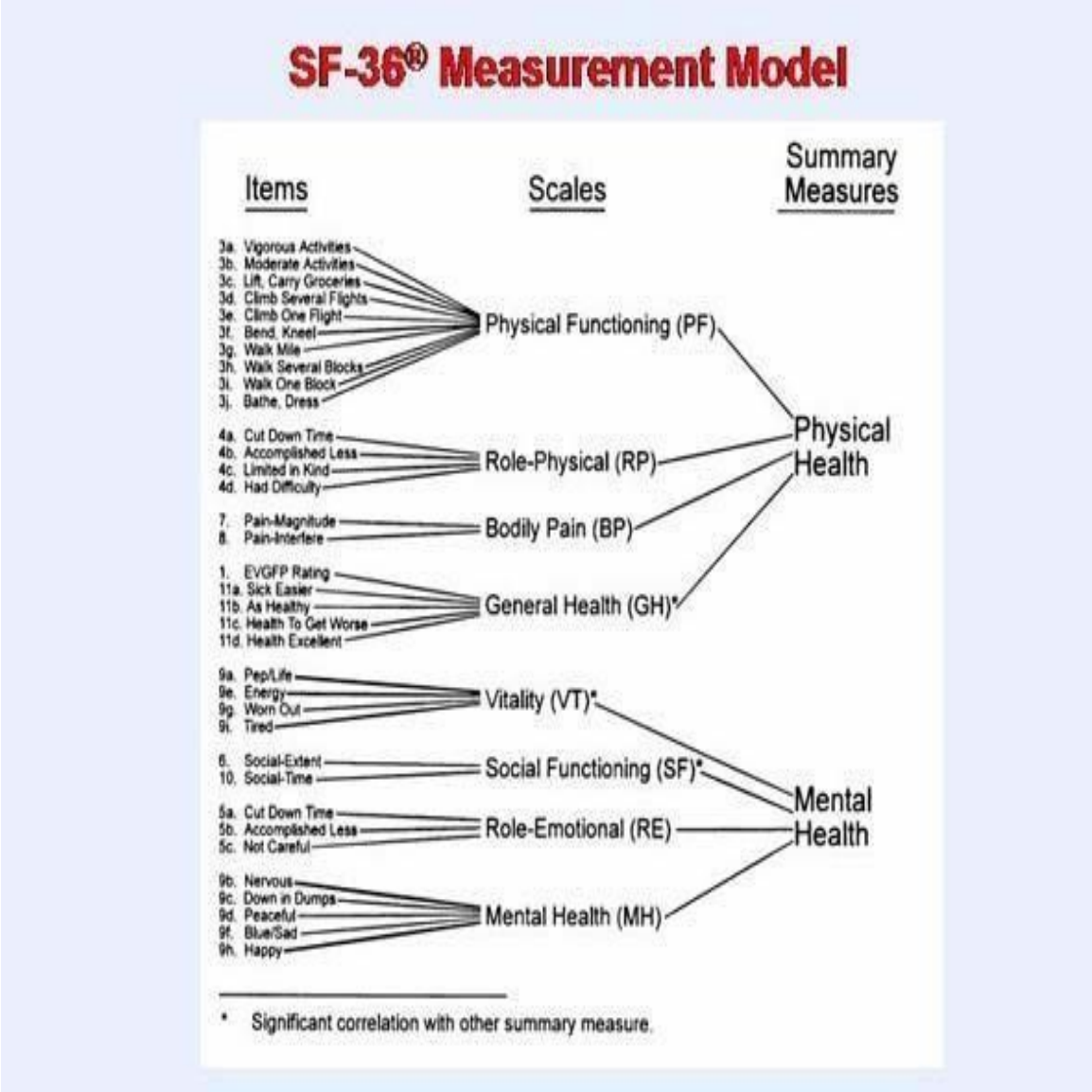


Figure 3.3

Short Form 36 (SF-36 utility)
http://www.sf-36.org/tools/SF36.shtml

The data from the SF-36 for each patient was categorised into five groups: 65-74 years, 75-84 years, >85 years and by M or F to identify if any these factors influence the views or problems encountered. Then, using a series of data queries with time, age and gender as independent factors, changes from baseline at timepoint 1 and timepoint 2 were captured and compared to the results at timepoint 3.

3.13 The analysis of the Interview Data.

Thematic analysis was chosen as the method of data analysis because it is widely used across the health sciences (Hoe, 2013) and suited the purpose of the study. As the author was a novice researcher the literature was searched to identify a suitable model as a guide. Two approaches came to the forefront right away. The first was the 'Framework' method developed by Jane Ritchie and Jane Lewis (2003). They provided a detailed process to follow for the development of themes and the construction of an index and how to develop a conceptual framework with which to guide the data analysis. However, it was rejected on the grounds the sample here was relatively small and the Framework approach can require a considerable amount of varied material to work with. The anticipated qualitative material here was to be quite tightly focused on a specific aspect of healthcare so would not need that level of organisation. The work of Braun and Clarke (2006) was then considered and agreed upon as the best method for this study. They provided a good overview of the role of qualitative research and a detailed explanation of the process of thematic analysis. Also attractive was that they took an educational stance – 'that learning to properly undertake thematic analysis is a core skill of the new qualitative researcher' (p4). While some social science commentators consider thematic analysis to be best used within other analytic traditions (such as Grounded theory) Braun and Clarke argue that 'thematic analysis should be considered a method in its own right' (p4).

It was a relatively straightforward process and put and emphasis on all of the respondent's voice being heard. 'Through its theoretical freedom, thematic analysis provides a flexible and useful research tool, which can potentially provide a rich and detailed, yet complex account of data' (Braun and Clarke, 2006, p5). They stated that there were two levels of analysis at which themes could be identified. The first a relatively straightforward 'semantic' level where a surface (explicit) understanding is enough, or a 'latent or interpretive level' which offers more in-depth analysis (p13). This study, given the nature of the enquiry and the relatively short interview time, took a semantic level approach. The statements provided by the patients were accepted at face value with patterns and themes forming as the amount of material grew. A six-phase guide to data analysis was provided and followed here, this is how each stage was undertaken (Braun and Clarke, p18)

Phase One. The researcher familiarises themselves with the interview material but also employs other sources such as early information gathered during the research problem formulation and any preliminary ideas emerging during the interviews. In this study, as the interviews were transcribed chronologically, they were read and re-read immersing the researcher in the material. Ideas for potential codes began to emerge from the start, such as reference to *difficulties with diet while on Warfarin*, and *limited pain relief*, which were also found in later interviews. The transcripts were read in full, omitting no material, and they were checked against the original audio recording to ensure this.

Phase Two. This phase sees the development of the initial codes, that is, the individual ideas that have been mentioned across many interviews. It is a process of clarifying, separating, and organising the material amassed in phase one into ideas and concepts that are discreet and distinct from each other. The codes were 'data-driven' – from the bottom up. They were arrived at manually; highlighter pens were used to colour-code the transcripts and ideas/codes were cut and pasted into groups. In order not to lose context – the whole human being behind the codes – each respondent's transcripts was kept at hand to illuminate understanding.

Phase Three. In this phase, all the codes were allocated to large groups to form overarching themes, in order to structure and provide a deeper meaning of the sometimes factual statements and the subsequent codes expressed by the respondents. For example, *stalwartness* described the many codes referencing the role of the patients' 'resilience' and 'just getting on with things'. Each code was found a home under one theme or another, some being reallocated on further consideration to get the best fit. They were written onto post-it notes and hand sorted into groups, where necessary, some large groups were divided to produce a clearer theme. Supporting quotes from the text were numbered and colour coded to match the themes.

Phase Four. In this stage, with the help of a deeper knowledge of the material, the work of refining the themes and getting best fit for each code is continued. The themes were considered against the whole person transcripts and some changed and refined.

Some early themes were reviewed and became two distinct themes allowing for more a more nuanced understanding of the material. By the end of this process, the overall picture of these patients' experiences became clear.

Phase five. This is when the themes were named and used to provide the broad brush strokes of the patients' stories. Effort was made to ensure that each theme was not too broad, failing to encapsulate a range of ideas or feelings at a level that was meaningful. It should be noted here that although this study deals with human emotions related to this treatment programme, many of the codes and, therefore, subsequent themes lean towards the concrete, the practical, which sets it apart, to some extent, from a traditional qualitative study.

Phase six. In this phase, writing the report, the researcher has drawn together all the material available and incorporated it into two findings chapters. She interpreted the material and drew conclusions, ending with recommendations which will inform more 'patient-centred' future practice.

3.14 Interviews with staff

Anecdotal evidence from across the clinics concerned suggested that the clinicians (e.g. doctors, nurses) showed varying degrees of knowledge about of the social and personal impact the switch had on their patients. This may be related to the fact that little research had yet been undertaken, so the medium and long-term Quality of Life impacts were not commonly known for DOACs patients. Therefore, these interviews aimed to draw out the views of the clinicians and make a comparison with the information volunteered by the patients. For example, do both parties identify the same key issues or areas of improvement or concern? To draw upon the views and experiences as well as concerns of key staff involved in the care of lifelong anticoagulated patients, focus groups were first considered. But due to staff work commitments they proved impossible to arrange, so four staff members were interviewed individually. The group consisted of one doctor (the team consultant), a pharmacist and the two clinic nurses. (See Appendix Two for the interview schedule). The interview data generated was processed and analysed separately

from the patient's interview data. The process again followed the Braun and Clarke model. A comparison was then made between the patient's views and the data provided by the professional staff. Common and divergent views and levels of understanding were identified.

3.15 Role of the researcher

That the researcher took part in the interviews was considered a potential ethical issue as she was known to some of the group members. For example, they may not have wished to display a lack of knowledge about the topic in front of her (or indeed other colleagues). The researcher is, for this part of the research, an 'insider' researcher. The dilemma such researchers have was one of having 'insider status' as described by Corbin-Dwyer and Buckle (2009). 'Insider research refers to when researchers conduct research with populations of which they are also members, so that the researcher shares an identity, language, and experiential base with the study participants (Asselin, 2003 and Shamloo *et al*., 2019).

However, they argue that 'the insider role status frequently allows researchers more rapid and more complete acceptance by their participants. Therefore, participants are typically more open with researchers so that there may be a greater depth to the data gathered' (Asselin, 2003). It was anticipated that it would be the case here as the researcher was known to be an expert in the research topic although from only one clinical perspective. Asselin goes on to support the positive aspects of being an insider researcher. 'Being a member of the group under investigation does not unduly influence the process in a negative way. Disciplined bracketing and detailed reflection on the subjective research process, with a close awareness of one's own personal biases and perspectives, might well reduce the potential concerns associated with insider membership'. (Cracknell, 2010). To help mitigate this issue, the researcher undertook interviewer training at the University of Westminster. Interestingly, no resistance or issue was raised about researcher's role, in fact the reverse was evident, Staff and patients expressed great interest in the research and were glad the subject was being studied.

This chapter outlined the research design and the methods employed detailing the mixed methods design, its origins, its relevance to this study and general characteristics. The following chapter details the ethical implications of the study.

Chapter 4 - Ethics and Governance

4.0 Ethical approval

Ethical approval for the study was granted by the University of Westminster and the Integrated Research Application System (IRAS). In addition, the Imperial NHS Trust Research and Development Office were asked for and granted permission to conduct the research during anticoagulation clinic working hours on the Trust's site. The participants were provided with a summary sheet of the study background, information about the study, and contact information in case of concerns emerged. A consent form for participating and a consent form to inform their General Practitioner (GP) of their involvement in the study were provided. See Appendix 13. The patients and staff will be provided with a summary of the findings in due course.

The data and personal information were dealt with in a strictly confidential manner in accordance with the information governance rules set out by the trust, the university, and General Data Protection Regulation (GDPR) as it is applicable to NHS trusts in the UK. Respondents were assured that their names and other personal information would be dealt with in the strictest confidence. This aspect includes the principle of trust in which I assured the participants that their cooperation would not be exploited for personal gain or benefit, by deceiving or betraying them in the research route or its published outcomes. The principle of voluntary participation was explained, as was their right to withdraw from the study at any time. The principle of informed consent statement was attached to the questionnaires and verbally explained to the interviewees. Both principles entailed explaining the research process and its purposes to the participants.

4.1 Data collection and storage

This was a low risk study. All the scales used with the participants have been validated and are deemed to be reliable and widely used within the research community. The interview schedules were designed to be neutral and non-invasive. One factor, however, that needed to be considered was the risk of fatigue or the time burden to the patient. This was assessed on a case by case basis. The researcher looked for signs of tiredness or of the patient being uncomfortable. The purpose and duration of the study was explained verbally as well as with information

leaflets. The storage and use of personal information with regards to patient confidentially was also explained in the leaflets to the patients, who were given a copy of the patient information sheet (Appendix 6) and consent form (Appendix 8). The questionnaires were administered, and the interviews undertaken by the researcher. The data has been handled in accordance with the six Caldicott principles (Sinclair, 2013) and the University of Westminster's code of practice. The data collected was anonymised and given a key code number. The key code was held securely by the Director of Studies at Westminster University, Dr Patricia Maitland and kept separately from the data.

The hard-copies and the transcribed reports from the patient interviews and group discussion were stored on a password protected recorder and on an encrypted memory stick, which was kept in a locked safety filing cabinet at the University. The information gathered using the memory stick, digital recorder and patient survey was electronically transcribed at the earliest opportunity using Dragon® auto transcription software. It was saved to a restricted drive on the University of Westminster's secure server. This drive was viewable only by the researcher and will be kept for 5 years in accordance with the UK Data Protection Act of 1998, after which all data will be deleted from the drive. The hard copy of the raw data will be disposed of using confidential waste shredders.

In formulating the Quality of Life survey questions for the patients, care was taken to consider the following:

- Invasion of privacy
- Sensitive questions
- Voluntary participation
- Informed consent
- Benefits to patient
- Risks to patient
- Benefits to NHS Trust
- Risk to NHS Trust
- Patient confidentiality
- Patient consent.

The standard complaints procedure was available to the participants if requested: they may contact the Ethics department at the University of Westminster. The Faculty Dean, Prof Annie Bligh, the University of Westminster sponsor, was the point of contact for any complaint. Alternatively, the Imperial College Healthcare NHS Trust patient advice and liaison service (PALS) or complaints team could also be contacted.

As this research involves the elderly the researcher is mindful of any potential distress which might result from the study (Green and Thorogood, 2018). Should participants require follow-up support following the study, they would be referred to the anti-coagulation or cardiac arrhythmia team for clinical and social support. The team, which comprises medical staff, was best equipped to manage or change anticoagulation therapy if required by the participants.

4.2 Project governance, management and support

The Short Form 36 measurement scale (SF-36) is validated in the UK for use in QoL studies either in person or via telephone, in both paper and electronic formats. Dr Trudy Edginton and Dr Maria Woloshynowych (University of Westminster) acted as advisors for the administration and data analysis, likewise, the administration and analysis of the PSS and CFQ. The researcher was granted Student Academic Research License by Optum, the company which publishes the scales, allowing access to the Short Form 36 instrument along with scoring materials. The identification of patients who are suitable for switching from Warfarin to DOACs is currently performed by the anticoagulation nurses and clinicians. All background investigations, such as checking patient clinical relevance to the study (age etc.) and data-analysis was carried out by the researcher. Dr Patricia Maitland advised on the qualitative data collections and analysis. Dr Abdul Shlebak, Consultant Haematologist (General Haematology, Obstetric Haematology, Haemostasis and Thrombophilia) and Lead Laboratory Clinician at St Mary's Hospital, Imperial NHS Trust, acted as a local research advisor.

Other occasional advisors were Dr Frances Akor, Consultant Pharmacist for Anticoagulation at the Imperial College Healthcare Trust, and Ms Jo Burke, Lead Anti-Coagulation Clinic Nurse. Any input to the research based on their area of expertise was ad hoc or on pre-scheduled dates, depending on their availability. Anticipated peripheral support for this study was provided by the University of Westminster's Doctoral Researcher Development Programme. They include workshops on ethical issues, analysis of statistical data, academic writing, and the dissemination of findings.

4.3 Dissemination of findings

In the first instance, the findings will form part of a doctoral research degree and written up as a thesis for submission, and may be published on the University's repository Westminster Researcher and on EThOS. As St Mary's hospital is a stakeholder, summary findings of the report will be discussed with participating clinical staff and members of the steering group. The findings may then be used to inform clinical decisions with regard to patient anticoagulation care with DOACs, to revise policy on patient-centred care, and possibly on policies regarding self-monitoring of oral anti-coagulation especially in the elderly (>65 years). Based on the findings of the report, a set of clinical recommendations will be produced to facilitate these clinical changes.

As the targeted age group of the study is over the age of 65 years, a plain English summary, as opposed to an electronic version, was printed in leaflet/flyer format, and given to all participating patients. A summary of the findings may also be posted on 'The Source', the Imperial Healthcare NHS Trust website, and submitted for publishing. The summary may reassure the patients that their on-going medical care is not just based on the risk/benefit of the new drug, but that the best clinical outcome (i.e. improvement in health and Quality of Life) is also considered.

Publication of the findings in professional journals will also be considered.

Chapter 5 - Findings Part One:

The first patient interview at the time of the switch to a new drug regime.

5.0 Introduction - Participants and Procedure.

As discussed above, this study is a mixed-method exploration of the views and experiences of older patients living with AF who have been on a long-term Warfarin treatment plan. This chapter reports the findings from the first interview with 20 of the 56 participants. The interviews were held at the time of the patient's switch-over to a new drug regime. A second interview followed three months later and is reported in the next chapter. During the interviews, the Perceived Stress Scale and a general health measure were administered, both of which are fully reported in Chapter 7 but are also briefly referred to here. The four staff interviews are drawn on briefly when exploring the effectiveness of information and communication between staff and patients. To provide context, the patients' general health and medications, apart from Warfarin, are first outlined. Their experience of life on Warfarin is next explored: how it impacted on their daily routine and implications for their family and social life, and how well they managed self-medication. Then their expectations, if any, of the new drug regime are explored. Finally, the effectiveness of information provision in its various forms is discussed.

The data were analysed using the Clarke and Braun 2006 guidance for the development of themes emerging from the interview material. The full process has been set out in chapter three. To understand how the main themes were arrived at, see Appendix 14, tables 1 and 2 which show the main themes and supporting codes.

5.1 Managing Complexity – living with multiple medical conditions while on Warfarin.

Given the age of the sample it is not surprising that they were experiencing a wide range of medical conditions in addition to AF, including arthritis, high blood pressure, chest infections, high cholesterol, and asthma. It was reported frequently by the interviewees that one condition could pave the way for another; the older the patient the more medical conditions they disclosed. Importantly, treating their other conditions conflicted frequently with taking Warfarin. For example:

> *'I get these chest infections all the time, it's horrible, and sometimes I'm up all night coughing. The antibiotics will get rid of the infection, but my*

INR is up and down because of it. My wife is not very well either and we keep passing the chest infection back and forth, it's like a vicious cycle'. MK, man 86ys.

'Every time I take antibiotics, my INR goes up, and I keep getting all these infections, especially when it's cold like today'. SS: woman 82 yrs.

It is clear therefore, that AF is not the only medical issue that many have to manage. This needs to be kept in mind when exploring how they have coped to date and their responses to the new drug regime. It seems to be a balancing act:

'I take atorvastatin, tramadol, metformin, amlodipine and Salbutamol; Sometimes antibiotics and vitamins, but I have to be careful because my INR is always out of range'. GD, man 65ys.

'Hypertension, diabetes and epilepsy, and I was only recently diagnosed with ADHD as well. I have a grandson who is 7, he is so much like me, and my daughter told me that K has ADHD, so I went and got tested and imagine my surprise to be told at 64 that I have ADHD'. BP, man 65ys.

Despite the multiple illnesses, when asked about their current state of health, most interviewees declared that they were 'fine' or 'okay'. In many cases it was only when direct questions were asked, often when completing the stress and health scales, that pain and other discomforts were disclosed. There was a tendency for many within this group to dismiss joint pain and body aches as part of ageing, to be coped with by self-medicating or quiet endurance.

5.2 Stalwartness

This reticence to complain, to be *stalwart,* emerged as a theme in both the first and second interviews and is explored more fully in chapter six. It is important to note that this overly-positive response cannot be regarded as 'denial' as such on behalf of the patient – they understood how ill they were – but rather a need not to dwell on their illness and not to bore other people by complaining. There is also a desire

to be normal – not always being seen as a patient and having a sense of control over their lives. However, once they began to talk freely multiple issues emerged, along with the difficulties encountered coping with them.

The real life facing many of the interviewees was difficult and uncomfortable. This man's response was typical and tells of the impact of having several conditions:

> '*Oh yes, I have high blood pressure, high cholesterol and arthritis. I also have diabetes and every now and again I get these bad chest infections, especially when it's cold or damp like today. I get all these ache and pains, so depending on what they give me, the INR can be sky high'.* AB, man 91ys

Two factors in particular emerged as prevalent and, at times, difficult to cope with: living with pain, and poor quality of sleep. Both tested the patient's stalwartness. Pain was the most frequently occurring complaint with over half of the patients experienced it in varying degrees, and it had a direct impact on their quality of life. For some it was acute, the result of a recent operation, for others chronic pain accompanied arthritis. Typically, these patients complained of several pains:

> *'I have pains all down my back, in my hands and in my knees, I used to play rugby with my son as recent as 3 years ago, we used to go for a scrummage and that, but I can barely make it up the stairs most days'.* BP, man 65ys.

> *'I had hip replacement surgery about 6 months ago, so I can now get to the shops up the road and back with my stick, but I have to stop when I feel the pain coming on…... I rest a bit then I carry on. It can take a while but it's important to keep active'*. OG, man 82ys.

The degree of pain endured while on Warfarin is worth exploring because most pain relief medications have an adverse effect on the Warfarin patient's INR. They were therefore underused, leaving the patients with little relief. Successful pain management become a more important factor after the switch.

Another frequently raised factor, which strained their positive attitude to life, was poor quality sleep caused by constant pain. This was a typical comment:

> *'I don't sleep much these days. Sometimes I only sleep 3 or 4 hours a night, and even then, I have to sleep propped up by pillows in a sitting position, it's very painful'*. MF, woman 65ys.

The theme of stalwartness was reported by many but not all. Some, often the older patients, found life very trying indeed and felt little sense of control over their bodies.

5.3 Loss of Control – the domino effect

Contrary to the theme of stalwartness, a significant minority of patients said they were only barley coping. Physical illness was not the only factor of concern and for several not the most pressing. At points during the interviews some participants were quite emotional with a few revealing psychological issues of concern. Approximately a third reported feeling lonely or being down in spirits or depressed at times; social isolation, it transpired, was a major factor in the lives of several. Along with this was a feeling of a loss of control, not just over their physical pain but also their social life and a dislike of having to receive help with daily tasks. The resultant loneliness clearly had a profound impact on some. For example:

> *'I get upset, sometimes. I don't think that I have much control. I feel so depressed all the time. I sit in all day and then go to bed cause I'm widowed you see. I don't think that things are going my way, I don't see a future actually. I just wish I had an answer to it all. Just so much going on'.* JW, woman 82ys.

Others talked of the simple daily living activities being difficult to negotiate alone, at times physically and emotionally exhausting. For example:

> '*Ever since she [his wife] passed away, it's been really hard, I find it hard just doing day to day stuff'.* AB, man 86ys.

Limited mobility was also mentioned by some as another cause of isolation and a major restriction on family interaction. This woman told of her plight:

> *'I can't walk very far, I need help getting dressed and all my relatives live so far away, and we never had kids. I get really lonely sometimes. I looked after my husband for 24 years before he passed away'.* SS, woman 82ys.

All the participants, to some degree, felt restricted or not in full control, for example in eating, or rather in their choice of food being limited because of their medication. A kind of domino effect that they could not control was established – their life-saving medication led to major implications for their general health. Just under half stated that they experienced problems with food interaction and how 'getting it wrong' can impact their lives:

> *'Warfarin affects everything, from what pills I can take for my pains, to what type of vegetables I can have'.* JW, woman 90 yrs.

> *'The hardest part is trying to co-ordinate the diet for taking Coumadin with a diet for diabetes'.* ML, woman 89 yrs.

A result of a restricted vegetable intake was, for several, the difficulty of maintaining a healthy weight. Patients who had embarking on a weight loss regime had to have their INR closely monitored at the clinic as their weight reduced. For example:

> *'The doctor told me that I had diabetes, he said that I am now at an even greater risk of a stroke. So, he suggested that lose some weight by gentle exercise and a change in my diet, but I noticed that kale, liver, and green tea would wreak havoc with my INR. It was later when I spoke to the nutritionist at Hammersmith that I was told that all the green leafy vegetables are a no go. That made dieting very difficult'.* KS, woman 65ys.

To compound matters for those who wished to lose weight, they said that if they exercised regularly they needed a higher Warfarin dose. Not being able to do even light exercises such as walking was reported as being one of the major daily problems because it hindered other health-promoting activities.

The sense of reduced control extended to mild and serious physical reactions to Warfarin. One side effect, and one of the most unpleasant and embarrassing, was

the propensity to bruise without knowingly sustaining an injury. Several participants reported bruising even after a mild knock or even dental treatment:

> *'My face was really swollen and bruised after having dental work done while I was taking Warfarin. It really looked awful'.* GA, man 68 yrs.

It was not the discomfort that caused them anguish but having to explain the bruising to others, often healthcare professionals, and the questions that might follow. A few wondered what people might think had happened to them; had they been a victim of domestic abuse perhaps. This could lead to a negative impact on their self-image:

> *'I was embarrassed and worried. This was when M (his wife) was alive; we had a home visit to decide if she should go into care, and I had a black eye. I just get these bruises all the time. I was worried that she (the nurse), would think that M had hit me and take her (M) away…. She died a few months later, but at least she died at home, like she wanted'.* FM, man 91 ys

Light-headedness caused by Warfarin was also a complaint by several patients. It could occur at any time, but most participants seemed to be aware of the danger points for their dizziness:

> *'……and just getting up quickly from the bed would make me lightheaded'.* FM, man 91ys

As well as bruising, cuts and bleeding are a constant fear of those taking Warfarin, more than half of these patients reported some form of bleeding. It could happen at any time without warning during regular activities such as a visit to the dentist. For example:

> *'My only issue is my bleeding gums; the dentist says it's related to Warfarin because I have healthy gums……usually when I brush my teeth, but they can start bleeding if I have any course or hard food, even toast can aggravate my gums'.* AG, woman 71.

Fortunately, most cuts were dealt with without hospital admission, and this sample did not report many emergency hospital visits due to bleeding. While not life threating in itself, bleeds caused considerable distress and discomfort.

Two patients experienced less common side effects, but nonetheless distressing:

> *'I developed dermatitis since being on Warfarin, which affects my quality of life at this stage. I feel like people are always looking at me, I detest Warfarin'.* GD, man 65ys.

> *'…. it's called priapism (a persistent and painful erection of the penis), apparently it's a rare side effect so I guess that makes me special (smiles)'.* BP, man 65ys.

It is clear from these interviews that life on Warfarin for a good number of patients can be difficult, with a range of physical and social consequences that, if not life threatening, make daily life uncomfortable and reduce their sense of control.

5.4 Freedoms Lost – the impact on social and family life

Further restrictions were cited by some patents. Leading a fully integrated social and family life was impacted negatively by their Warfarin regime.

> *'I used to play rugby with my son a lot, but because of all the pains in my joints, I can't go up to the field much',* BP, man 65ys.

In addition to participation in sports, travel was also affected. Simply taking a holiday became a major undertaking, particularly for long distance visits. Patients travelling to different time zones had to ask the clinic about the timing of their dose. Time differences of up to six hours were relatively easy to manage, they said, but travelling from London to New York (five hours behind London) as one man wanted to do, required him to calculate the time difference in order to take his medication on time. Some altered the timing of their doses gradually (e.g., two hours earlier or later each day) in the run up to their holiday and reversed it when returning home. Long range travel was curtailed, as for this man:

> *'I mean it's difficult to travel to see my family in Barbados, the GP says it's too long a flight and I am at risk of a DVT'.* RB, man 84 yrs.

It is important to note that it is not only the medication itself that has an impact on their movement, but the whole clinical process proved burdensome for some:

> *'I'm a solicitor, so I could be called away in the middle of the night for a consult, so having to come to the clinics every other week sometimes gets in the way of trials or client visits. I usually have to plan my travel around the clinics or sometimes I miss the INR test at the clinic'.* HM man 66 yrs.

Importantly, it is worth noting that several patients expressed little difficulty with travel arrangements, for example:

> *'I'm sure that there are people worse off than me, I still travel every now and then and I'm not dead yet (laughs)'.* GD, man 65 yrs.

Another factor that impacted on the social life of a few was that mixing alcohol and Warfarin can be problematic. This woman seemed to know the risks but had a drink regardless:

> *'My INR is always up and down; I enjoy a tipple every now and again, which causes it to shoot up as well. This blooming Warfarin seems to shoot up for no reason, so I'm interested to see what happens with this new one'.* MR, woman 65ys.

For another woman, the occasional drink was hard to avoid given that she worked in a pub:

> *'Because I'm working in a pub, punters sometimes buy me a drink or two when they get the rounds in, but I know that I can't drink like I used to because drinking causes the INR to be so out of control. I mean I have one here and there, but I do worry about it all the time, especially as I am getting older'.* KS, woman 65ys.

It was a risk, but one that some patients were prepared to take. Happily, there were no reports in this study of any serious side effects as a result of dose manipulation or

alcohol. This is an indication of Warfarin's long reach into people's lives and that a domino effect can easily begin.

The impact on families also needs to be noted here. They were often involved in the daily care of the patient, with emergency hospital visits from time to time in cases of a bleed, then nursing the patient while they recovered at home. However, the participants were sometimes not the only patient in the household:

> *'I take care of my wife, she has dementia, arthritis, diabetes, you name it. I used to miss a lot of the clinics and my Warfarin was all over the place…...it's funny, she was always looking after me, I never even imagined that I would have to look after her……...39 years married this July'.* JP, man, 73ys.

Caring for his wife had a negative impact on his own health routine.

5.5 Self-Reliance is Key – but within a partnership

Despite the considerable medical and social difficulties faced by these patients, a culture of 'you just have to get on with it', of self-reliance, prevailed. While each respondent had their own way of managing their medication, two factors became clear as key to their wellbeing: 1) being organised, and 2) the importance of the role of an efficient GP's surgery to support their own efforts. Being organised took several forms. Many respondents talked of their methods of self-medicating, with most integrating the Warfarin into a daily hygiene routine such as brushing their teeth:

> *'I have no difficulty taking Warfarin: the tablets are small and easy to swallow'.* OG, woman 65ys.

Mitigating against this sense of order, however, was forgetfulness, the most common reason for missing a dose. Sometimes it was what could be called 'medication fatigue':

> '*Sometimes I forget to take my Warfarin, I take 8 tablets a day, some before meals, some in the morning and some last thing at night. It can be annoying trying to keep up with which ones to take'.* MF, man 73ys.

Other patients took the possibility of forgetfulness into account and were well organised taking their Warfarin regularly. This lady did have help however:

> *'Yes, I have a pill box that my husband always checks and stocks up. He is a bit younger than me and is registered as my care-giver. He comes with me every week to my appointments'.* AB, woman 91ys.

Being organised included knowing their condition well enough to be able to successfully manipulate their table dose. Almost all admitted to changing the dose of their medication without medical intervention or advice:

'If I've been out drinking, I sometimes don't take the whole tablet, I will break it in half. I've had this heart problem and been on Warfarin for so long, that I feel confident to swap and change, it's always all over the place anyway….'. GD, man 65ys.

The clinic check-up was generally viewed in the same light, as just a small inconvenience worth putting up with if planned well:

> *'I usually have my blood test on the way to work, it only takes fifteen minutes and they give you a little pin prick and they give you the results straight away'.* GA, man 65ys.

5.6 Partnership in care – having a good GP.

The need for good organisation went beyond the patient's own sphere of control to the medical support offed by the NHS. Self-reliance could take them only so far; a good, easily accessible, well equipped, GP surgery was also essential. One much approved of organisational feature was the increased use of technology. An older respondent praised the new machine at his GP's surgery which tested his blood with a finger prick test, and provided immediate results so that his doctor could adjust his levels of Warfarin if necessary:

> *'It is so much easier than the old one [machine]. You had to wait for them to warm up and check the machines which took ages, but these ones are just like my diabetes one at home. They put your blood on a little strip thing and you get the result, amazing'.* GB, man 81ys.

Interestingly, the smooth running of their medication regimens is not, it seems, according to these interviewees, depended on age. Both the older and younger participants talked of the need of being well organised. The main difference was that with the older patients they were generally organised by others.

5.7 Responses by sex and age

As well as whole group responses as set out above, the interview data were examined by age and sex to see if any difference in views between the sub-groups could be identified. Some small differences were seen. Patients aged 75 years or over were more likely to show openness to being switched from Warfarin to DOACs, but the reason for this finding is unclear. It is possible that Warfarin-related food restrictions are more of a burden for elderly patients who may prefer traditional green leafy vegetables, so the switch was made more attractive to this group. However, several patients under the age of 75 were also open to change, so it is important not to make too much of this finding.

When it came to identifying the differences across the age groups with regards to the main themes discussed above, a few findings are noteworthy. The views and issues could be found across the whole group, though with some patterns forming between groups. All patients, but with varying degrees of enthusiasm, said they were 'fine' until more detailed questions were asked. The culture of stalwartness was true for the older and younger patients alike. However, when the interview revealed personal distress or sadness, it was noticeable that the patients who were in the 65-74 age group made fewer references to symptoms of anxiety or depression than those over 75yrs in similar circumstances. It was also noted that patients over the age of 85, as would be expected, more frequently reported poor functional status. Life was more difficult all round; mobility difficulties were more

pronounced, pain was often present, and more in this age group tended to live on their own increasing their sense of isolation:

> *'I have so much pain all over, I don't get much sleep ever since my hip operation. If I stay on Warfarin, the cardiologists said I will not be allowed to have Naproxen, which really helped me before I was on Warfarin'.* JW, woman 90 years.

> '*Bingo on a Thursday, but not much else since my husband died, I don't always get to go as well. My only daughter moved away when she got married*'. AB, woman 68ys.

A sense of freedoms lost because of the medication was slightly more pronounced in the younger group, as they also reported more activities, they had wished to do but were prevented from doing so. They also seemed to have more questions for the nurse and consultant, the older patients being more accepting that a switch would be in their best interest.

No clear pattern of differing views between the sexes was identified, however some small tendencies emerged. For example, men more often reported being socially active than women, so felt marginally more restricted by the Warfarin regime. Conversely, the woman more frequently raised the issue of being alone a significant amount of the time. This was most commonly noted in those who had lost a partner or other social support. Importantly, more women revealed concerns about a decline in mental health and wellbeing, linking with a feeling of not being in control of their own body. The men detailed more negative impact from the Warfarin regimen than the women. This may be related to their more active lifestyle, and wishing to undertake even more activity but feeling prevented from doing so. Interestingly, there was no division between the sexes when it came to concerns about the new medication. In particular the often voiced concern, 'how will I know if it is working'? was evenly spread across the sample. While small differences can be identified across the ages and sexes related to some themes, it needs to be remembered that this is a small sample and, like all interviews, is dependent on how the participant was feeling on the day.

5.8 The provision of information

One goal of this study is to improve, where needed, the patient-facing services provided by the haematology clinic. To this end, questions were asked about the amount, method of delivery and appropriateness of the information available about AF, about the switch-over, and about the new drugs prescribed. The topic was raised at the time of the switch and again at 90 days. To avoid repetition, this analysis combines material from both first and second interviews. In addition, material from the clinical staff's interviews is included to provide a rounded picture.

Most of the participants voiced at least a minimal understanding of their medical condition (AF) which necessitated their being on Warfarin, and several were well informed. Many had lived with AF for a long time and knew the condition well, including the possible health crises that they were susceptible to:

> *'I have been taking Warfarin every day for 15 years to reduce my risk of stroke and am very pleased to say that I have never had one'.* BP, woman 77ys.

In general, the patients showed a good understanding of the medical care required to keep them stable although, importantly, there was a leaning toward the younger patients being better informed. Three themes emerged related to the provision and source of their information: that the *material was current*; *was age appropriate* (method and clarity); and a culture of *'learn as you go'* prevailed. First, it became clear that that for several patients their original information, provided when they were first prescribed Warfarin, which for some was over 15 years ago, was now old and had not been updated. Unless they asked staff about something, specific little or no 'refresher' material was forthcoming; the habit of just asking the nurses about any emerging issue was well established. There appeared to be a general assumption among patients and staff that they knew 'all about it' by now.

Secondly, age appeared to impact the level and depth of knowledge and an understanding of the benefits and risks associated with Warfarin and the new

drugs. The older patients, 75+, demonstrated poorer knowledge than their younger counterparts; indeed, the knowledge level among older participants appeared to be quite superficial and fragmented. Many could not explain with any degree of precision the rationale for taking Warfarin and the associated risks. Some were reliant on others for help:

> *'My daughter is a nurse, so she has told me a lot about it'.* OG, woman 84ys.

The younger participants, under 75ys, were more knowledgeable, and a small group was very well informed, talking of their use of the internet and having read widely on the subject.

The third theme, common across the group, was that, in their view, the best source of information was experience, not only their own but that of others. Being in the older age range of the general population increased the likelihood their of knowing other people in their daily life who were also on Warfarin and experiences were shared. Some patients had become skilled in self-monitoring, developing a reliable sensitivity to their own wellbeing:

> *'Over the years, you learn more from other patients and the clinic. I learn as I go as well. Sometimes I know the dose change before the nurse tells me'.* AC, man 82ys.

However, informal information sources had risks. One lady, who had been on Warfarin for years was made unnecessarily anxious:

> *'What's worrying me is that lots of my friends and people I've met tell me that they would never take Warfarin as they've heard terrible things about it. I've heard rumours that it's been used as rat poison or could cause me to bleed to death. It seems a very unpopular drug'.* AM, woman 85 ys.

It was understood from these interviews that formal information, regardless of the source, had its limits in keeping patients safe – personal vigilance was always required:

> *'I was told to watch out for major bleeding from my stomach or bowel, which is a potential complication of taking Warfarin, but luckily I have never suffered anything like that'.* SC, woman 82ys.

5.9 The Switch Itself – the level of perceived understanding of the reason for a switch and the process

These patients had good recall about why they had switched drugs. Several listed the following reasons: poor compliance with Warfarin, pain that could not be relived with other medication, problems with food interfering with the Warfarin, bleeding, and bruising. Most participants agreed with the doctors that a switch was required, but some without much enthusiasm based on not really seeing a problem. However, overall, there was a general expectation voiced that they thought things would improve for them over the next few months as a result of the switch.

Regarding information provided about the switch-over there was generally an expression of satisfaction across the group regardless of age, sex, or state of health. The information had taken the form of discussions with their GP, consultant, and nurses at the clinic, but the delivery varied in effectiveness. Some professionals, it was said, explained things better – in more detail – than others. In addition, there were leaflets for the patient to read at home and share with family members. Importantly, it appeared that the speed of delivery (too fast) and the amount of information (too much) impacted, for some, on the comfort and effectiveness of the experience:

> *'It was all explained to me at the time by the nurse at the clinic. I'm not 100% with all the information and leaflets and stuff, but it all seems ok so far'.* ML, woman 89ys.

> *'Like I said, it was the clinic that explained it all to me. The GP didn't explain it as well as the nurse. I came last month for my check up and she (the nurse),*

took her time and made sure that I know not to skip a dose or take two if I forgot'. DF, woman, 84ys.

5.10 The clinical staffs' view of information provided.

Each week the staff saw dozens of Warfarin patients and between four and eight on DOACs. Their own information sources about the administration and use of Warfarin and the new medications came primarily from brochures and factsheets supplied by the pharmaceutical companies concerned and a booklet prepared by the Trust. The doctor kept his knowledge updated by reading journal articles on the topic and consulting the NICE guidelines. On-line information, which they said was plentiful, was also consulted. Interestingly, no one reported being on a training course or expressed a need for more information; they felt sufficiently well informed. The team's lead nurse had also prepared an information pack for the patients. The staff confirmed the patients' accounts of the process of information delivery: that conversations were had in the weeks before the switch, and written information given to the patients at each stage.

5.11 Trust is the key to understanding

Importantly, despite the abundance of information in various paper and electronic forms, the key to good information exchange, claimed the staff, was trust, namely their relationship with the patient which had been built up over the years. The trust between patient and nurse was crucial, they argued, in the patient agreeing that something was going wrong with their existing programme, and so considering a new drug, and then going ahead with the different treatment. Reading about the medications was not enough; patients needed to be able to ask questions, sometimes repeatedly. Without the human interface the information exchange would have been much more problematic.

5.12 Summary

Warfarin as a lifelong medication has a long reach into people's lives. As well as the cardiac therapeutic impact, themes emerged from these interviews indicating that it

can profoundly affect many aspects of the patient's daily routine, their comfort and their sense of wellbeing. The interviews reveal the high degree of comorbidity among these patients, and how one condition often triggered another. Despite this, there was a culture of stalwartness across the group, and a high degree of trust in the medical staff who cared for them. Living with Warfarin meant a constant alertness for harm, and a degree of loss of control over their bodies and their lives. This extended beyond family life to relationships in the outside world, where they thought that the occasional results of treatment, bruising and bleeds might draw unwanted concern from others.

Self-reliance was a major theme, but just as frequently raised was the need of a good GP to confide in and for clinical support. The provision of information was reported as good but variable, and to some extent depended on when the patients had been put on Warfarin, with the more recent cases tending to be better informed. There is a need however, for age-appropriate information (e.g. large font and layman's terms) to be available. There are just a few differences between the men and women with regards to the main themes. Some are related to age, but none were unexpected. There was no difference between the sexes or age groups when it came to concerns about the new medication, which ran through the whole group. The concerns focused on the monitoring of the effectiveness of the new medication.

These patients indicated that to be effective and to keep their anxiety to a minimum, the information needed to be *detailed,* with questions anticipated and answered in *simple* language; *unrushed* with time to answer questions, and *repeated* at several sessions. That is, conducted through face-to-face conversations with both clinicians and nurses, on more than one occasion, and with opportunities to ask questions, even extending for some time after the switch. Communication also needed to be in both a verbal and written format. Plain language leaflets were required for the patient and, just as importantly, for their family to read and retain.

The next chapter reports on the second patient interview at 90 days, and the emergent themes between the two sets of interviews are compared.

Chapter 6 - Findings: two

The second patient interviews 90 days after the switch, and the clinic staff interviews.

6.0 Participants and Procedure

At the heart of this chapter are the patient's observations about their lives during the first twelve weeks after switching medication, and how this compared with life on Warfarin. The first interviews, at the time of the switch, were reported in the previous chapter and surfaced several key themes which dominated their thinking. Three months later additional themes had emerged. This analysis is followed by an exploration of the clinic staff interview data and continues from the previous chapter. A decision was made to integrate the staff material within the body of the patients' findings in order to make comparisons and to avoid the repetition of themes within the thesis.

As stated in the methods chapter, the same twenty patients participated in a second interview. During the first interview, as part of the consent process, the patients provided their contact information, also giving permission to be contacted at 30 days (for the questionnaire to be administered) and 90 days (for interview and questionnaires) to explore their experience of the new medication. Since some of the patients were not due to return to the clinic at the 90 day point, eight of the 20 were interviewed by telephone. As this was the third time the researcher and patient had talked on this subject it was considered that the relationship was strong enough for a telephone interview to produce good information. This proved to be the case, and no patient expressed reservations about a telephone interview. The interview began with a personal reintroduction by the researcher, and a summary of the purpose of the interview and research aims. In addition to the interview, the patients were given an appointment by the clinic staff to attend the anticoagulation outpatients' department at St Mary's Hospital in order to answer any clinical questions they might have. The perceived impact that switching to a new drug regime had had on the patient's health and their life in general was discussed, as was their satisfaction with the service provision from the anticoagulation team at the St. Mary's Hospital. The interview material is initially reported as whole group responses; then by sex and age (65-74ys, 75-84ys and 85+).

6.2 General health after the switch.

As expected, the range of age-related medical conditions listed at time one remained unchanged: diabetes, high blood pressure, arthritis, general pain, recurrent chest infections, high cholesterol, and asthma. However, it is important to note that several conditions were reported as being less severe. The reasons why this was the case was not always clear, but several signs and symptoms were reported as being, in the patients' view, positively impacted by the switch to the new drugs.

6.3 Stalwartness – a continuing theme

In the previous chapter it was reported that the patients, when asked how they were, often replied 'I'm fine' but on further probing reported discomfort or had a range of other medically related worries. This was also evident throughout the second interviews; a culture of 'keep calm and carry on' was expressed by all ages and both sexes. *Stalwartness* continued to pervade the conversations. For some, this took the form of not complaining to the clinical staff about their personal or social issues. Interestingly, no interviewee stated that the healthcare staff were unhelpful, but rather that they had sense of stoicism and did not want to bother them.

However, some concerns were raised by the patients, but these were about the 'system', for example, too long a wait to receive a GP appointment. This initial positive response when asked about their health was, however, undermined somewhat when they began to talk in more detail about their chronic medical conditions. This reticence to complain to staff was not always in the patient's interest, for during one or two interviews comments made were so concerning to the interviewer that referrals were made to clinical staff for further investigation. This theme of outward stalwartness is important here as it can in mask a patient's real situation and lull their clinicians into believing that all is well, and only when the patient's test results are of concern is there a fuller conversation with the patient. This tendency for some patients to underplay their complaints is known in healthcare research, and was one reason for including scale questionnaires in this study. These provided an additional data source to complete the picture, and were gained obliquely so did not suggest that the participants were complaining about their lot. The scales also acted as useful prompts during the interview, thus capturing additional rich data.

6.4 A leap of faith – responsibility for own wellbeing and a reduction in dependence on healthcare professionals

Possibly the most important feature of the new regime was that the patients no longer needed to attend clinic regularly for a check-up. The responsibly for their welfare was, therefore, now moved onto the patients themselves. For some this

was a significant change, while in the majority of cases the routine of self-medication was reported as presenting no problems once it had been established. Those who lived alone felt the burden more acutely; that it was very much up to them to get the tablet taking 'right', as there was no one to support or remind them. While this had been the case when they were on the old Warfarin routine, the clinical check-up had always been there as a backup. The lack of regular clinic check-ups added a new level of anxiety. 'How will I know if I am ok?' was repeated by the majority of participants of all ages. For example:

> *'Yeah, I feel fine, but I was really worried at first, …. I'm not sure if they [the new drugs] are working? It was really a leap of faith, after being on Warfarin so long, but it's no different to the blood pressure ones, cause they don't test for those ones. (laughs)…. It's all fine, I am getting used to them'.* BP, man 65ys.

For others is will take a little longer to feel confident:

> *'I understand a lot more about the new tablets now, but I am still not used to them. I guess it will take time. The clinic nurse said that I can come in or call if I have any questions. That helps, but I still get anxious cause I'm not sure it's working'.* JW, woman 82ys.

Despite these worries they adapted and kept going:

> *'So far so good, thank God. No, I haven't been back to the hospital since the last time. It's getting a bit warmer so the pains in my hands are not too bad now. I can take the naproxen now too, I had to stop it for a while, but the GP has put me back on it. So, it's all good thanks'.* VP, woman 89ys.

One new responsibility raised as a concern by several was that for the medication to be effective, it needed to be taken at the same time each day. It was mostly the older participants who mentioned it, and their main concern was poor memory – forgetting to take the tablet or taking two by mistake. Some patients had, therefore, developed techniques to help themselves:

> *'I take so many tablets, some before meals and some after meals, I tend to try and keep my tablets in a set order on the kitchen counter, but if someone tidies up and moves things around, I can get a bit muddled….'.* FM, man 91ys.

It is important to note that having to keep to a strict timetable was not enough of a problem that they reported regretting the switch. The earlier theme of being well organised remains as important as ever.

6.5 Liberation – regaining control

The majority of these patients talked enthusiastically of a newfound freedom now that they were liberated from attending regular healthcare appointments. Most were very happy with the greater flexibility provided by the new regime. With the weight of the old restrictions lifted many took up opportunities to visit friends and relatives in other parts of the country, or to just be a tourist:

> *'It's made a difference; not going to the clinics, I can actually make plans'.* BP, man 65ys.

> *'My holiday to Turkey is booked for next week, this is such a big deal! I've wanted to go for a really long time. I'm still worried about getting sick on holiday, but I don't have to worry about travelling. I am so excited. I think it's been more than 15 years…...since I went abroad'.* HM, man 66ys.

Each of these improvements, small as they might seem to an outsider, represents a new freedom and opportunity to enlarge their lives. The loss of control over their movement which emerged as an issue in the first interview was reversing - choice had been restored:

> *'…...France, Ireland, back to London for 2 weeks, then I'm back to France again for my nephew's wedding…...yes, it's been a great few months'.* CO, man 67ys.

It is important to note that those who reported increased liberation were those who had already experienced a good deal of independent living. For many who had reported living relatively isolated lives, the older patients, their situation had changed little. The new liberation of movement was absorbed into the lives of these participants in differing degrees; some were better able to benefit than others.

The situation was slightly different when it came to enjoying relief from the side effects of their old medication as the benefits appeared to be more evenly spread across the sample. Many patients talked of their improved wellbeing as a result of fewer negative interactions with other medicines. Recurring pain had been the most reported issue at time one, therefore the wider range of pain relief medication now available to them was embraced. This new ability to control their pain is a significant finding and is one that impacts on almost half of the participants. This is no small achievement, as many first reported living lives in quiet but substantial discomfort and, for some, in distressing levels of pain:

> *'…. By the time the pain comes on it can be too late to take anything. But at least now I can take some really strong stuff that I couldn't before…...no it doesn't happen as much, cause I tend to take the Naproxen, but when it does happen it's pretty painful'.* VP, woman 89ys.

The pain reduction led, in some cases, to improved mobility and to a much welcomed greater social interaction:

> *'I had so much pain in my knees and hips before, and I would get very stiff joints in the mornings. I still have some pain, but no way like it was before. I've started walking to the shops on the Highstreet, it's about 100 yards away, it was near impossible before'.* OG, man 82ys.

Others were freed from the dietary restrictions that Warfarin had required. Their food choices had opened up, and for some this was a life changing freedom as well as the pleasure of more varied meals:

> *'My diet is going ok; it's amazing all the things that I can eat now. I've lost almost a stone'.* ML, woman 89ys.

Closely linked to diet was the added benefit of now being able to drink alcohol. Again, it went beyond the simple enjoyment of wine or beer, but it helped with a newfound confidence in social situations, and the opportunity for companionship in an expanding social circle. They were becoming normal again:

> *'I even had a tipple on the weekend. I went to my mate's pub and had a gin or two……no I still used to have a glass of gin before, but it would completely mess up my INR for about 2 days. It's good to be a enjoy a drink now'.* GD, man 65ys.

These are just a few examples of how the reduction of side effects offered broad benefits. In the first interview patients talked of a domino effect; one illness impacting on others; and one negative effect of Warfarin leading to other issues, so decreasing their ability to be comfortable and mobile. So, life, they felt, was closing in on them. A reverse domino effect was now reported, with one symptom reduction leading to an opening up of parts of their lives which they thought they had lost. An example of this is the improved sleep patterns for some:

> *'The night sweats still happen, but I'm not dripping in sweat like I used to the nurse said to keep an eye on it, but it seems to be getting better. At least I can get more sleep now'.* AB, woman 91ys

It was not made explicit why their sleep had improved, but since many were now undertaking more exercise that may have played a role. Leading on from this, several patients reported improvements in their sense of wellbeing and how life was, for several, simply more comfortable – even if they had no major health improvements. For example, one woman was delighted that there was a significant improvement in her appearance – her hair had begun to grow back:

> *'…...it's only a few millimetres but my hair has started to grow back'.* MR, woman, 65ys.

What may appear to be small changes can have huge implications for these patients. This can be easily missed by the clinician whose primary concern is managing the patient's major, even life-threatening condition.

6.6 New beginnings

Small liberations led some patients to report quite complex pathways to better health, with the removal of the perceived barrier, real or imagined, created by the need to take Warfarin. Some were now able to face up to other health issues for the first time in many years. It appeared that improvement in one area of life raised their spirits to such a degree that they were prompted to review other areas that had been burdensome. The impact seemed to be cheering for a significant number, and a new start seemed to be offered. For example, this woman talked of reversing old bad habits:

> *'I think I used my health problems as an excuse for a long time. I ate poorly, and I never really worked out. But I think it's time for a change. I was talking to my GP about all the green foods that I can eat now, and she suggested a whole lifestyle change to help control my diabetes. So far so good'.* KS woman, 65ys.

This man was also very clear about the positive impact:

> *'I'm not sure how much weight I've lost now, but my trousers are definitely looser. I'm really surprised, cause its literally just been a short walk to the shops and a few light exercises once a week at the gym. I can't really do too much. But yes, I'm really pleased'.* MK, male 68ys.

Two virtuous circles seem to be at work here. One is that better access to pain relief is leading to increased mobility and better quality sleep.

> *'I can walk to the shops now (new pain relief) and take my time shopping, I used to have to be aware of what foods to get so I just had a routine of getting the same things every time. But I can take my time now and buy different things'.* GA, woman 69ys.

A second circle relates to the wider availability of healthy foods, weight loss, improved appearance, and subsequent growth in confidence:

> *'My (blood) pressure for the most part is ok, and I still have some pains from the arthritis, but I am eating more greens now which I couldn't do before, so my cholesterol has gone down…...yeah I have noticed a difference'.* AB, man 91ys.

6.7 Liberation for some was a loss for others.

It is important to note here that a few patients were less enthusiastic about the switch, claiming that they had not been unhappy on Warfarin. However, it became clear that the loss of Warfarin was not the problem, rather it was the change of the health care process. While heralded as a great improvement for many, the absence of the weekly clinical check-up was major loss to others. It had become clear during the first interviews that several patients lived relatively isolated lives, and while not the main purpose of the weekly check-up at clinic it was, for some, an important social event. It is important to note that these patients did not report any physical difficulties associated with the switch, but this does not diminish the importance of the missed social experience for this small group of patients. The loss of the clinic would have been noted less but for the isolation experienced by several patients:

> *'I feel like I do nothing all day. I have no kids and I'm widowed, so I don't really have much to do, or people to visit. It can get very lonely*'. SS, woman 82ys.

> *'Every other Thursday they send the bus to pick me and take me to the clinic. It's nice because I get to catch up with the other patients on the round. We have a good chat. We talk about knitting, our aches and pains and things like that. Mary used to be a nurse, so sometimes we badger her with questions. Poor Mary, she's a good sport'.* GA, woman 69ys.

The following case illustrates many of the concerns voiced by this group:

'I really preferred to be on Warfarin, the old system, it's a reassurance to know what your INR is'. MP, woman 85ys.

It is noteworthy that her switch did not occur after a period of discussion, but suddenly as a decision by the consultant three days before a knee operation in order to minimise the risk of haemorrhaging during or after the operation. This was standard practice for patients on Warfarin. The consultant used this opportunity to switch the medication rather than resume Warfarin post-operatively. The patient, a woman of 85ys, had been on Warfarin for 17 years and had been more than 75% outside of her Warfarin therapeutic range for the past 12 months.

MP reported that she was very unhappy with the switch to DOACs. She lived alone with no children or family and, as well as AF, suffered from diabetes, high blood pressure and rheumatoid arthritis. MP had recently had both knees replaced due to severe pain from her rheumatoid arthritis in her joints. She was also taking multiple medications for her complex range of illnesses. It was therefore predicted that there might be interactions between the Warfarin tablets and the pain medications. While she understood the reason for the switch, she said that she missed the contact with the nurses she has known for a long time and trusted., She complained that she had had pains and had to wait 15 days for a doctor's appointment instead of talking to 'her nurse'. She said that she was constantly unsure of whether the new medication was working and had no one to tell her it was ok. It was not just the lack of reassurance of a friendly figure that troubled her, she said that she was very lonely and missed the interaction on the NHS transportation bus, which took her to her weekly appointments at the anticoagulation clinic. The bus journey with the other patients with whom she had forged a friendship over the past 17 years was a chance to catch up with her friends, some of whom were also elderly and house-bound, and to share her experiences of being ill. Essentially, she now considered herself a shut-in and had become very sad. MP still suffered some discomfort in her knees but, on a more positive note, said that felt she was getting stronger all the time

6.8 Responses by age and sex.

The themes reported here were broadly true for all the participants irrespective of their age or sex; however, there were notable variations between some groups. For example, the much-voiced concern about the lack of regular monitoring was a greater concern of the over 75s of both sexes, although the difference is slight, as several 65-70 year olds also voiced concern. As might be expected, the loss of the bus trip to the clinic was more often voiced by the older participants who were also more likely to live alone. But again, this is not hard and fast, as some younger participants also felt the loss.

6.9 Overall satisfaction with the switch.

In order to gain a group perspective on the level of overall satisfaction with the switch, the second interview schedule (90 days) included one scale item asking the patient to score themselves as: 1 = very unhappy - 7= very happy. The data was analysed by both age and sex and the response was overwhelmingly positive on both counts. See Figure 6.1. Almost all of these patients rated themselves as happy and a few as very happy, there was little difference when analysed by age and sex. This overall positive view is in accord with the interview material.

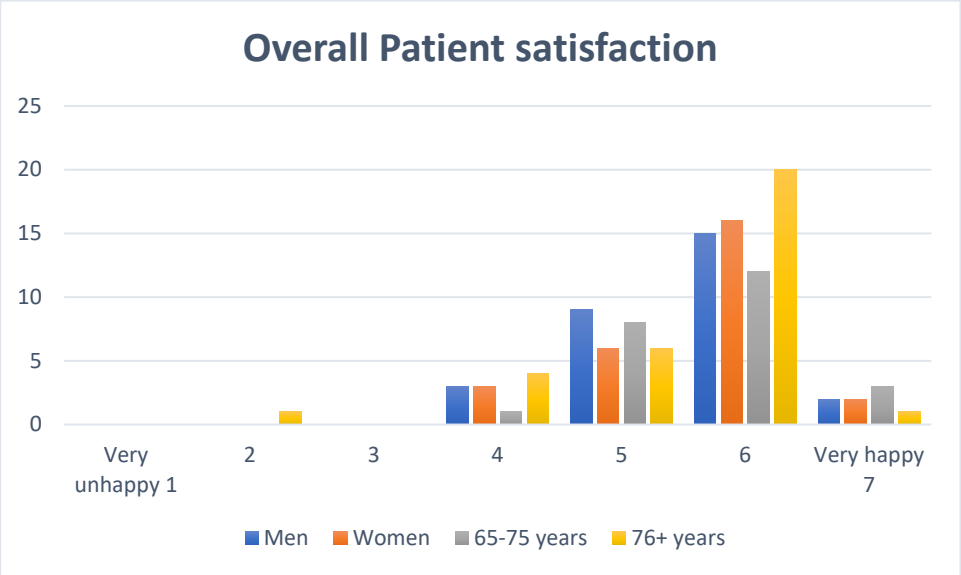


Figure 6.1
Patient Overall Satisfaction with the switch, separated by age and sex

6.10 Comparison of findings from Time One and Two.

While the themes emerging during the second interview were similar in many respects to the pre-switch conversations, they took on a new and, overall, more positive perspective. One theme remained unchanged, however, that of 'stalwartness'. The participants sense of 'carrying on no matter what' remained just as evident three months later. This appears to be both a benefit as they step into the unknown of a new medication regime, presenting a potential problem if taken too far and difficulties are not expressed to their clinical staff. The theme of 'loss of control' voiced at Time One was, for many, reversed, with a feeling of regained control over their own bodies and parts of their lives. Overall, the patients reported improved wellbeing, mainly resulting from their new drugs, and a reduced area of conflict with a range of food stuff and medication. For some, it felt like a new start to take back more control over their lives. This resulted for many in a freeing up of their time to allow travel and make plans away from home.

However, the very change that liberated many patients created a problem for others. The old routine of clinic visits had clearly supported many somewhat isolated patients, but the gap left by the new regime for some patients' lives could not be filled by the clinic. Rather, it could be argued, this fell in the domain of their GPs' responsibilities. The improvement of service in one area, with the reduced need to visit a clinic, also created a need for services (not necessarily provided by the NHS) in another aspect of the patients' lives for some patients.

This research suggests that the strongest influencer on the patient's wellbeing is not a single factor standing alone, for example now being able to eat a wider range of vegetables, but rather the interaction or combination of several factors – a positive domino effect. However, underpinning all of this are the patient's personal domestic circumstances which so often determine the level of support they could expect.

This next section reports on the data gathered from the four staff interviews.

6.11 Staff interviews

The staff interviews were conducted by the researcher at the Anticoagulant Clinic at St Mary's, Paddington. As mentioned in Chapter 3, a focus group was originally planned, but due to difficulties with the staff rotas the interviews were carried out individually. It was originally hoped the eight staff would be interviewed but, for the same reason, only four were available. The aim was to explore how the staff received information about the new DOACs, any concerns that they may hold about the treatment plan, and their perception of the patients' responses to the new medication. Their views about the provision of information were discussed in the previous chapter. In addition, the interviews aimed to explore any concerns they might have about patients switching from Warfarin with regard to wider health issues and any emerging social implications. The interviewees had considerable experience of working with DOAC patients – between 3 and 8 years. Two were anticoagulant nurses, one a pharmacist, and the fourth a consultant haematology doctor. Two were men and two were women. Each week they saw between four and eight DOAC patients.

At each clinic visit, the patient's compliance (blood test) with the Warfarin regime is recorded electronically. Following this, the computer will then provide an alert if the patient shows difficulty in compliance. The nurse then talks with them about their difficulties with the treatment and can refer them to the consultant for further discussion and a decision. (It was claimed that often the nurse, who may have known the patient for many years, could tell without the aid of the computer that the patients were not coping on Warfarin and would refer them to the consultant.) This process would take place a few weeks before the switch. Written information would be given to the patient at each stage, and a time offered to come into the clinic with any questions. Their GP would also be made aware of the switch, and would also be offered information if required when they take on responsibility for the prescribing. With regard to the decision to switch to DOACs, the staff made it clear that it would be made on clinical grounds, with the patient's personal life only being considered if it was deemed to be the cause of their poor compliance – for example the patient's poor drug time keeping, or a medical emergency occurring.

6.12 Awareness of the impact of the new medication on the patients.

At the time of the switch staff reported that the psychological or social impact on the patient as a result of the change was not generally taken into account. The clinical data was all that mattered:

> *'Not as much as would like, you tend to get to know the patients over a course of several years, but I tend to assess the patient's clinical need for the medication …… and whether or not they qualify under the rules and guidelines for switching to the new medication'.* Consultant.

However, on reflection, as a result of their growing experience with these patients, the team thought that wider considerations should be made relating to the patient's domestic circumstances. But these considerations were unlikely, unless extreme, to override the person's clinical needs. Despite the small role that social factors played in the decision, the team were aware of several factors, the foremost of which was the lack of future clinic monitoring sessions and the anxiety it generated – for both staff and patient. The lack of regular check-ups generated four areas of concern. The first was the team not being aware of a patient's non-compliance (adherence), and so other medical issues could follow:

> *'Accidently overdosing or their missing doses is my biggest fear'.* Nurse.

Linked to this issue of over or under-dosing is the lack of reversal for the new medication which could be a problem although only in an emergency. Bleeds resulting in a need for emergency treatment were generally considered by staff to be a result of overdosing, so timely tablet taking was key to success. However, small domestic mishaps such as a cut with a potato peeler could also create an emergency situation. Despite this, these drugs were considered to be relatively low risk:

> *'Mostly in an emergency, but it's a pretty stable drug. The medication should be out of the system in just over four hours'.* Nurse.

While the risk was low risk, it was still a risk. The consultant had a more general concern for his older patients:

> *'Older patients are prone to falls and can get quite nasty cuts and bruises, so particularly for those and trauma patients, the lack of reversal may be an issue'.* Consultant.

The risks did not, in the view of this team, outweigh the benefits. It was more a matter of the patient getting used to a new routine and being alert enough to maintain it.

The second concern was the patient being anxious about knowing if the medication was working. While the staff felt confident that the majority of the patients were coping well with the change, it was acknowledged that other issues might weigh on the patients' minds. The nurses had some sympathy with their anxiety. The third concern was that potential warning signs of distress, not all of them medical, could now easily be missed until their GP may picked it up:

> *'Sometimes I find bruises on the patients or find out information during the chats that I would have missed otherwise. Sometimes it's nothing to do with the Warfarin, these patients may be experiencing abuse or loneliness, these are the signs that may be missed without a clinic'.* Nurse.

While not frequent, it happened often enough to be raised as a concern. Finally, the withdrawal of a social support provided by the clinic visits concerned the nurses. It was not simply the medical consideration of no regular check-ups, but the team recognising the social role the visits fulfilled:

> *'The older patients struggle with not coming to the clinic. Some are widowed or shut-ins – so they complain about not having the clinics'.* Nurse.

> *'To be honest most of the issues are social problems, but there are issues such as the reduced access to the medical team that can cause some patients to be overly anxious'.* Nurse.

The complexity of settling down to a new medication programme was well understood by the consultant:

> *'It often depends on a whole host of extenuating circumstances such as other medical conditions, as well as the social and psychological condition of the patients. …persistent pain, or loneliness… all of these a can have an impact on how the patient responds to changes in their routine, not just to changes in their medications'.* Consultant.

6.13 Positive aspects of the switch

The clinical team were clear that the switch had several benefits for the patients, and they were the same as those reported by the patients. For example, the patients having more time to themselves, and not being restricted by clinic visits, was considered a major benefit for most patients. This was linked with a keen awareness that this is an older population, who were relatively isolated at home and they liked the social interaction of the hospital trip. Possibly the most positive impact recognised by the staff, because of the multiplier effect of additional positive implications, was that the new medication had fewer issues around interference with other medicines and types of food:

> *'I think the fact that DOACS are more stable is a high plus for these patients'.* Nurse.

The full implications were understood as the Consultant said:

> *'The patients now have a wider selection of medication and diet options that they were previously excluded from. Especially the patients that suffer from chronic pain, they can now have access to stronger more effective pain relief that was not allowed to be taken with Warfarin'.* Consultant.

It is interesting to note that while this benefit is acknowledged and given its huge implications for the patients, it did not come top of their list of benefits.

6.14 Could the trust do more?

It was clear from the team's responses above that they understood the patients' needs for on-going support, particularly among the over 80s. But, importantly, they considered that such support needed to be easy to access and located in the community rather than with them. In reality, this support was currently, as far as they were aware, sporadic, and dependent on the patient's GP practice or community nurses:

> *'There is of course always more that the Trust should be doing, but the reality is that there is insufficient funding to ensure patients in the community are compliant with their medication'.* Consultant.

Given that the issues for limited community care were often financial, one nurse offered a solution: that the reduced clinic time due to these patients not coming in for regular check-ups would generate a financial saving which could be redirected:

> *'I think that some of the savings gained from switching to these new drugs should be spent on community nurses to check up on these patients. I think that there is such a post code lottery when it comes to access to social care. The trust should consider more community based care. Patients may even do better being cared for in their own homes and free up much needed bed space'.* Nurse.

One practical suggestion was offered – that the patients could be reached by telephone, not necessarily by the Trust, but perhaps from the community:

> *'Maybe check up on them more after the switch or have a team of admin staff that call them routinely to see how they are getting on. It would be interesting to see how they are doing six months, a year or two later. For younger patients I think they will be ok, but the older ones should be checked on. Definitely worth doing'.* Nurse.

6.15 How the staff and patients' perceptions compared

There was a good deal of commonality between the views of the clinical staff and their patients, which was to be expected given the long relationship. The fundamental benefits of the new medication were understood by both groups, as were the patients' reservations about the new responsibility of unsupported compliance with the treatment. The patients, understandably, provided more detailed and nuanced information about life after the switch than the staff. The one area where a gap in perception was evident was in the breadth and depth of the impact on personal achievements enabled by the new medication's lack of conflict with many formerly incompatible foods and medicines. According to the patients, some outcomes were life-changing and had a positive impact on wider health issues. However, this information could not routinely be made known to the staff given the time constraints of their clinic interview.

In the next chapter the findings from the questionnaires (PPS and SF-36 scales) administered during both the first and last interviews are discussed.

Chapter 7 – Findings three:

Scale Data Analysis

7.0 Introduction

The responses from the patient interviews reported in the previous chapter allowed for important themes associated with living with the new medication to emerge. Patients spoke openly and sometimes in an unreserved way which allowed the issues to be explored thoroughly at an individual level. However, it was considered important that this idiographic (personal) material should be supported with nomothetic data (general statements) in order to gain a fuller picture of the patients' perceptions towards their medication routine and their general health.

This chapter reports on the findings of the two questionnaires used as survey instruments for this study: The Perceived Stress Scale and the Short Form 36 (SF-36) Health Survey. The two scales were administered to the 56 participants (29 men and 27 women) three times: at the switch over, then at one and three month time points.

7.1 Findings – Perceived Stress Scale (PSS)

As discussed in the methods chapter, the aim of using the PSS scale was to ascertain the level of stress these patients considered themselves to be under before and after changing to the new medication. The scale is a short one, just 10 items, and produces one overall score. It does not subdivide the score into smaller units, so the findings are relatively straightforward to present. The findings of the PSS scale show that, overall, the perceived stress of all 56 participants reduced between Time1 and Time 3, - ninety days later. Of importance to note is that the greatest reduction was between Time 1, at the switch, and Time 2, four weeks later. See Figure 7.1. The decrease in score was quite marked. The reported reduction in anxiety happened quickly, within the first four weeks, and stayed down, but with the level of anxiety falling only a little further between two and three months post switch.

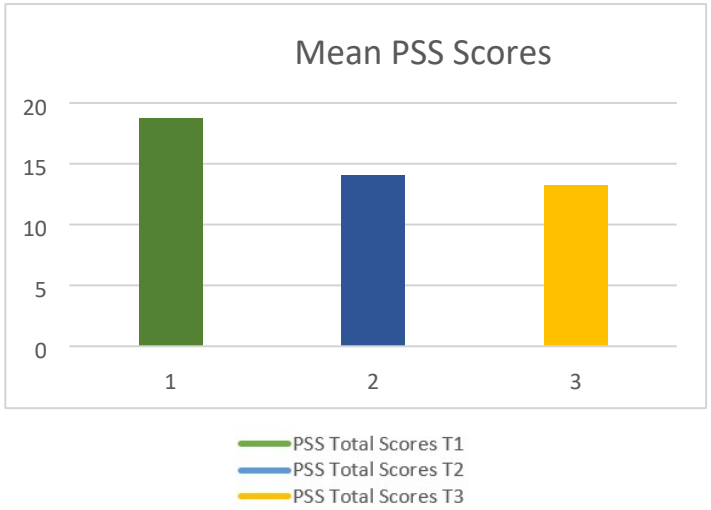


Figure 7.1
Mean PSS Scores

In order to compare the data at each time-point and determine how much the three groups differ, statistical analysis of the average PSS scores at each of the three data time-points using one way anova was undertaken. The results are shown in Appendix 15, Table 1, which shows that the F crit value between the groups is lower

than the F value between the groups. Because the calculated value of F from the PSS data is larger than the value in the F table, there is proven variance between the populations being explored to a 95% confidence. This indicates that the results are robust, and not random or due to chance.

The F crit value represents the point of intersection of the data, and the F value represents the ratio of variance (should be close to 1.0). A one way ANOVA was conducted to compare the mean PSS scores at each time point and showed a significant difference, F (2,110) = 13.79, p < .001 - See Appendix 15, Table 2. Therefore, as seen in Table 7.1 the mean of the total scores for each time point shows that there was a general consensus among patients of feeling less stressed 90 days after switching from Warfarin to DOACs, and that this was statistically significant, not arrived at simply by chance.

7.2 Age and Stress Scores

Figure 7.2 shows that the observed changes are maintained across all age groups at the point of the switch, at week four (T2) and at 12 weeks later (T3) (See Appendix 15, Table 3).

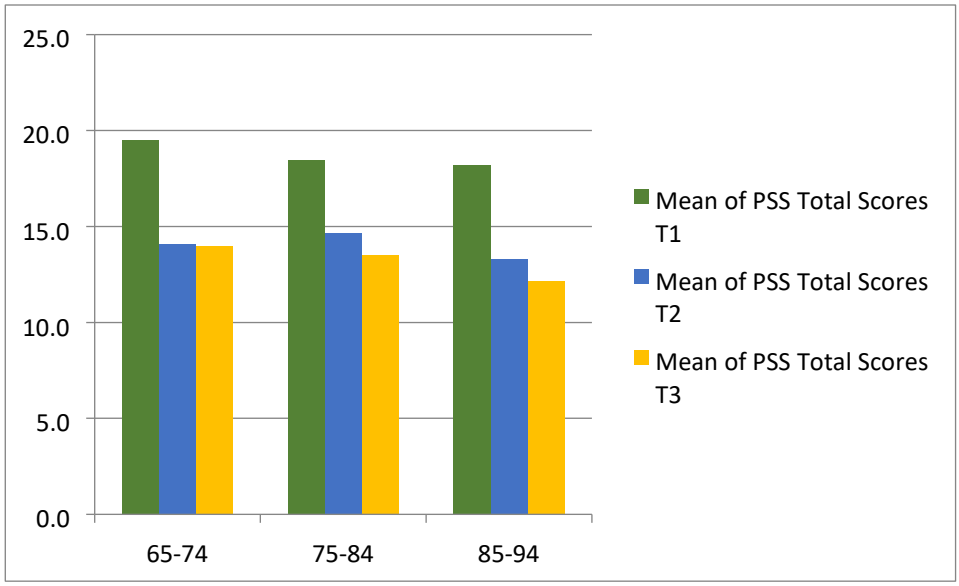


Figure 7.2
Mean PSS Scores by Age.

In all groups the most marked change is within four weeks of the switch. Interestingly, the 85-94year age group recorded the lowest stress scores at all points, though the difference is minimal between groups. There was an overall decrease in the stress scores by approximately 5%, which is significant (See Appendix 15 Table 3).

The patient's self-reported outcomes may be related to a perception of life in general being less stressful anyway. Given the small sample size it is important not to read too much into this small difference between the age groups. The fact that the patient's stress level is determined by a spectrum of confounding factors may contribute to this result, not simply their change of medication.

7.3 Sex and stress scores

Figure 7.3 shows that across the time points there was only a marginal difference between the total stress scores in males and females. And as was reported for age, both sexes responded in a similar way across the time points; that is, the biggest change was within the first four weeks.

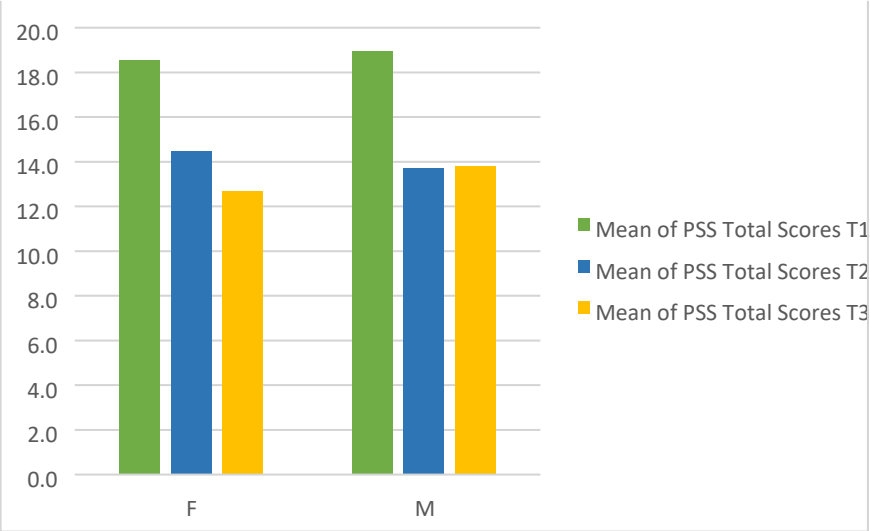


Figure 7.3
Male and female scores for 3 time points

In Figure 7.4 the picture is broadly the same when the data is analysed across age and sex. However, while the 65-74ys, and 76-84 year olds present only marginal

changes in their stress reduction after week four, women aged between 85-94 continue to reduce their stress over the 12 week period. Interestingly, the men in that older group show a slight increase of stress at time three.

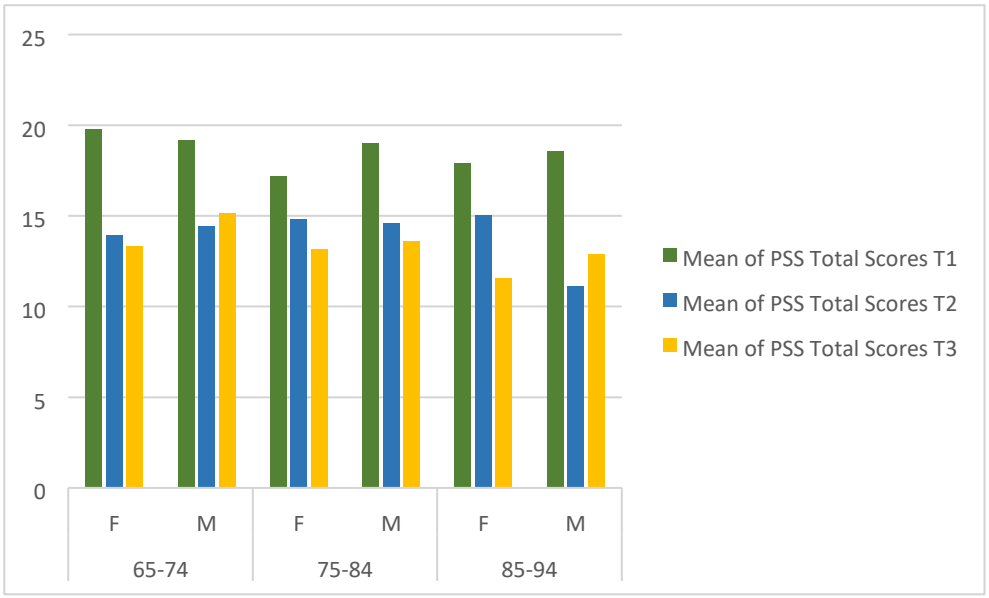


Figure 7.4
Scores by age and sex

It is worth noting that based on the analysis of the overall data from the switch over point compared to day 90, there were no significant changes in the responses for any individual each PSS scale item when analysed by both age and sex together. The factors of age and sex do not appear to have a significant effect on these patients' perception of their overall level of stress.

7.4 Short Form 36 (SF-36) Health Survey

Turning now to the second questionnaire administered at the same three time points, the Short Form F36 (SF-36), which is an indicator of self-reported overall health status. The scale divides into two sections: the physical component scores (PCS) 18 items, and the mental component scores (MCS) 19 items, each with answer options from a min of 2 and a max of 5.

7.5 Results - whole group

Matched-pairs *t*-tests were calculated for both the PCS scores and the MCS scores. The results are presented below in Table 7.2. Noticeable were the reductions in the mean PCS and MCS, but the difference between the total group scores (times 1, 2 & 3) groups was not significant.

Component	Difference	*t*-value	*P*-value
PCS	1.80	1.877	0.063
MCS	0.73	0.789	0.437

Table 7.2
Results of matched-pairs *t*-tests
PCS = physical component scores, MCS = mental component scores

The combined scores for the SF-36 for each participant at each of the 3 time points (n=169), 51 (91%) of the 56 described their health as moderate. Figure 7.5. This is consistent with the number of participants who first expressed views of satisfaction with their overall health then later expressed dissatisfaction with some aspects of their health and social circumstances. See Appendix 15, Table 6.

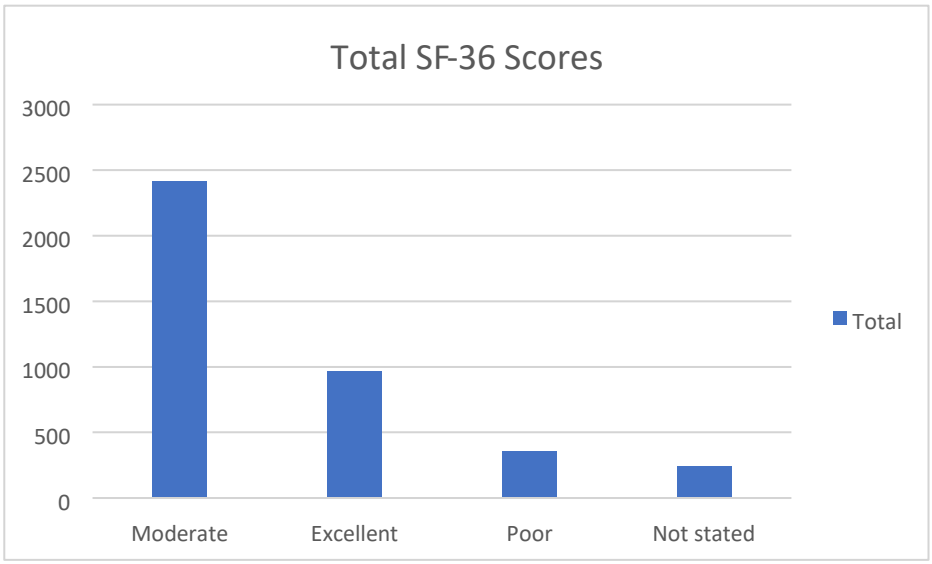


Figure 7.5
Mean SF 36 scores for overall health – the whole group

7.7 Results by age and sex

Older patents in the study, 85 years and over, showed a greater satisfaction with taking the old medication Warfarin ($p<0.008$), with fewer reported Warfarin-related issues ($p<0.001$). This may be associated with comorbidities, social or other reported psychological issues relating to loneliness and isolation and a liking for the regular clinic visits required for Warfarin therapy. This age group of Atrial Fibrillation patients (>85 years), interestingly also had a decreased perception of potential benefits from switching from Warfarin to Direct Oral Anticoagulants ($p < 0.001$), and also showed markedly less interest in potential side effects or safety-related issues of DOACs ($p < 0.001$). Perhaps there were used to living with risk.

The men and women had very similar reactions to each other, with very close mean SF-36 scores. Females, however, scored very slightly higher, that is more positively, for both the MCS (mental health) and PCS (physical health) domains. This was supported by data generated from the ProCore® software, which compared the results from this study, to other studies conducted on Atrial Fibrillation patient populations of the same age, using the same SF-36 questionnaire (Hayes, et al., 1995). In this study, females (n =27) scored an average of 40.8 for **physical health** issues and 37.7 for their **mental health**. The males (n=29) scored an average of 39.9 for **physical** and 36.5 for **mental health**. See Appendix 15, Table 7.

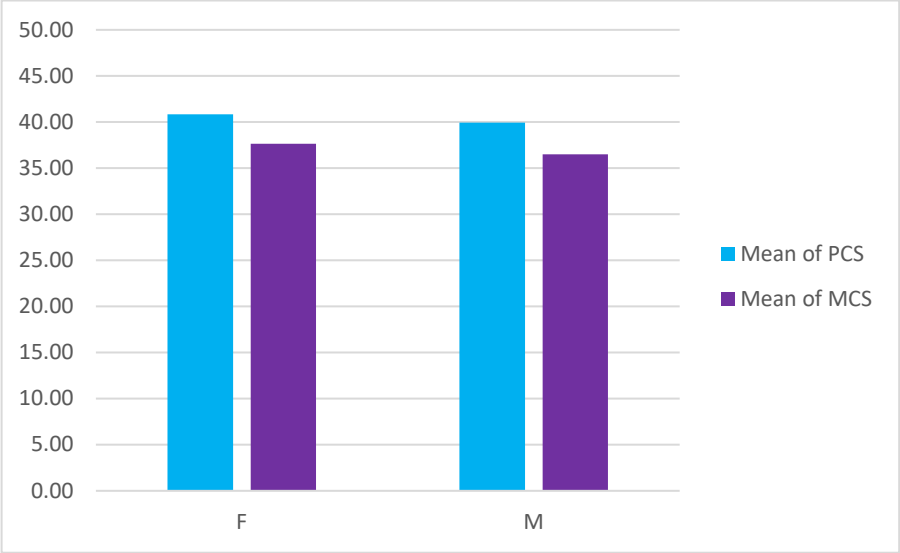


Figure 7.6
Mean PCS & MSC scores combined time points – Male and female

There was no significant difference between men and women with the mean overall therapy switch satisfaction ($p = 0.624$). Of note is that the women reported a greater number of problems associated with their Warfarin therapy than men ($p = 0.047$, Mann–Whitney U test). Conversely, the women were significantly more concerned about the switch (side effects, monitoring, etc.) than men ($p < 0.001$). The potential benefits associated with the switch from Warfarin to Direct Oral Anticoagulants in both men and women were remarkably similar ($p = 0.276$).

Bodily pain was the most reported domain of this scale, with almost 50% of all participants across all age groups reported having either a chronic or acute pain. Consistent with the results from the Perceived Stress Scales, a mean of 27% of all participants reported being emotionally affected by events that had happened in the preceding 30 days of the study. See Appendix 15, Table 8.

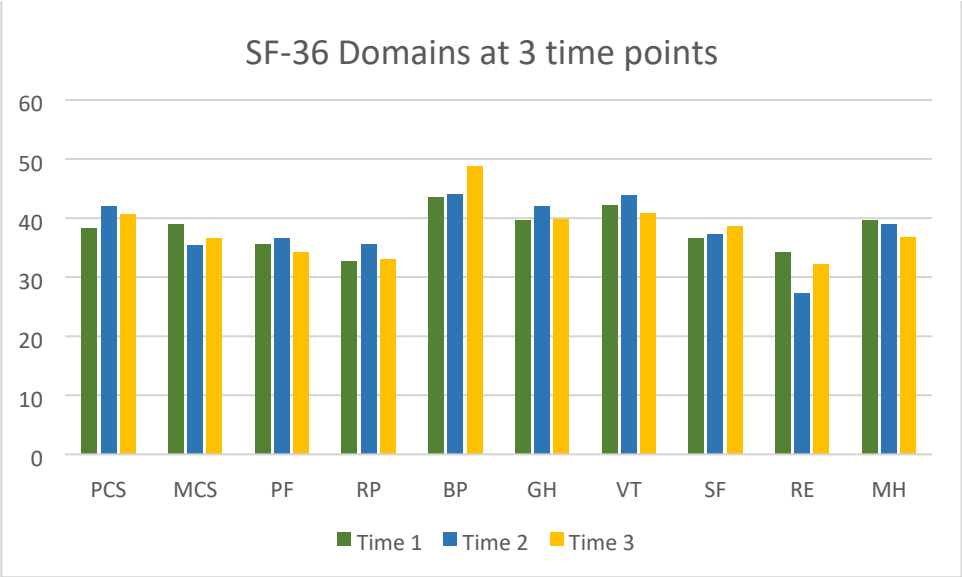


Figure 7.7
SF 36 Domains at 3 time points
PCS, physical component summary; MCS, mental component summary; PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health

7.8 Duration of Warfarin therapy and quality of life

The patients who had been taking Warfarin for more than 10 years were reportedly less accepting of the adverse side effects it brought, for example, interactions with other medications, their diet and pain relief restrictions. Therefore, it was considered of value to explore this further here. On the SF-36 scale, a 'p' value of 1.0 is the maximum score achievable for a patient satisfied with being on Warfarin. It was noted that the longer the patient had been on Warfarin therapy, the lower their satisfaction with it ($p = 0.026$).

Interestingly, whilst there was more apprehension around switching to a new medication in the >85 year group, there was no direct correlation noted, between years on Warfarin and the patient's satisfaction with the new medication they were switched to. The apprehension appeared to be linked to 'a change' rather than 'the change'. This is further substantiated by the fact that the overall satisfaction of the medication switch, when the patients were asked about information provision and

overall understanding of the new DOAC therapy, gave a ‘p’ value of p = 0.879, with is a positive finding. See Appendix 15, Tables 9a & 9b.

7.9 The total SF-36 score by sex and employment status.

During the first interview the employment status of the participants was discussed, the sample was then divided into ‘retired’ and ‘working’. Along with ‘male’ and ‘female’ these subgroups were analysed by each patient’s total SF-36 score (satisfaction score). The satisfaction score directly correlates to the Quality of Life of the participant. The findings showed that retired men had a better overall satisfaction score compared to non-retired men, but this association was not observed among the women. Men living in cohabitations or in mixed arrangements also had a higher score and therefore a better quality of life, than those who lived alone. Interestingly, women who lived alone had a median score and did not show a clear overall satisfaction or dissatisfaction with the SF-36 scores. With regards to their self-reported level of physical activity, the men and women who stated they did not practice regular physical activity tended to have lower overall score. Women who reported good physical and psychosocial health were more likely to have a higher total score then those who did not. For men, the highest total score was associated with those with higher socioeconomic conditions (e.g. income, education, occupation, and neighbourhood).

Gratifyingly, the most commonly reported overall patient perception was a positive response, as 30 of the 56 participants (54%), noted that there were fewer food, drink, and concomitant medication interactions to contend with. They also noted that they could be prescribed a wider spectrum of medications post switching than when they were on Warfarin. Most commonly, these were prescriptions relating to arthritis, general pain, and recurrent infection (usually antibiotics).

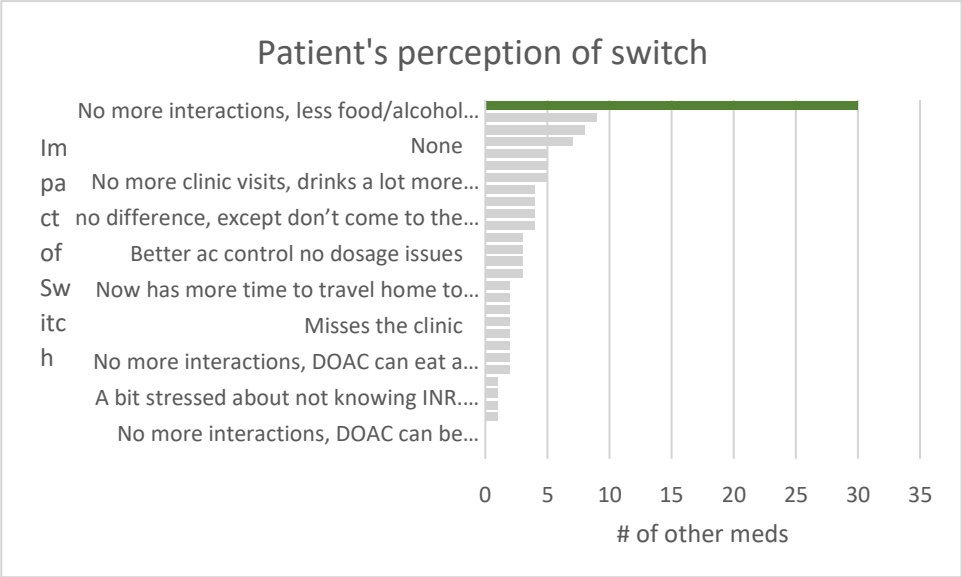


Figure 7.8
SF 36 Patients on multiple medications perception of switching

7.10 Conclusions

The findings from both sets of scales are consistent. The Perceived Stress Scale shows a notable positive impact, a reduction in stress levels, right at the start of the new treatment that was sustained for at least three months. This pattern held true even when the data was analysed by sex and age. Interestingly, there was slight tendency for the older female participants (85+) to show lower stress levels at the start and a greater reduction in stress at time points two and three.

The findings from the SF-36 questionnaire indicate that the participants were, overall, reasonably positive about their state of health, with most rating themselves as 'moderately healthy'. Slightly more declared themselves to be in 'excellent health' than those who claimed to be experiencing 'poor health'. This was despite about half the group experiencing bodily pain at the time of the study. These findings were largely unchanged when analysed by sex and age. These results are supported by the work of Chiong and Cheung (2013), whose results confirmed no significant difference between the sexes. Concerns about mental health were less frequently reported as troublesome than physical illnesses. These findings are supported by similar studies, for example Campos et al (2014) who found a direct link between physical activity and the quality of life in the elderly, with particular

reference to the impact on the following domains: '*autonomy; past, present and future activities; death and dying; intimacy; mental health; vitality; and psychological'.* These interesting findings support the decision here to include scales as a research tool; they have provided statistically sound evidence of a perceived positive change after the switch which supports the interview material.

The discussion and conclusion chapter which follows will combine the findings from the interview materials and scales, and will draw conclusions about the participants' perceptions of life on their old and new medication. This is followed by recommendations for the future care of patients switching from Warfarin to new anticoagulant therapy

Chapter 8 - Discussions and Conclusions

8.0 Introduction

This study explored the perceptions of 56 AF patients who switched from Warfarin medication to one of the new DOACs. In this chapter the findings are discussed in relation to other research on the subject, and to current NHS policy on the long term care of these and other AF patients. Recommendations are made with the aim of helping translate the findings into practical support for all such patients. Finally, the limitations of the study are discussed. The aim of the study was to undertake a

qualitative exploration of the perspective of a sample of patients who were required to switch from a life-long treatment plan on Warfarin to a new drug regime on one of three of the Direct Oral Anticoagulants (Apixaban, Rivaroxiban or Dabigatran). The aims and objectives were achieved, with several key themes emerging from the data which will inform healthcare professionals of their patients' views, and which will aid them significantly in providing a more patient-centred treatment plan.

8.1 Context

At the time of the first interviews the majority of this sample had multiple co-morbidities, with many concomitant medications, and these did not change over the three month duration of the study. Often patients had to juggle their medication; each tablet had its own requirements (for example, to be taken pre-meal, post meal, twice a day, four times and a day, first thing in the morning or last thing at night). This presented the patients with a complex schedule of medication to maintain, which for many became a struggle. Adherence to long-term Warfarin therapy remains challenging due to the risks of anticoagulant-associated complications and the burden of monitoring. The patients here expressed a variety of reasons for having missed doses, including forgetting to take their tablets, self-adjusting their dosage in order to consume alcohol, or missing a dose because of personal circumstances such as travel. A few patients reported missing a dose of Warfarin deliberately in order to allay the side effects of Warfarin. Adherence was measured by the clinic staff by asking the patient whether they thought they were excellent, moderate, or poor in taking their medication, and why. Poor adherence leads to poor anticoagulation, which is reflected in the patient's blood test results. Among this sample, the anticoagulation team anecdotally noted that adherence was one of the most common reason for poor INR results.

These participants stated that various factors affect adherence, possibly related to cognition (poor memory) and also to physical, functional, and psychological status plus outside influences. Horstmann (2019) undertook a European study and showed that of 94% of patients were receiving oral anticoagulants for 12 months following a stroke. Unexpectedly, physical, and functional problems, more than

cognitive performance, were associated with discontinuation of anticoagulant therapy at 12 months; adherence tended to be better with DOACs than under Warfarin. That finding is very different from the sample reported in this study who did not show any signs of needing to discontinue their oral anticoagulants. Were they just lucky or were there other factors involved? It is difficult to assess adherence objectively; there may have been a selection bias in the present study, as patients with a cognitive disorder were excluded for reasons of feasibility (ability to complete the questionnaires).

The patient's satisfaction with their pharmacological treatment should be considered as an important factor in clinical practice. This is because satisfaction with, and preference for, a given drug regimen may have a significant impact on medication adherence. In similar clinical studies a higher medication satisfaction in patients is associated with better anticoagulation control (Choi *et al*., 2014). Therefore, patient satisfaction with their anticoagulant therapy should be considered an important factor in encouraging optimal medication adherence.

8.2 The broad research objectives and findings:

> *To explore the participants' perceptions and understanding of the new treatment and its impact before and after the switch using a qualitative approach, with a sample of 20 patients, who will be interviewed at the time of the switch and 90 days afterwards.*
>
> *To ascertain the impact of switching for 50 patients by assessing quality of life and the perceived stress at three points: baseline (immediately before the switch), then at 30 and 90 days into the new treatment regime, using standardised scales.*

The objectives were achieved, and, in addition, a further informal conversation accompanied the administration of the scales at the 30 day point. The requests for interviews were met with enthusiasm, indeed several people said how good it was to have the chance to voice their feelings on the subject of their treatment. This produced rich data.

8.3 The emerging themes:

I'm fine – coping with multiple conditions

A theme which permeated all these interviews was that of *stalwartness, self-reliance* and, importantly, '*learning as you go'.* Early in the analysis this culture of *'carry on no matter what'* was regarded as peripheral to this research, and simply an interesting cultural phenomenon of older people, some of whom could remember WW2 and the depravations that followed. They saw themselves as resilient. It was perceived as merely providing a cultural context to the other findings. However, it soon became clear when considering the current NHS plans for managing chronic and long term conditions that resilience is an important and necessary personal attribute to hold. The Department of Health in fact declares its aim to cultivate such feelings of resilience and independence in order to deliver more cost-effective treatment in the future.

The NHS report *Long Term Conditions Compendium of Information (2012)* provides an overview of the situation at present regarding the numbers and treatment of patients in the UK with a long term condition (LTC). A key observation is that the population at large, with or without and long term conditions but particularly those in middle age, must take greater responsibility for their health. This can be achieved, the report argues, if the onset of any long term condition can be delayed for as long as possible thought public heath interventions such as exercise and other healthy living programmes. This would appear to support the views of many in this sample, who relished their newfound ability to self-medicate after the switch and to take more responsibility for themselves, but with the caveat that they should not be left to cope alone. They wanted to have on-going contact with the NHS at times of need, and simply for reassurance. The findings reported here go some way to support the conclusions drawn by the NHS report that patients with long term conditions want the following:

- to be involved in decisions about their care – they want to be listened to.
- to have access to information to help them make those decisions.
- to receive support in understanding their condition and confidence to manage it.

- to receive support for joined-up, seamless, self-care services (NHS England, Annual Report, 2012, p4).

The authors of the report's claim that the best way forward for the older population is to delay the onset of any chronic condition would be sympathetic with this sample. Many patients talked of a 'new start' health-wise, and the all-round improvement to their health after the switch from Warfarin. Some chronic conditions were reversed slightly, such as increased mobility and reduction in pain. Others were slowly improving their health through weight loss, hence decreasing the likelihood of developing diabetes and lowering their blood pressure, and so reducing the chances of suffering a stroke.

They were in fact, through their own sense of wellbeing, delaying the onset of a new long term condition. Foot *et al*., (2014) argue that this cannot be achieved by the patients alone and that they need to be supported in their self-management claims. They also report on patents retaining control of their own health care. The key factors to successfully assisting patients are to have a personalised care plan, structured education for staff and patients alike and, importantly, peer support. (p25). Each of these goals would be supported by these patients.

Concern about welfare of elderly patients within the NHS and the wider society is regularly reported in the headline news, and many research papers are emerging to discuss elderly care (NHS Safeguarding, 2018). Studies such as the one by Pillemer *et al*., (2016) show the problem of neglect and abuse of the elderly to be a worldwide phenomenon. Understandably, most studies are organisational reviews at the level of actual abuse, not at sub-optimal care or at the point where older people find themselves in *potentially* difficult circumstances.

The NHS's safeguarding report (2018) confirms this. They list over eight types of abuse and neglect, though reporting is retrospective; little has been written about the inadequate, though not culpably bad, care offered to the elderly. There is no suggestion that the patients in this study are not treated with genuine care and professionalism by the clinic staff. However, both patients and staff identified a potentially problematic area for the elderly patients after the switch: that of missed

doses and lack of self-care (medicine wise) for those who live alone (Callewaert and Callewaert, 2011; Pillemer *et al*., 2016).

8.4 A leap of faith

This theme of trust in the judgment of clinical staff was true for the whole sample – they were taking a leap of faith with regards to trusting the new medication. Anxiety about the new venture at the point of the switch was very real, however, and only thinly disguised if at all. The anxiety voiced by this sample about not knowing whether the new medication would work, and would continue to work, is not unexpected or unusual. Brosschot *et al*., (2016), who undertook an evolutionary theoretical research perspective to study anxiety, concluded that to feel anxious and concerned in the face of uncertainty, the unknown, is the 'default' position for all humans. It is not 'generated' by the stress producing factor but rather 'uncovered' as it is our natural, risk adverse response to threat.

It is not surprising, therefore, that the whole sample here expressed some degree of concern at the new treatment. Brosschot's theory might also account for the swift reduction of anxiety, as recorded in the questionnaire data, that during the first few weeks of treatment the previously unknown medication became commonplace in their lives. The interviews echoed this, with nearly all expressing satisfaction with the new medication, some almost immediately, while for others it took a week or two.

The presence of anxiety is all too often regarded as par for the course and not always addressed by heath care staff. Mohlman (2013) reports that it is not only medical staff working with older people who may miss signs of anxiety, but psychologists who have been slow to recognise the frequency of anxiety and its impact on the elderly. Even mild anxiety, according to a report by the National Institute of Mental Health (2019), can have a knock-on effect, inducing, in some people, feelings of fatigue, poor sleep or simply feeling restless (Mohlman *et al*., 2013). The anxiety reported by this sample at the start of their new treatment, although brief in some cases, should not be dismissed as inconsequential, and steps need to be taken to provide reassurance at the outset of the process.

Attempts have been made to reduce a patient's anxiety by offering technology-assisted self-testing for anticoagulant patients at home, with some positive results. Kuljis *et al*., (2017) interviewed 17 patients who were using self-testing at home to monitor their dosage. They were concerned with the lack of information about the patient's perspective regarding low clinical engagement and the reliance of education programmes, rather than asking the patients themselves how things were going. While the self-testing was valued by the patients, they also valued the clinic time for the same reasons given here: trust, reassurance, and the human contact. For self-testing by patients to be taken up in any numbers by the patients, the researchers argued that support needs to be the clinic as well. The role of the patient taking more responsibility for their own health was understood and valued but it must be performed within a framework of support.

8.5 A new start for many but not all

A theme of better times ahead or a 'new start' for many of the patients in the lower age range is echoed, although to a more limited extent, in the older participants' responses. This was, to a major extent, due to the reduction of pain resulting in the now wider availability of improved pain relief. More than half the patients lived with varying levels of pain, which inevitably would have a direct impact on their wellbeing, particularly in mobility and quality of sleep.

Twenty percent reported a recent operation, whilst others were experiencing physical pain due to other medical conditions such as arthritic joint pains and lower back pain. Untreated pain can become chronic and greatly diminish their quality of a patient's life (Cracknell, 2010). This sample is typical for this age group across the general population, with arthritis as one of the most common causes of pain in the elderly; results from a study reported musculoskeletal disease causing joint pain, inflammation, and stiffness (Bowling and Gabriel, 2004). Patients who initially rated themselves on the scales as having chronic or acute severe pain, also reported being limited in their ability to perform daily tasks such as walking 50 meters, carrying a small bag of groceries, doing household chores (particularly vacuuming) and the ability to wash themselves. This reduction in the ability to perform daily activities accounted for just over a third of the participants. The patients' general

outlook on life before the switch, for those who experienced chronic pain, was lower than those who did not have pain related limitations, as indicated by the SF-36 Health Survey scores. The ability to perform even moderate physical exercise: walking, performing domestic chores, participating in social activities, and maintaining an independent lifestyle had the biggest impact on the patients' general outlook on life.

This sample was not alone in their responses; Dueñas *et al.,* (2016) found links between pain intensity and a patient's perception of wellbeing. Patients in this study also reported a poorer quality of life than patients with moderate and less frequent pain. Their pain had a greater impact on the physical dimensions than on the mental ones. The researchers also found that in relation to pain intensity, symptoms of anxiety or depression and emotion-focused coping strategies are the variables that most affected the wellbeing of patients – all of which was voiced by the participants of this study. Sleep disorders, often linked to pain, may increase levels of stress and, accordingly, such disturbances can made it difficult for patients to perform simple tasks. They may even impair their cognitive ability, in turn affecting everyday activities in the workplace and at home (Dueñas *et al*., 2016). The new freedom from much of their pain was a major benefit for these patients, and the impact was life-changing in some cases. Importantly, this may also help the patients delay the onset of other conditions due to their increased mobility and subsequently decrease in pain, allowing them to seek out and extend social contact. Improved quality of sleep also enabled them to lead a fuller life despite their complex conditions.

8.6 Sex and age - differences in perspective.

The interview and questionnaire data and the scales data were examined by age and sex to ascertain if any observable patterns emerged. This met the requirement of the fourth objective: '*To explore any effects of gender and age on measures of quality of life and perceived stress before and after the switch'.* Interestingly, very few authors have published research relevant to this topic that report observed differences by age or sex in treatment, or responses to switching medication. The elderly, as far as this area of research is concerned, seem to be regarded as a homogenous group. While it is acknowledged that the interview sample was rather

small to identify any major differences between the sexes or across the ages it was worthwhile exploring to identify if any patterns emerged.

Some difference could be identified, mostly related to age; more of those over 75 voiced greater concern about the lack of monitoring after the switch. Importantly, key to their complaint was the loss of the social aspects of the bus trip to the clinic. This loss increased their sense of isolation, which was particularly hard for those who lived alone. It also reduced their opportunities for obtaining medical advice. It is important to note that anxiety, related to the cancelation of clinic visits as discussed above, was prevalent across all age groups. There were only small differences between the sexes on any issue, and none that could be regarded as a clear pattern, suggesting that other factors such as living alone, general health, and level of pain may be better variables by which to examine any further qualitative research material.

With regards to the scale data, however, the picture was a little more interesting. This was supported by data generated from the ProCore® software, which compared to the results from this study to other studies conducted on Atrial Fibrillation patient populations of the same age, using the same SF-36 questionnaire (Hayes et al., 1995). The Perceived Stress Scale showed a reduction is stress levels as soon as the new treatment began, which lasted for at least 90 days. Neither the patient's sex nor age changed this outcome; it was true for the whole sample. It is interesting that the older women (85+) not only showed lower initial stress levels but also recorded a reduction at one and three months. Despite having several medical conditions, the SF-36 questionnaire shows that they were reasonably happy with their sate of health, and this is in line with their stalwart attitude emerging from the interviews. Interestingly, as a group they were less concerned about the state of their mental health than their physical complaints.

8.7 Other work in this area.

When this research study began over seven years ago there were no published research papers exploring the perception of patients in this older age group who have switched to DOACs. However, during the research period a few papers have

been published, although none focused on the switch over itself and their methods were more restricted, being mostly short surveys not supported by interviews. Therefore, this study has further original knowledge to offer. The outcome is that this current research and that of others has now paved the way towards a practical understanding of the implications and impact on patients of being on anticoagulants and switching medication.

A number of studies on the topic of new anticoagulants, which are gradually replacing Warfarin, are now beginning to appear. Monz *et al*., (2013) assessed the impact of Dabigatran and Warfarin on health-related quality of life factors of 1435 patients with AF. Using a utility and Visual Analogue Scale consisting of five areas: mobility, usual activities, self-care, pain/discomfort, and anxiety/depression at three time points up to 12 months. Interestingly, the findings were a little different from those reported here. For example, there was no significant difference between the Warfarin or Dabigatran groups across any the five health dimensions at the three points including levels of anxiety. Also, of interest is that contrary to the finding here, their Dabigatran group did not report better pain control. However, as the two research methods were different it is difficult to make a direct comparison of the findings. Interestingly, one factor did appear to be consistent across the two research populations - that which this study calls *stalwartness* is also expressed in Monz's sample in the higher than might be expected HRQoL scores considering the number of comorbidities reported.

Fumagalli *et al*., (2014) used PSS scales to study the psychological effects of life on anticoagulants when comparing groups of elderly, atrial fibrillation patients on DOSCs with those on Warfarin. They argued that DOACs could be used more extensively with elderly patients and set out 'to determine whether new oral anticoagulants have greater psychological tolerability than Warfarin'. Their sample was smaller (15 on Warfarin and 15 on DOACs) and older (81+ys) than the study reported here and did not interview the patients. But their PSS scales reported findings similar to those observed here, that the DOASs group expressed, among other things, less stress than the Warfarin group. 'They concluded that NOA have a positive psychological impact when compared with Warfarin in elderly patients' (p99). Patel *et al*., (2015) reports a longitudinal study at Kings Collage Hospital, London, where they studied the dosage and monitoring level of compliance of AF

patients. Some of the findings resonate here. The Kings College team highlighted the discovery of the following health care issue:

> *'We were surprised that an individualized dosing strategy was not recommended for these new anticoagulants when they were introduced into clinical practice. Although the dosing strategy adopted was based on data from large clinical trials, clinical trial populations do not necessarily represent real world populations, especially older and frail people who commonly use these agents'. (*p1*)*

The relative lack of understanding and the lack of action taken to address the needs of older patients would appear to be widespread. That they may require more sensitive person-centred treatment was also noted by Patel and colleagues. This supports the findings here which show that, even in the most caring of clinical environments, older patients need more help than younger ones if they are to successfully manage their own medication programme.

A study close to the aim here was undertaken by Bartoli-Abdo *et al*., in 2016 (of which Patel was a team member) but it differed considerably in methodology and in some outcomes. With a research team from Kings Collage, London they involved 32 people, fifty per cent each of AF and venous thromboembolism (VTE) patients in order to monitor their responses to switching from Warfarin to a new anticoagulant. The patients had, however, already been on the new medication for several months by the time they joined the study. Four focus groups were held, lasting 90 minutes, at two anticoagulation clinics: at King's College Hospital NHS Foundation Trust, London, Denmark Hill and Princess Royal University Hospital, south London. These patients were paid £30 each for their time. (It is noteworthy that the current study did not offer an inducement.) The focus of the group interviews was the value patients placed on VTE against other treatments, their experiences with the new medication, how well they managed it and their level of satisfaction with the new treatment (Auyeung *et al*., 2016; Mabley *et al*., 2019, p63). The patients were seen once only and always in a group.

The results for the Kings College team were, in some ways, similar to those reported here, but did not go as far in fully exploring the life-changing impact of the switch on various aspects of their patients' lives. In common is that the patients had all successfully incorporated their anticoagulant drugs into their wider array of medications and saw no major difficulties in adhering to the treatment plan. Some similar small difficulties were reported, such as clinical appointments for monitoring getting in the way of work and travel. Both samples reported anxieties about how they would know if things were 'all right' without regular testing. They also reported a high level of trust in the care staff to keep them safe from harm. (Also reported by Patel *et al*., 2016, p65). Like the sample here, they reported a high level of compliance after the switch with just a few stating they manipulated the doses to help manage life events.

Their findings also supported the view of the current sample, that of desiring more long-term support even if in-clinic testing was not required. Telephone helplines and occasional meetings were put forward as options. Bartoli-Abdo *et al*., acknowledge that while many of the experiences regarding this type of therapy are known about '…. they nonetheless deserve attention….' if a better service is to be delivered (Patel *et al*., 2019, p66). The Kings sample was small and acknowledged as a limitation, as was the fact that the participants were self-referring and so may not be representative. In addition, there was no attempt to further analyse their findings by age or sex. While the findings of Patel *et al*., may support many of the findings of the study reported here, the St Mary's study aimed to and was successful in gathering more soft, personal material that underpinned the lives of these patients. Patel *et al*., (2019) member of the Kings College research team, returned to the data set and published more findings but they were restricted to clinical issues.

Bajorek *et al*., (2018) explored patient's preference for Warfarin versus newer anticoagulants, using vignettes and interviews with a group of patients on the old and new treatments. Both samples of patients professed satisfaction with their current medication but mostly, it was thought, due to familiarity and not wanting to try something new. Interestingly, similar themes emerged to those reported here, patients claimed that they 'just accepted that things were as there were, nothing you can do about it'. In addition, it was also found that the regularity of the blood testing

was a comfort for those on Warfarin and those on one of the DOACs talked of liking the simplicity of the new regime and the reduction of the Warfarin side effects, but some missed the comfort of the clinic visits.

Most recently, Ng, *et al.,* (2019) compared the quality of life and treatment satisfaction between patients on Warfarin and direct oral anticoagulants in a cross-sectional study. Their findings showed no significant difference between the two groups on physical and mental satisfaction but, despite this, the DOACs group reported being more satisfied with their treatment than the Warfarin patients. Perhaps related to this was the Warfarin patients significantly higher hospitalisation rate due to adverse events. This last finding of higher satisfaction with the new regimen resonates with the findings reported here.

While research studies in this field are still few, notice is now being taken of the patients' perceptions of the old and new treatment programmes. There would seem to be a consensus that this group of older patients show personal resilience in the face of comorbidities, but some do miss the comfort of clinic visits. Importantly, there would appear to be growing evidence that they are generally happier with their new anticoagulant programme than on Warfarin.

8.8 Staff perceptions of on-going care for older AF patients.

These findings are the result of meeting the second research objective:

> *'To interview the medical and nursing staff to explore their level of knowledge relating to issues faced by the patients with regards to safety and compliance, as well as their awareness of the social implications of switching patients to DOACs'.*

Pirmohamed (2006) said that due to the frequency of contact between the patient and the nurses in the specialist anticoagulation clinics based in a primary care NHS hospital, they are able, through building a trusting relationship, to effectively and safely manage anticoagulation patients who require a multi-disciplinary or multifunctional approach. It would appear that the frequency of contact with the

same staff and subsequent trust is key to patient's continued health then and now. Trust of course requires stability, such as the same team with low staff turnover within the clinic team in order for trust to build. It was clear from their interviews that the staff at St Mary's anticoagulant clinic cared very much about their patient's welfare. Though this was in the best interest of and at the heart of each patient's treatment plan, it was, however, necessarily limited to clinical concerns. Noticeably, concerns relating to bleeding were not often mentioned by the patients and have not been directly linked to improvement of patient satisfaction in this study. However, it is worth noting that concerns of bleeding play a role in deciding the prescription given to AF patients for the primary prevention of stroke.

The staff were aware of some of the personal, non-medical consequences related to the switch, but were less alert to the wider implications which sometimes lasted for the rest of the patient's life. The increased sense of personal responsibility the patients voiced after the switch was acknowledge by the staff, and some concerns were shared, particularly those of not knowing if all was well with their medication. However, it was left more at the level of voicing concern than of having a strategy in place to help them. To be fair to the staff there is no easy answer, as the only plan was that the patient should keep in contact with their GP. A similar finding was discussed by Glasziou *el al*., (2013) when exploring the rise in diagnosis and decline (as they saw it) in 'care'. They state that we need to get better at working *with* the patient, to sharing knowledge of the risks of treatment as well as the benefits, so that the care plan can be shared. This is in line with the tone of the already cited NHS report on long term care:

> *'Patients universally say that they wish to be treated as a whole person and for the NHS to act as one team. Despite this, those people who have more than one condition, particularly older people, face an increasingly fragmented and 'specialised' response'.* (NHS England Annual Report, 2012) p3.

It could be said that the staff did appreciate the patient's difficulties, but it could be argued that they did not fully understand the sometimes positive impact of the switch on many aspects of the patients' lives. The impact of Warfarin into people's lives was not always fully understood, nor was the new freedom of the new medication.

The provision of information to the patient is linked to the roll of the staff. The patients reported being quite satisfied with the amount and format of the information provided but some room for improvement was noted. The information provided was generally paper-based but a link to a website was also given. Elsewhere, more sophisticated methods have been tested with similar patients. Denizard-Thompson *et al*., (2012) worked with 91 patients in America who were educated about good anticoagulant compliance via handheld personal computers during clinic visits. The computer-assisted strategy was received positively by patients and staff and they claimed that the learning was sustained over time. It was cost-effective with regards to clinic time and resources, with the patients undertaking all three modules with little assistance from the staff.

One factor that the St Mary's participants tell us is important to them but is not raised in Denizard-Thompson's study, is a face-to-face relationship which led to the building of trust. In addition, the patients here required repeated 'top ups' of information over time to keep them reassured. It would be difficult to see how the older patients in this study would cope with a much high level of technology assistance despite the attractive elements of the technological approach regarding cost and freeing up of resources (NHS England Annual Report, 2012).

8.9 Should more people be switched?

Given the positive response of the majority of these respondents to the new medication, what might the future hold of other AF patients? Martin Cowie, (2012), Professor of Cardiology at Imperial College London (Royal Brompton Hospital) and colleagues from other leading institutions, reported on the progress of the new DOACs (*NOAC innovation in anticoagulation report.* 2014). Their concern was that many people who could benefit from appropriate anticoagulation medication were not receiving this treatment. The general tone of their paper was that more people could be helped and so avoid the high attendant cost of their required monitoring while on Warfarin:

> *'Routine anticoagulation monitoring adds significantly to the cost of Warfarin treatment. Treatment with NOAC therapies means that routine anticoagulation*

monitoring is not required, and therefore, NOACs may present a release of capacity opportunity for local health services' (p 29).

It should be noted that the report was commissioned and sponsored by the pharmaceutical industry.

The findings here might support Cowie's conclusions, in particular in the light of current thinking about patient-centred healthcare. As the overall response of this sample to has been positive in both practical and psychological ways, perhaps there is room for a discussion within the NHS about switching over more patients. These additional switchers might be selected by their Consultant or GP, but the decision to switch them could now beneficially be based on personal issues and well as clinical factors. Taking this idea further, patients might be allowed to self-select into a DOACs programme based on their being well informed about the impacts of Warfarin and the new DOACs.

The choice might also be offered to newly diagnosed AF patients. The cost for this change would, of course, have to be a consideration, as the newer medicine is more expensive than Warfarin. To date, however, there are no firm figures on the costs of such a move that go beyond the cost of the medications. A study needs to be conducted that takes into consideration the reduced cost of the patient no longer requiring weekly monitoring and the reduced incidences of emergency admissions. More research is also required into UK patients' perspectives of the medication change-over.

The calculation of the financial benefit to patients switching from Warfarin to DOAC as recommended by NICE takes into account the Quality Adjusted Life Years (QALY) of each individual patient. The QALY combines both quantity and health related quality of life (QoL) into a single measure of health gain in years. This was scored using 'perfect health' as 1 and death as 0. This Figure was then used to calculate the QALY-ICER which is the Incremental Cost effectiveness ratio. The QALY is the recommended measure of the national institute for clinical excellence (NICE) to measure the cost-effectiveness of treatments for patients, especially in life-long conditions such as AF. It also allows for benefit versus harm analysis as well as allowing for a broader comparison between patient groups. The expected

QALY for patients switching from Warfarin to DOAC according to NICE 2012 is shown in Figure 8.1 below.

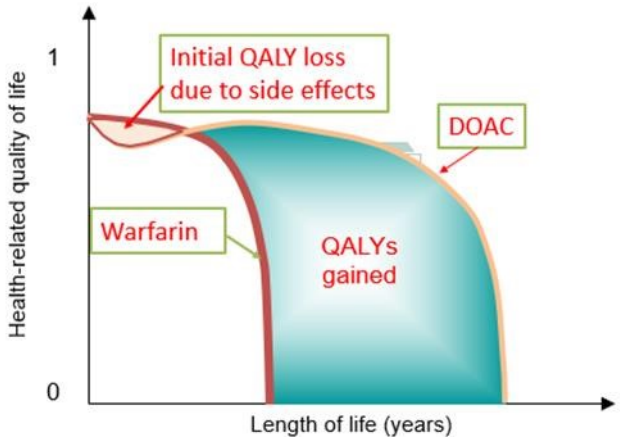


Figure 8.1
QALY of switching to Anticoagulation Drugs
Adapted from (NICE, 2012)

Research has begun elsewhere on this topic, for example Elewa *et.al*., (2014), surveyed 260 patients in Georgia, USA to ascertain their level of satisfaction with Warfarin and their views on switching to Dabigatran. The study was a short questionnaire-based study administered to outpatients. No interviews were carried out. The findings report that although the majority of patients claimed to be satisfied with Warfarin most said they would be willing to move to the new medication. Fewer follow-up appointments was cited by patients as the main attraction, but they would also welcome the reduced negative interaction effects with other medications and with some foods which would normally have an impact on the effect of Warfarin. It is interesting to note that Elewa *et al*., respondents would forgo the comfort of the staff interaction during routine monitoring in order to have the freedom of choosing a greater variety of foodstuff, which is similar to those reported here. Unlike the patients in the current study, these American patients had an additional barrier to overcome before they could change medication, that of cost. The new medication was almost three times more expensive than Warfarin, so some patients, despite wishing to switch, did not do so for financial reasons.

The switch is not without complications, particularly for the elderly; Elewa *et al*., also quotes Eikelboom *et al*., (2011) who reports an increase in bleeds in older patients. This is not an issue that emerged in the St Mary's sample. However, if they had been studied for longer that the 90 days, it is possible more incidences of bleeds might have been reported.

Real life has intervened here in a somewhat dramatic way. This thesis was at the point of completion when the COVID-19 virus was at its height in March and April 2020. This impacted immediately by curtailing all patients' visits to UK hospital clinics for INR monitoring. Several clinics in London moved into the community but the decision was also made to switch many patients from Warfarin to one of the new DOACs which require no clinic visits. The high cost of such a switch becoming secondary to patient and staff safety. This may herald the increased use of DOACs in the future.

8.10 Conclusion

The findings show a clear overall positive response to the switch to the new medication, and that the patients felt a considerable reduction in their stress levels almost as soon as the switch was achieved. This was true across both sexes and ages groups. The findings show an overall satisfaction with the care they received at St Mary's and a high level of trust between staff and patient. It is clear that the anticoagulant clinic at St Mary's is performing well in supporting their patients who switched from Warfarin to a DOAC. However, more consideration could be made with regards to the patients' dietary preferences and/or restrictions before starting anticoagulant therapy, as well as to their age-related needs, comorbidities, and domestic circumstances. With all these in mind a fuller care-plan could be developed that would help the patients adhere to the new medication.

8.11 Recommendations

Any change in healthcare practice will often require a reallocation of resources or an increase of funding, or both. Some of the recommendations set out below could be achieved with small changes to practice, given the goodwill of staff concerned. However, others would require the cooperation of other parts of the NHS, necessitating considerable management time and multi-discipline involvement. Cross-discipline cooperation can be very hard to achieve, and will require a strong case to be made for the added expense of time and effort. With regards to funding, some savings will be made within the anticoagulant team budget due to the reduced number of clinic appointments required for the switched patients. However, the risk is that that money will be re-absorbed into the general budget. A way needs to be found for it to be protected for the use of switch patients.

A key finding is that patients differ in their care needs depending on their age and complexity of comorbidities, and that happily this is now being more widely recognized within other health care professions. A recent overview of the care received by anticoagulant patients is *Excellence in anticoagulant care* (2016), published by The NHS London Clinical Networks. Its overriding theme is that:

> '*An excellent anticoagulation service should be built around the needs of its patient population, and commissioners should actively involve patients and carers in the design and improvement of services*'. (p7)

Components of an excellent patient-centred anticoagulation service would include, as the report stated: convenient services close to home, good GP services, and rapid access to expert support when needed. Clinical staff should be innovative when designing communication channels with their patients, including greater use of telephone contact to save time and travel. More 'one stop' provision to help the patient, especially the old and frail, and more convenient appointment arrangements were also called for. Finally, a clear 'care pathway' should be developed for each patient. All of these factors have also emerged from the current study.

However, it is important to note that despite the good intentions of the London Clinical Networks report, the practice on the ground currently remains traditional and not particularly patient centred (Gbadamosi *et al*., 2015). In the light of many NHS reports on good governance and many publications of improving practice, it might be worthwhile before setting out the recommendations, to consider that many patient care systems and departments, such as the link between the NHS and the council (which supports the patient outside of the hospital), are not linked up in a way which enhances good value for the patient. Gbadamosi talked about the difficulties the NHS faces when implementing change, listing ten common reasons why bottom-up change, even small changes, are so often thwarted. In order to be able to discuss let alone implement even the smallest of changes outlined in these recommendations Gbadamosi's ideas need to be considered. One in particular is the stifling of innovation by the system itself:

> '*Senior leaders are trapped in inflexible processes. We fail to embrace ways of taking part in low coat, low risk experiments to test ideas. We must utilize the diverse experiences of stakeholders - our patients'.*

Likewise, Alderwick and Ham, (2017) reported on quality improvement in the NHS. They listed lesson for leaders which focused on relationships and culture, in particular the involvement of patients and their carers, and that stated their care package should work as a whole system (Alderwick and Ham, 2017).

In the study reported here, the supposed greater ease of use of DOACs reflected in greater satisfaction in this sample but did not always improve adherence or quality of life for everyone. The introduction of DOACs, intended to simplify follow-up for the physician, may have had the collateral effect of making the prescription of oral anticoagulants more complicated by reducing contact with healthcare professionals. The findings are clear, that good adherence to any medication routine is complex even for the most cognitively aware and robust patient. It is recommended that a series of discussions among healthcare professionals within the Trust be held and focus on the way in which elderly patients, particularly those who are frail or house-bound, are monitored following the switch to DOACs. To facilitate this there follows a number of recommendations.

These recommendations are based on patient and staff concerns and the researcher's interpretation of the evidence generated here. For clarity, the recommendations have been divided into three areas:

- Local research
- Local anticoagulant clinical practices
- Implications for the NHS

While at this stage these first recommendations are regarded as local, but it is anticipated that some could be used to inform the healthcare process of similar patients across the NHS. In the first instance, they will be used to inform the patient-centred pathway already in place at St Mary's, and the two hospitals in Lewisham where the researcher works.

8.12 Local research.

The first recommendation involves making use of this sample of patients' preference for informal learning, many participants talked of learning so much from each other, for example, on the bus ride to the clinic, this knowledge base should be unitised. It is important for the medical team to draw on the years of unique experience that these patients have to offer from living on either Warfarin or the newer anticoagulants. This study has gone some way to inform us of the impact of the switch, and has provided insights into how some patients cope with their medication treatment plan. Importantly, their coping mechanisms sometimes include methods of self-management which are not what the doctors would recommend or even approve of, though the patients continue to employ them all the same. For example, awareness of how, when, and exactly why they manipulate their medication dosage to suit their daily activities might be very useful information for the clinical staff to know – and enable them to prepare for. The difficulties of taking the correct dose at the right time when faced with work or travel arrangements or simple forgetfulness are unique to each patient. However, it may be that a pattern of behaviour is discernible across a particular group. Each patient in this study has worked out a way to survive their medication without too many mishaps. How they do this, and the risks involved, is well worth exploring further.

This is a small study and limited to patients over the age of 65, therefore, it is recommended that a research study be set up with older AF patients to meet in a series of group discussions. The focus groups should be divided into sub-groups: men and women; age 65/74, 75/84, 85+ and, if possible, a group of patients who live alone and another for those who live with another; also, if possible, groups of people with different types and numbers of co-morbidities. The reason for these subgroups is to gain a wider and deeper understanding of some of the key themes identified here. A group facilitator would encourage them to talk about their personal coping methods and to ask questions. It should be a 'safe' environment, so the patients can talk freely without sensing any disapproval or concern from the group organiser. They should be encouraged to talk openly about any of what might be called 'rule breaking' or 'work-arounds' that they need to employ for their medication to meet their personal needs. A second line of discussion would be the gathering of any hints or tips about how to manage one's life which on such medication. For example, tips with regards to eating, exercise and travel would be invaluable. It is anticipated that the patients would have insights that could be incorporated in the preparation of a booklet for patients living with this type of long term medication. After approval by health care professionals, it could be distributed to existing and newly diagnosed AF patients. It is hoped that a patients' groups at the researcher's NHS Trust in south London will be set up in the near future.

8.13 Local clinic-based recommendations.

Longer switch over patient consultations are recommended. When a switch to new medication is under consideration, a series of conversations should be held with the patient about the clinical necessity of the change and also about their domestic circumstance. How they will achieve treatment compliance should be explored. The clinician should not assume that the patient has a clear idea of what is involved. For example:

- What process will the patient use in order to remember to take their medication?
- What difficulties does the patient think *may* emerge and how will they cope with them?

A personalized healthcare/anti-coagulation plan based on personal circumstances could then be developed.

8.14 Development of a global/national DOAC registry

Currently, INR results for Warfarin patients are monitored and trended on popular hospital databases such as the INRstar® or DAWN® software. Additionally, these patients are issued with a record book ('yellow book') in which patients can keep a contemporaneous record of their INR, taken at home or in a hospital or clinic. The record book can be transferable between various hospitals and clinics. However, patients who have been switched from Warfarin do not have a log or record keeping method. As there is an increased interest in the use of direct oral anticoagulants as an alternative to Warfarin therapy, it is therefore a recommendation that a global or national database for DOAC patients be introduced to the NHS. The need for such a registry is evidenced by the introduction of the Dresden DOAC registry in Germany, which has been cited as '*an invaluable source of information in emergency situations*' (Beyer-Westendorf *et al*., 2014).

As this research was conducted within Imperial NHS trust, which is a world-renowned teaching hospital and innovator in technological and medicinal advances, it may be prudent to approach specialists in anticoagulation who work at the trust such as Dr Shlebak, a specialist consultant in haemostasis and thrombosis, and who kindly assisted with this study, Dr Mike Laffan (Professor of Haemostasis and Thrombosis), or Professor Martin Crowie, a Consultant Cardiologist, for assistance with setting up such a registry.

8.15 Assistive technology

It is recommended that research be undertaken into a method of assistive technology, such as a handheld device, that will allow patients to self-monitor direct oral anticoagulants at home and so reduce their anxiety. When identified it might well be of support to some of the participants, such as the ones who are overly concerned with the loss of the Warfarin testing, though not to all (NICE, 2014b). Given the advanced years of many of the participants, some would not be able to cope with the technology but undoubtedly some would. Additionally, according to research elsewhere, clinicians working in an emergency or trauma setting would

welcome the ability to rapidly detect the presence of DOACs when deciding pathways of treatment (Ebner *et al*., 2017). This, however, is a difficult task. While there are guidelines for medical staff to help support and train patients in self-monitoring who are on Warfarin, such as the London Clinical Networks, there is no equivalent for patients on the new anticoagulants. This results from the issue of anticoagulation being complex, and made even more difficult by the nature of the DOACs, whereby they are licensed for use without monitoring. This may be due to the fact that each DOAC dose has a targeted mode of action within the coagulation pathway, is rapid in onset, and has a predictable removal time from the body via the kidney, usually 2-4 hours. However, according to Padrini (2019) it is possible for patients to inadvertently overdose DOACS, particularly those patients who have impaired renal function. Padrini revealed that 43% of patients with atrial fibrillation and renal impairment were at an increased risk of overdose and haemorrhages. A handheld device with the capability of detecting and quantifying DOACs would therefore be of benefit to a population of over a quarter of DOAC users (Padrini, 2019).

8.16 Better information.

It is recommended that printed information leaflets and web sources are made available to both new switchers and those remaining on Warfarin, as their existing information may well be out-dated. These should contain information about the AF condition as well as the medication. A further leaflet should also be provided for the patient to give to their carer or any other person close to them the aim being to inform the non-patient about the condition and implications of the medication. The information would be similar to the patient leaflet, but would be addressed directly to the patient's supporter/friend/family so that they feel the information is specifically for them. Both should be written in an appropriate way to help with understanding, such as using plain language, perhaps using larger lettering, and with easy references.

8.17 Linked up working – reaching out to patients

It is recommended that the help of Community nurses is enlisted because they are familiar with treating patients with similar personal and medical circumstances. DOAC patients could be added to their list of medical patients requiring home visits

for follow-up or simply just to check on. This would be independent of whether the patients had other conditions. It is also recommended that a service of dedicated anti-coagulation healthcare workers routinely phone DOAC patients once a month for at least a year post switch. These callers could be medically trained personnel or other healthcare staff who have had training to identify at-risk patients or those in need of a home visit or referral.

It is recommended that a dedicated hotline for patients who have questions or concerns regarding their anticoagulation therapy be set up. Patients should also be able to receive advice or referrals on non-anti-coagulation issues such as loneliness, transportation access, medical personnel access, entitlement to benefits, weight loss, or age-relevant local social activities. This would necessarily need to serve as a referral resource as well as an immediate source of reassurance.

It is recommended that an intervention to support patients who are newly switched from long-term anticoagulants (e.g. Warfarin) to long-term DOACs be set up that offers face to face contact delivered within a social setting. Suitable locations would be in a recreational/non-clinical community setting such as a local fire station, hospital, church or school, that elderly people could attend weekly for tea/coffee and sandwiches and a chat with people of the same age group and circumstances, and so develop a more community-like sense of belonging. This would also be a point of contact for those who are coping on their medications, but are dealing with non-prescriptive issues such as loneliness and depression.

Patient-led support groups have been a feature of NHS life for many years. However, to date there are no community based support groups for AF patients in South London. Worrall *et al*., (2018) undertook a review of the research on self-help groups of patients with mental health problems and found many positive outcomes (Seebohm *et al*., 2013). There was good scientific evidence, they argued, to support the view that support groups were successful. They cited researchers who found that groups could help people develop an improved sense of personal value and belonging and improve their social networks (Worrall, *et al*., 2018). They also enhanced feelings of control and resilience (Seebohm *et al*., 2013).

8.19 Reversal of DOACs

Within the medical community, the uptake of the use of some DOACs, despite their many benefits compared to Warfarin, has been slow. As discussed in earlier chapters, one of the most commonly cited reasons for this is the unavailability of an approved reversal method or antidote for these particular DOACs. In May 2019, the first reversal for Rivaroxaban and Apixaban (Andexxa®), was proposed to the National Institute of clinical excellence as a possible reversal but was declined because:

'there is insufficient information on the rationale for scoping the use of Andexxa®'. (NICE, 2019).

It is therefore the recommendation of the author that future pharmaceutical research be centred on expanding the development of suitable reversal of DOACs, as well as increasing the information accessible to clinicians on the scope and benefits of DOAC reversals.

8.20 Limitations of the study

The patients were seen on three occasions over a three month period, a relatively short time given that their medication plan was lifelong. With more resources, it would be desirable and beneficial to visit them again at 12 and 24 months to learn how those who claimed they were experiencing a new lease of life had actually fared over a longer time period, and how the older patients were coping in the face of reduced clinical support. Finally, an alternative research methodology, but again depended on increased resources, would have been a case study approach which would gain a deeper understanding of some of the profound changes that the new medication brought to the lives of these patients. Notwithstanding these limitations the study has generated new and valuable information and clearly demonstrates the value of patient-centred investigation in this area.

Chapter 9 - Self-Reflection

9.0 The start of the journey

This chapter presents my personal reflection of completing this Professional Doctorate, charting my personal development and growth as a researcher. I am really pleased to have reached the conclusion of this thesis; this is an enormous achievement for my entire family who have been supportive whilst I pursued this self-funded study. I am a wife, mother of three and have worked full time as a Specialist Biomedical Scientist in haematology for the last 17 years.

The progression of this thesis has been a journey. At times it was very difficult, frustrating and tear inducing, but also gave me the joy of discovery and hugely increased my knowledge of the subject researched. I have always been an 'adapt as you go' kind of person, and not always good at forward planning. However, over the last six years I have come to realise the value in getting to know my personal and professional potential. David A. Kolb in 1984 said: 'Learning is the process whereby knowledge is created through the transformation of experience'. How right he was!

Being the eldest child and grandchild to a very large and extended family has its challenges. I often feel as if I have a lot of responsibilities in maintaining communication with all the siblings and relatives. My main priority has always been

to make sure that my husband and children are cared for, however, I also have routine financial obligations to several relatives. This has not always been easy, especially as this course was almost all self-funded for 6 years. For years, I have worked two jobs in excess of 50 hours a week as a routine, to accommodate my responsibilities. What I learned from that was the need to plan, right down to the last detail, and to cooperate with those who can offer support.

At the start of my studies, I worked in the NHS as a Junior Biomedical Scientist, my husband worked full time as a Metropolitan Police Officer, and we had two children. While my employer was positive about my research plans, they could not fund them. At the time, my husband and I were required to participate in a work shift pattern which includes day and night shifts during the weekday and on weekends. My university attendance for the first two years was often before or following a 12 hour night shift.

Two years into the studies and whilst on maternity leave with my third son, I was promoted to Senior Scientist in the NHS, a role I kept for two years. This new role helped me develop skills which were also useful in my studies: conflict resolution, working with various IT platforms, managing a budget, people, and time management and most important of all - multitasking. Again, my employer was enthusiastic about my research which led to some fruitful discussions. Later I left the NHS and joined a private medical laboratory on Harley St (HCA). This laboratory offered shift patterns which, most importantly, allowed me to attend the NHS anticoagulation clinics at St Mary's to collect data for this study. Work at HCA also taught me the value of communication and engaging with the users of the service, producing efficient and quality results. All of which I have been able to apply to my studies. They also offered some funding for my studies.

In 2018 my husband joined the Ministry of Defence as an Armed Police Officer, which is a really big achievement and had a positive impact on the whole family in part due to the more regular hours and increased ability to time manage. In December 2018, I returned to a new job in the NHS and was promoted to the senior role of Blood Transfusion Laboratory Manager for two NHS Hospital laboratories

(Queen Elizabeth Woolwich and University Hospital Lewisham), with a total rotational staff responsibility of 28 scientists.

It is worth noting here that during my interview for the job, my research was discussed and recognised as important and received informal support with a request for me to share the findings with the Trusts. Most usefully, I have been the master of my own time schedule during this last vital year of study. Looking back, I am pleased that I was persuasive enough about my research to bring all my employers along with me, in spirit at least.

9.1 Looking to the future, the role of research in my profession

The importance of research intelligence has always been important in healthcare to determine strategy formulation as well as patient care management policies. In recent years, the importance of research has become far greater than previously as part of the decision making process for all aspects of patient care. At the start of my studies I had ambitions around self-progression as well as helping my patients, but also, I wanted to promote my profession. This, in my view still needs doing. For example, the results generated by biomedical scientists influence 75% of all clinical diagnosis in the UK, however there are very few people who are aware of who we are and the work that we do and as a result, the pool of applicants for the profession each year is declining which will in turn impacts on standards. Often patients are asked to list the staff involved in their care and only 5% would list the scientists, the laboratory or even the results. It was, therefore, a dream of mine as a junior scientist to be able to have a platform from which I could promote this section of healthcare and also increase awareness of Biomedical Science as a career option in young people entering university.

Now that I have progressed to the level of management, I would like to apply lessons learnt from this doctorate journey such as critical analysis and review of data, time management skills, the ability to prioritise the order of deadlines, to my new role as Blood Transfusion Manager and hopefully promote the profession as a career choice.

9.2 My academic learning

Before engaging in this research programme, I had only basic research skills gained during my Master's degree but had a desire to find out what happens to vulnerable members of the community who have reduced access to medical/healthcare professionals following a change in their life-long medication regimen. The taught modules, which made up the early part of doctoral programme, improved my academic learning and raised my confidence in many ways including an understanding of the importance of how to undertake qualitative research and how to manage a research project over a long time period. I was new to the process of critically reviewing the research of others but now find it a valuable skill.

I have also found it useful to learn from the experiences of others and I have been very lucky to have formed a bond with the other students in the class. I have learnt various perspectives and approaches to problem solving and critical thinking. Conducting this research using validated questionnaires has introduced me to some of the most popular qualitative and quantitative research tools and methods. I therefore gained practical experience whilst administering questionnaires, as well as data analysis skills.

I was very concerned about the possibility of not completing this course due to time constraints, work and family commitments and the financial pressure. However, early into the course (second year), I was encouraged to perform a SWOT analysis as part of the *Professional Development* module. This later proved to be invaluable, as it quickly emerged that some of my ordinarily routine tasks would have to be curtailed, postponed, or delegated in order to complete this study. I needed to get structure and routine into my daily activities, so I implemented forward planning, Figured out what changes can be made in my work and home life, As much as possible, I have maintained links with family and friends who were my support team for the duration of the course and tried to maintain a healthy balance of diet and exercise as well, although not always successfully.

I was under no illusions that this course was going to be an easy one, far from it. I remember in my first year during a Q&A session following a lecture with Dr Patricia Maitland, who later became my project supervisor, she said 'Completing a PhD or

Prof Doc is a test of endurance and perseverance as well a love of learning'. Six years in and my work-life balance has been greatly impacted as well by the time I have set aside for studying, researching, and writing. I made monthly schedules to include all work and family related events, these are posted on the family fridge.

A copy of the schedule is also given to my child-minder. Additionally, I synchronized the iPhone calendar time-table for my husband and I, in order to better manage the pick-up and drop-offs of the various activities of the kids such as scouts and swimming etc. This introduction of my new organisation skills has greatly improved the routine running of the day to day tasks and work hours and has gone some way to reducing stress in the household. I have learned the art of delegation, a skill that will no doubt become invaluable in the future in my role as a Blood Transfusion Manager.

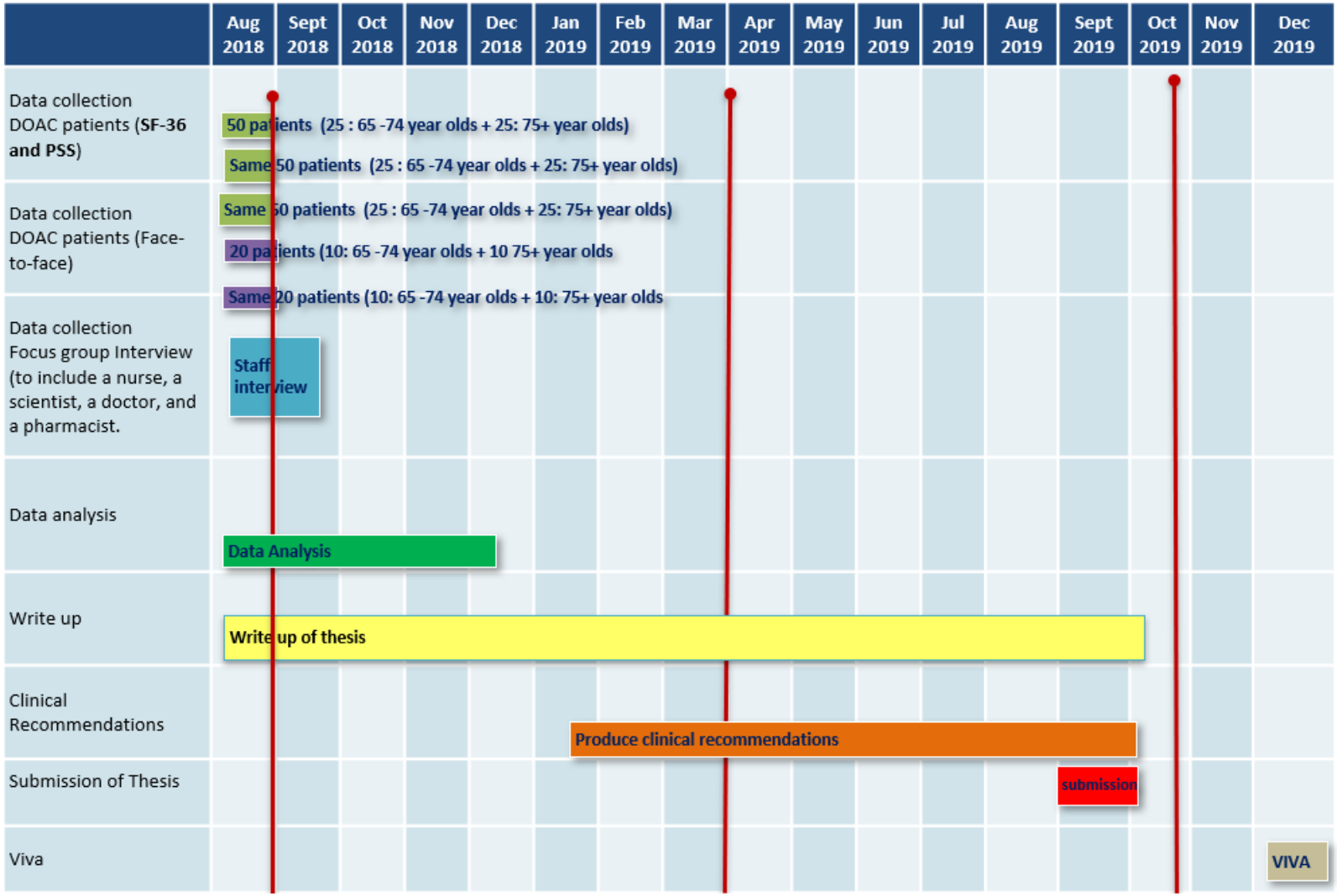
I am happy to conclude that I am generally a happy and grateful person but now also a more questing one. I stand back and think more critically about published research papers, asking are they valid and useful? Along with this is a greater appreciation of the research (and researchers) undertaken within the health care sector as I know first-hand just how much goes into it. This DProf has undoubtedly been one of the hardest things I have ever done so. I will end with a quote from Cicely Tyson:

'*Challenges make you discover things about yourself that*

you never really knew'.

APPENDICES

APPENDIX 1 - Gantt Chart



APPENDIX 2 - Question Guide for Clinicians and Biomedical Scientists Interviews.

Introductions and explanation about the aims of the research

Topic: Your experience of working with DOACS - as a group warm up covering:

Q 1. How long have you each worked with DOACS? (1a) In what capacity?

Q 2. Approximately, how many DOAC patients per week/month do you see?

Q 3. What information do you have available about the dosage, side effects, and other information relating to DOACs to help you?

Topic: DOACS itself – information provision.

Q 4. How and when is the need for a switch of medication first discussed with the patients?

Q 5. After the decision is made, how is the DOAC information generally passed to patients?

5a Do you think it is the right/ enough information?

5b How else might it be given?

Topic: The impact of the new medication

Q 6. What issues have you observed the patients encounter at the point of the switch?

Q 7. What do you know about the personal and social impact the switch has on the patients?

Q 8. What is the biggest impact you envisage that these drugs will have on the life of these (DOAC) patients?

Q .9 Do you think that the lack of monitoring of these DOACs could be an issue for these patients?

Q .10 Do you think the lack of reversal of these DOACs could be an issue for patients? If so, in what way?

Q 11. Is the social impact on the patient considered before the prescribing DOACs?

Q 12. What are the main concerns of patients being on DOACs?

Q 13. Do you feel that there is more that the Trust or coagulation department could do for these patients? **Close**

APPENDIX 3 - Question guide for the <u>first</u> patient interview.

Welcome given and the researcher repeats the explanation about the research that the patient was given at the time of recruitment. The information and consent form are then read by the patient and completed.

The patient's scale scores will be read by the interviewer before the qualitative part of the interview begins just to see if any areas of particular interest or concern can be identified.

Topic: Living with Warfarin

Q 1. You have been on Warfarin for some time now, can you tell me what that is like? For example, how does it impact your day?

- Prompt for examples

Q 2. Does having a drug regimen interfere or enhance with your lifestyle in any way?

Q 3. How do you get on with self-medicating – giving the medicine to your- self?

Topic: Information provision

Q 4. Thinking back to when you first started on Warfarin, how much information were you given?

4a How was the information provided? (leaflets/conversion/website).

4b Did you understand the information easily?

4c Were you give any more information after that time?

Topic: Current health self-assessment and expectations

Q 5. How much do you know about the condition (AF) that Warfarin helps you with?

Q 6. How many other medications do you take? Do you think you can name them?

Q 7. Do you know why your medicine is being changed?

Q 8. Do you think that switching to drug (DOAC) will change anything for you?

Q 9. What benefits are you expecting from the new drug, if any?

Q 10. Do you have any concerns about taking the new drug?

Prompt only if necessary:
reversal/antidote/adverse events/returning to Warfarin.

Q 11. Have you had any unexpected experiences or events since using Warfarin?

And finally

Q 12. Is there anything else you would like to tell me about being on Warfarin or your feelings about the change to a different medicine.

Thank you for giving your time to take part in this study, we will hopefully meet again in three months' time to see how the change of medicine has been for you.

APPENDIX 4 - Question guide for the second patient interview. (90 days post switch)

Welcome and a recap the first interview and any issues raised with be included in the discussion.

Topic: The switch over.

Q 1. How was the switch over for you at the time?

Q 2. Did you understand the reason for it?

Q 3. How long did it take to get used to taking the new medicine?

Topic: Living with the new medication.

Q 4. Now that you have been on your new medication for three months, how are things going for you?

Q 5. How are you getting on with the routine of self-medicating?

Q 6. How do you think switching to drug (DOAC) has impacted on your life?

Q 7. Have you had any unexpected experiences or events have you had since switching to DOAC?

Q 8. Are you glad you switched?

Topic: Expectations

Q 9. Are there any expectations that you had initially that have/haven't been met? If so, what are they?

Topic: Overall Satisfaction

Q 10. In broad terms, how happy are you that you made the switch to this new medication.

Very unhappy. 1 2 3 4 5 6 7 Very happy

Q 11. Is there any way the hospital could make your medication regimen better for you or others with the same condition?

Thank you for giving you time to take part in this study.

APPENDIX 5 - SF36 Questionnaire

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. *Thank you for completing this survey!*

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. Compared to one year ago, how would you rate your health in general now?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c. Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d. Climbing several flights of stairs	☐ 1	☐ 2	☐ 3
e. Climbing one flight of stairs	☐ 1	☐ 2	☐ 3
f. Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g. Walking more than a mile	☐ 1	☐ 2	☐ 3
h. Walking several blocks	☐ 1	☐ 2	☐ 3
i. Walking one block	☐ 1	☐ 2	☐ 3
j. Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

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(SF-36 Standard, US Version 1.0)

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	Yes	No
a. Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2
b. Accomplished less than you would like	☐ 1	☐ 2
c. Were limited in the kind of work or other activities	☐ 1	☐ 2
d. Had difficulty performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	Yes	No
a. Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2
b. Accomplished less than you would like	☐ 1	☐ 2
c. Did work or other activities less carefully than usual	☐ 1	☐ 2

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6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. How much bodily pain have you had during the past 4 weeks?

None	Very mild	Mild	Moderate	Severe	Very Severe
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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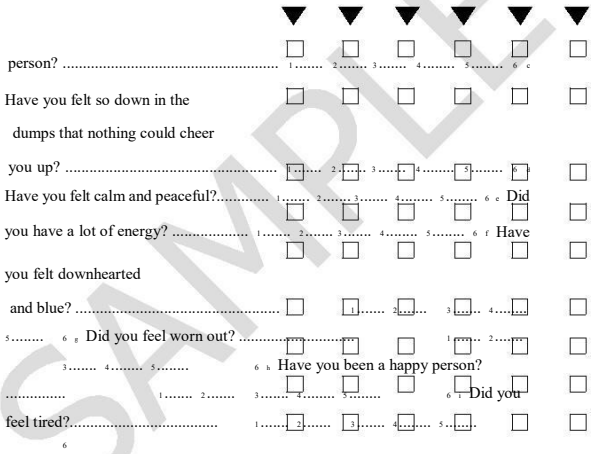
9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...?

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of pep?	1	2	3	4	5	6
b. Have you been a very nervous						



APPENDIX 6 - Information sheet for patient participants

UNIVERSITY OF WESTMINSTER

A study of the impact of substituting Warfarin with Direct oral Anticoagulants (DOAC), in Atrial Fibrillation (AF) patients over 65 years old: the patient's and clinician's perspectives.

Information sheet for study volunteers who will complete the scales and be interviewed

Chief Investigator: Patricia Richards

You are being invited to take part in a research study. Before you decide whether or not you wish to take part, it is important that you understand why the research is being done and what it will involve. Please read this information carefully and discuss with others if you wish. If you would like to ask questions about the research you can contact the study researcher, Patricia Richards without any obligation to participate. Please take time to decide whether or not you wish to take part.

What is the purpose of the study?

This study will look at the short term impact on the quality of life of 50 patients who are 65 and over and switching to the new Warfarin alternatives, DOACs. It will help us understand, from the patient's point of view, what it is like living on Warfarin and then switching to a new medication. This information will help us work better with patients in the future, so your assistance will be of value to many other patients in years to come. This research is being undertaken as part of the researcher's studies for Professional Doctorate in Health Sciences at the University of Westminster. It is being carried out at the Imperial NHS trust at St Marys, St Charles, and Hammersmith Hospital and Queens Park sites.

Why have I been chosen?

You have been invited to take part in this study as you are 65 or over and have been switched from Warfarin to DOAC.

Do I have to take part?

No, it is up to you to decide if you want to take part or not. If you decide to take part Patricia will explain the study to you and you will need to sign a consent form. If you start the study then change your mind that is ok, you are free to withdraw at any time without needing to give a reason. If you wish to withdraw you can request that any data, we collected from you is destroyed.

What will happen to me if I take part?

If you wish to take part in the study, you will be asked to complete an informed consent form. Patricia will then talk to you about your experience of switched from

Warfarin and ask you to compete some short questionnaires/scales about how you feel at the moment with regards to your general wellbeing and any stresses or anxieties you may have. It will take about 30/45 minutes.

A month later you will be asked to complete the questionnaires again which will take about ten minutes. Finally, in three months' time, Patricia will talk with you again when you can discuss how life has been on the new drug and you will complete the scales for the last time. Asking you to fill in the questionnaires/scales three times and talk with Patricia twice gives us some idea of any changes that you may experience over first three months of your new drug programme. Participants will be provided with a copy of their signed consent form

What do I need to do if I want to take part?

If you would like to take part in the study please tell the researcher, Patricia Richards, or email on patricia.richards@imperial.nhs.uk or by telephone (0203 312 1132).

What are the possible benefits of taking part?

You will have some private time to talk to someone who understands the drugs you are on and to discuss with them how you are getting on with the drugs - if they change anything you do socially and how they make you feel within yourself. When the study is finished all the research volunteers will be able to read about the results on the hospital website.

What are the possible risks and disadvantages of taking part?

They are no risks to you as the research only involves talking with the researcher. Nothing about your treatment will change.

What will happen if I don't want to carry on with the study?

If you decide to withdraw from the study, data obtained from you may be used to contribute to study results. If you do not want this to happen, you can request data that belong to you to be destroyed. However, once data has been anonymised and included in a dataset it is impossible to remove this data as we have no means of identifying which is, specifically yours.

Complaints

Any complaints you might have for this study will be fully investigated. If you have any concerns about study procedures you can speak to the primary researcher, Patricia Richard who will answer your questions. If you remain unhappy and wish to complain formally, you can contact Dr Annie Bligh, t Westminster University. A.Bligh@westminster.ac.uk on +44 20 7911 5000 ext. 65038

If you have any issues or concerns, please contact the patient advice and liaison service (PALS) or complaints team. Patient Ground floor of the Queen Elizabeth the Queen Mother (QEQM) building, St Mary's Hospital, South Wharf Road, London W2 1N. Phone: 020 3313 0088, Monday to Friday, 09.30-17.00. Email: IMPERIAL.PALS@NHS.NET:

Will my taking part in the study be kept confidential?

Yes, anything you say during the interviews will be kept strictly confidential. No one will be able to identify you at any time.

The University of Westminster has a standard confidentiality procedure for participants involved in research that adheres to the Data Protection Act. This stipulates how personal information is collected, used, stored, and disposed of during and following completion of research projects. Files will be encrypted, and password protected. Any information that is collected about you during the course of the study will be kept strictly confidential and secured within restricted areas and/or electronic files on computers that have restricted access. Each participant is assigned a unique code that is used on all data collected during the research. This code is then used to identify data in place of personal information. Only the researcher will have access to personal identifying data information.

No one will be identifiable from the collect data, written report of the research, or publications arising from it.

What will happen to the results?

Your interview material will be combined with that from the other volunteers and it will all be analysed as a group. The results will for part of my doctoral research for the University of Westminster. The findings will be used to help other patients. In certain exceptional circumstances where you or others may be at significant risk of harm, the researcher may need to report this to an appropriate authority, in accordance with the UK Data Protection Act 1998. This would usually be discussed with you first.

APPENDIX 7 – Staff Information Sheet

A study of the impact of substituting Warfarin with Direct oral Anticoagulants (DOAC), in Atrial Fibrillation (AF) patients over 65 years old: the patients' and clinicians' perspectives.

Information sheet for staff / study volunteers who will complete the scales only.

Chief Investigator: Patricia Richards

You are being invited to take part in a research study. Before you decide whether or not you wish to take part, it is important that you understand why the research is being done and what it will involve. Please read this information carefully and discuss with others if you wish. If you would like to ask questions about the research you can contact the study researcher, Patricia Richards without any obligation to participate. Please take time to decide whether or not you wish to take part.

What is the purpose of the study?

Generally elderly patients on Warfarin are routinely monitored in a clinic setting. The level of Warfarin, which is referred to as the International Normalised Ratio (INR) is used to determine whether the patient is being effectively anti-coagulated. Due to the many side effects of Warfarin, its documented interactivity with other drugs being taken by the patient as well as other reasons, patients are being switched from Warfarin to new Direct Oral Anticoagulants (DOACs). These drugs do not require monitoring and as such the patients are not seen routinely (once prescribed DOACs).

This study aims to look at the social changes in the quality of life of patients over 65 who have been switched, both from the patient's and clinical perspective. You are invited to be a part of focus group of NHS staff participants from a medical, clinical, pharmaceutical and scientific background, to discuss your experiences (anecdotal and otherwise), of patients who have switched, your level of interaction that you have with the patient post DOAC prescription, as well as any perceptions you may have on the quality of life of these patients.

Why have I been chosen?

You are an NHS staff member involved in the prescription, dispensing, care of, or testing of patients who have switched from Warfarin to DOACs.

Do I have to take part?

No, it is up to you to decide if you want to take part or not. If you decide to take part Patricia will explain the study to you and you will need to sign a consent form.

If you start the study then change your mind that is ok, you are free to withdraw at any time without needing to give a reason. If you wish to withdraw you can request that any data, we collected from you is destroyed.

What will happen to me if I take part?

If you wish to take part in the study, you will be given a staff participant information sheet which detailed how the focus group will be undertaken as well as the contact information for the research student Patricia. You will also be asked to complete an informed consent form, which will include permission for the research student to audio record the focus group discussion. Participants will be provided with a copy of their signed consent form

Please note that quotations from the transcribed audio recording may be used in the in written submission of the research to illustrate the findings of the patient study or supplement the final discussion/conclusions.

What do I need to do if I want to take part?

If you would like to take part in the study please tell the researcher, Patricia Richards, or email on patricia.richards@imperial.nhs.uk or by telephone (0203 312 1132).

What are the possible benefits of taking part?

You will be a part of an interesting discussion which may go on to inform NHS policies on the social effects of switching patients to Direct Oral anticoagulants as well as potentially help to improve the lives of the elderly patients seen by the Imperial NHS Trust. This study also forms part of a doctoral study for the research student; therefore, you will be assisting the researcher in completing her study. This study may form the framework for a larger future project looking at the social impact of life-long anticoagulants of the elderly, which is not possible to be done as part of this study due to time constraints.

What are the possible risks and disadvantages of taking part?

They are no perceived risks to you as this research only involves talking with the researcher.

What will happen if I don't want to carry on with the study?

If you decide to withdraw from the study, data obtained from you may be used to contribute to study results. If you do not want this to happen, you can request data that belong to you to be destroyed.

Complaints

Any complaints you might have for this study will be fully investigated. If you have any concerns about study procedures you can speak to the primary researcher, Patricia Richards who will answer your questions. If you remain unhappy and wish to complain formally, you can contact Dr Annie Bligh, t Westminster University.
A.Bligh@westminster.ac.uk. You may also contact the **Patient Advice and Liaison Service (PALS) or complaints team** on the Ground floor of the Queen Elizabeth the
Queen Mother (QEQM) building, St Mary's Hospital, South Wharf Road, London W2 1N. Phone: 020 3313 0088, Monday to Friday, 09.30-17.00. Email: **IMPERIAL.PALS@NHS.NET**:

Will my taking part in the study be kept confidential?

Yes. The University of Westminster has a standard confidentiality procedure for participants involved in research that adheres to the Data Protection Act. This stipulates how personal information is collected, used, stored, and disposed of during and following completion of research projects. Files will be encrypted, and password protected. Any information that is collected from you during the course of the study will be kept strictly confidential and secured within restricted areas and/or electronic files on computers that have restricted access.

What will happen to the results?

Your interview material (audio recording), will be analysed thematically, with the results used to supplement the findings, discussions and conclusions drawn from the patient interviews. The results will for part of my doctoral research for the University of Westminster. The findings will be used to help other patients. In certain exceptional circumstances where you or others may be at significant risk of harm, the researcher may need to report this to an appropriate authority, in accordance with the UK Data Protection Act 1998. This would usually be discussed with you first.

APPENDIX 8 - Patient Participant Consent Form

Participant's key code __ __ __

Title of Study: A Quality of Life study of the impact of substituting Warfarin with Direct Oral Anticoagulants (DOAC), in atrial fibrillation patients over 65 years old, at Imperial NHS Trust.

Lead researcher: Patricia Richards Please initial

I confirm that I have read and understand the information sheet dated ..... (V2) for the above study and have had the opportunity to ask questions. ------

I have had an opportunity to ask any questions and I am satisfied with the answers given. ------

I understand I have a right to withdraw from the research at any time and I do not have to provide a reason. ------

I understand that if I withdraw from the research any data included in the results will be removed if that is practicable (Once anonymised, data that has been collated into other datasets may not be possible to remove). ------

I consent to my general practitioner being informed of my study participation and results.

I give the researcher permission to contact me on 2 future occasions ------

I would like to receive information relating to the results from this study. ------

I understood what will happen in the event of disclosure of sensitive information. ------

I give permission for my interviews to be audio recorded. ------

I confirm I am willing to be a participant in the above research study. ------

I note the data collected may be retained in an archive and I am happy for my data to be reused as part of future research activities. ------

I understand that my anonymised words may be used as quotes in the final research report or publications. ------

Participant's Name_____ **Contact number** _____

Signature: _____ **Date:** _____

Researcher's Name: _Patricia Richards_ **Signature:** _____**Date:** _____

If you have any issues or concerns, please contact the patient advice and liaison service (PALS) or complaints team. *Patient Ground floor of the Queen Elizabeth the Queen Mother (QEQM) building, St Mary's Hospital, South Wharf Road, London W2 1N. Phone: 020 3313 0088, Monday to Friday, 09.30-17.00. Email: IMPERIAL.PALS@NHS.NET:*

APPENDIX 9 - CONSENT FORM Staff participants

Participant's key code _ _ _

Title of Study: A Quality of Life study of the impact of substituting Warfarin with Direct Oral Anticoagulants (DOAC), in atrial fibrillation patients over 65 years old, at Imperial NHS Trust.

Lead researcher: Patricia Richards **Please initial**

I have been given the Participation Information Sheet and/or had its contents explained to me. ------

I have had an opportunity to ask any questions and I am satisfied with the answers given. ------

I understand I have a right to withdraw from the research at any time and I do not have to provide a reason. -------

I understand that if I withdraw from the research any data included in the results will be removed if that is practicable (I understand that once anonymised data has been collated into other datasets it may not be possible to remove that data). -------

I would like to receive information relating to the results from this study. -------

I give permission for my focus group discussion to be audio recorded. ------

I confirm I am willing to be a participant in the above research study. ------

I note the data collected may be retained in an archive and I am happy for my data to be reused as part of future research activities. ------

I understand that my anonymised words may be used as quotes in the final research report or publications. ---

Participant's Name: _____

Participant's contact number _____

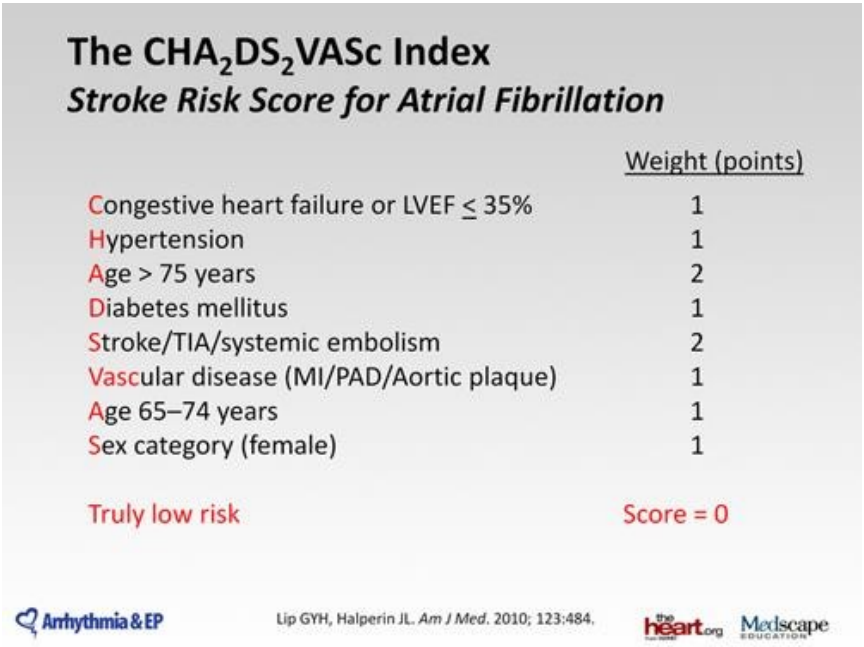
Signature: _____ **Date:** _____

I confirm I have been provided a copy of the Participant Information Sheet approved by the Research Ethics Committee for use by staff and colleagues and its contents have been fully explained. I have been given an opportunity to ask questions, which have been answered.

Researcher's Name: _____

Signature: _____ **Date:** _____

APPENDIX 10 - CHA_2DS_2VASc and HAS-BLED Scores Index



Lip GYH, Halperin JL. Am J Med 2010; 123:484

HAS-BLED

Letter	Clinical Characteristic	Points
H	Hypertension	1
A	Abnormal Liver or Renal Function	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly (age > 65)	1
D	Drugs or Alcohol	1 or 2
Maximum Score		9

Ruff, C.T. American College of Cardiology, September 26, 2011

http://afibprofessional.cardiosource.org/Hot-Topics/2011/09/Which-RiskScore-Best-Predicts-Bleeding-With-Warfarin-in-Atrial-Fibrillation.aspx

APPENDIX 11 - Perceived Stress Scale (PSS)

Perceived Stress Scale

The questions in this scale ask you about your feelings and thoughts **during the last month**. In each case, you will be asked to indicate by circling *how often* you felt or thought a certain way.

Name _____ Date _____

Age _____ Gender (*Circle*): **M F** Other _____

	0 = Never	1 = Almost Never	2 = Sometimes	3 = Fairly Often	4 = Very Often
1. In the last month, how often have you been upset because of something that happened unexpectedly?	0	1	2	3	4
2. In the last month, how often have you felt that you were unable to control the important things in your life?	0	1	2	3	4
3. In the last month, how often have you felt nervous and "stressed"?	0	1	2	3	4
4. In the last month, how often have you felt confident about your ability to handle your personal problems?	0	1	2	3	4
5. In the last month, how often have you felt that things were going your way?	0	1	2	3	4
6. In the last month, how often have you found that you could not cope with all the things that you had to do?	0	1	2	3	4
7. In the last month, how often have you been able to control irritations in your life?	0	1	2	3	4
8. In the last month, how often have you felt that you were on top of things?	0	1	2	3	4
9. In the last month, how often have you been angered because of things that were outside of your control?	0	1	2	3	4
10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	0	1	2	3	4

Please feel free to use the *Perceived Stress Scale* for your research. The PSS Manual is in the process of development, please let us know if you are interested in contributing.

References

The PSS Scale is reprinted with permission of the American Sociological Association, from Cohen, S., Kamarck, T., and Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior, 24,* 386-396.

APPENDIX 12 - Comparison of Warfarin and DOACs

Warfarin	NOAC	Source
Has little or no renal toxicity	May cost long term renal and liver toxicity	
Adverse effects		
Liver Dysfunction : the risk is the same as with the NOACs.		McNaughton, R. & Shucksmith, J., 2014. Reasons for (non)compliance with intervention following identification of 'high-risk' status in the NHS Health Check programme.. Journal of Public Health, Issue fdu066, pp. 1 - 8.
Bleeding: equal to **Rivaroxiban** & **Dabigatran, and** more bleeding than **Apixaban**		
Requires Monitoring	Does not require monitoring	Bauer, K. A., 2013. Pros and cons of new oral anticoagulants. American Society of Haematology, Volume 1, pp. 464 – 470
Takes 3 – 5 days to be effective	Active in 1-3hours	Lip, G. & Halperin, J., 2010. Improving stroke risk stratification in atrial fibrillation.. American Journal of Medicine, 123(1), pp. 484-488.
Has an effective rapid reversal/antidote – vitamin K	Has no effective rapid reversal/antidote	Lip, G. & Halperin, J., 2010. Improving stroke risk stratification in atrial fibrillation.. American Journal of Medicine, 123(1), pp. 484-488.
Has multiple concomitant drug interactions	Has minimal concomitant drug interactions : particularly p-glycoprotein inhibitors and platelet therapies.	Bauer, K. A., 2013. Pros and cons of new oral anticoagulants. American Society of Haematology, Volume 1, pp. 464 – 470
Narrow therapeutic range	Wide therapeutic range	Hodder, S., 2013. Somerset CCG - Prescribing Formulary – February 2013, Sommerset: Somerset Clinical Commissioning group.
Unpredictable dose requirements		
Costing		
Cost 7p per day (3mg) (US$0.22 per day)	Cost £2.52per day (3mg) ,(US$4-8 per day)	http://www.chemistdirect.co.uk/warfarin-tablet-3mg/prd-mjp
Warfarin is £426 per year	Dabigatran £920 per year	www.gp-update.co.uk GP update accessed 22/3/15
	Rivaroxiban is £58.80 for a pack of 28 15-mg tablets and £58.80 for a pack of 28 20-mg tablets	http://www.chemistdirect.co.uk/warfarin-tablet-3mg/prd-mjp
Physiology		
Works by reduced synthesis of factors II, VII, IX & X	**Dabigatran** – Direct FII inhibitor **Apixaban, Rivaroxiban and Endoxaban** – Direct FXa inhibitor	Ganetsky, M. et al., 2011. Dabigatran: review of pharmacology and management of bleeding complications of this novel oral anticoagulant. Journal of Medical Toxicology, 7(4), pp. 281-287
Causes allergic reactions in some patients	No known allergic reactions reported to date	Lip, G. & Halperin, J., 2010. Improving stroke risk stratification in atrial fibrillation.. American Journal of Medicine, 123(1), pp. 484-488.
Bio-availability -100%	**Dabigatran** Bio-availability – 3-7% **Rivaroxiban** Bio-availability – 80 -100%	Bauer, K. A., 2013. Pros and cons of new oral anticoagulants. American Society of Haematology, Volume 1, pp. 464 – 470
Metabolised in the liver (CYP2C9)	Metabolised in the liver (**Dabigatran** – hydrolysed in plasma/liver and **Rivaroxiban** – CYP3A4, CYP3A5 & CYP2J2).	Jenkins, L. et al., 2005. Quality of life in atrial fibrillation: the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. American Heart Journal, 149(1), pp. 112-120.
Excretion via kidneys 90 – 100%	**Dabigatran** excretion via kidneys 80 -85% **Rivaroxiban** excretion via kidneys 66% **Apixaban** excretion via kidneys 25% **Endoxaban** excretion via kidneys 60%	Bauer, K. A., 2013. Pros and cons of new oral anticoagulants. American Society of Haematology, Volume 1, pp. 464 – 470

Warfarin	NOAC	Source
Adherence		
Long term social studies done	No long term social studies done.	Kumar, A. et al., 2014. IMPACT OF PILL BURDEN AND SOCIO-ECONOMIC STATUS OF PATIENTS ON ADHERENCE TO PHARMACOLOGIC THERAPY IN ELDERLY. West London Medical Journal , 6(1), pp. 33-44.
Poor adherence readily rectified	Poor adherence potentially fatal	Davis, R. et al., 2012. Prevalence of atrial fibrillation in the general population and in high-risk groups: the ECHOES study. Eurospace, 14(1), p. 1553–1559.
	Discontinuation of NOACS due to adverse effects higher than warfarin. With **Dabigatran** discontinuation rates higher than direct FXa inhibitors	Heidbuchel, H. et al., 2013. European Heart R hythm A ssociation Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation. Euopean Society of Cardiology (Europace), Volume 15, pp. 625-651
Testing		
Has an approved and well documented method of testing	No approved method of testing	Baglin, T., Kitchen, S. & Keeling, D., 2012. Effects on routine coagulation screens and assessment of anticoagulant intensity in patients taking oral Dabigatran or Rivaroxiban: guidance from the British Committee for Standards in Haematology.. British Journal of Haematology, 10(1), pp. 97-113
Dosage based on International normalised ratio (INR)	**Dabigatran** – 110-150mg BD for AF; 220mg daily for THR/TKR **Rivaroxiban** – 10mg once a day	Lip, G. & Halperin, J., 2010. Improving stroke risk stratification in atrial fibrillation.. American Journal of Medicine, 123(1), pp. 484-488.
Pharmacokinetics		
Pharmokinetically unstable	Pharmokinetically stable	Bauer, K. A., 2013. Pros and cons of new oral anticoagulants. American Society of Haematology, Volume 1, pp. 464 – 470
Long half life – patients are required to stop warfarin at least 3 days before a surgical procedure.	Very short half life (**Dabigatran** : 14 - 17hours **Apixaban**: 8 – 15 hours, **Rivaroxiban** 11 – 13 hours and **Endoxaban** 9 – 12 hours	Pirmohamed, M., 2006. Warfarin: almost 60 years old and still causing problems. British journal of clinical pharmacology , 62(5), pp. 509-511.
Has multiple Food interactions	Has no known food interaction	Hodder, S., 2013. Somerset CCG - Prescribing Formulary – February 2013, Sommerset: Somerset Clinical Commissioning group.
Vitamin K agonist	Not affected by the vitamin K pathway	Pirmohamed, M., 2006. Warfarin: almost 60 years old and still causing problems. *British journal of clinical pharmacology* , 62(5), pp. 509-511.
Adherence		
Long term social studies done	No long term social studies done.	Kumar, A. et al., 2014. IMPACT OF PILL BURDEN AND SOCIO-ECONOMIC STATUS OF PATIENTS ON ADHERENCE TO PHARMACOLOGIC THERAPY IN ELDERLY. West London Medical Journal , 6(1), pp. 33-44.
Poor adherence readily rectified	Poor adherence potentially fatal	Davis, R. et al., 2012. Prevalence of atrial fibrillation in the general population and in high-risk groups: the ECHOES study. Eurospace, 14(1), p. 1553–1559.
	Discontinuation of NOACS due to adverse effects higher than warfarin. With **Dabigatran** discontinuation rates higher than direct FXa inhibitors	Heidbuchel, H. et al., 2013. European Heart R hythm A ssociation Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation. Euopean Society of Cardiology (Europace), Volume 15, pp. 625-651
Testing		
Has an approved and well documented method of testing	No approved method of testing	Baglin, T., Kitchen, S. & Keeling, D., 2012. Effects on routine coagulation screens and assessment of anticoagulant intensity in patients taking oral Dabigatran or Rivaroxiban: guidance from the British Committee for Standards in Haematology.. British Journal of Haematology, 10(1), pp. 97-113
Dosage based on International normalised ratio (INR)	**Dabigatran** – 110-150mg BD for AF; 220mg daily for THR/TKR **Rivaroxiban** – 10mg once a day	Lip, G. & Halperin, J., 2010. Improving stroke risk stratification in atrial fibrillation.. American Journal of Medicine, 123(1), pp. 484-488.

APPENDIX 13 – GP Referral letter exemplar

REC ref: 17/LO/0290
IRAS project ID: 196397

<GP name and address>

<Date>

Dear Dr, <GP name>

Re: **Title of Study: A Quality of Life study of the impact of substituting Warfarin with Direct Oral Anticoagulants (DOAC), in atrial fibrillation patients over 65 years old, at Imperial NHS Trust.**

Your patient <Participant's name and surname>, DOB <DOB>, <Participant's address>, has volunteered to take part in a research study at St Mary's Hospital, imperial NHS trust. <He/She> has given us permission to contact you.

The study is designed to look at the short term impact on the quality of life of 50 patients who are 65 and over and switching to the new Warfarin alternatives, DOACs. It will help us understand, from the patient's point of view, what it is like living on Warfarin and then switching to a new medication. This information will help us work better with patients in the future; the data will be of value to many other patients in years to come.

This research is being undertaken as part of the researcher's studies for Professional Doctorate in Health Sciences at the University of Westminster. For more information, see the attached participant information sheet.

We have selected men and women, aged over 65 years. With the exception of participants excluded on medical grounds, all AF patients who are switching from Warfarin to DOAC, regardless of sex, race, or disability, will be included in the study and approached for participation.

At the end of the study, a copy of your patient's results letter regarding the measurements performed as part of the study; any abnormal readings will be sent to you.

If you feel that there is a medical reason that prevents your patient's continued participation in this study, or if you need further details, please contact the study consultant Dr Abdul Shlebak, Consultant Haematologist (General Haematology, Obstetric Haematology, Haemostasis and Thrombophilia) and Lead Laboratory Clinician at St Mary's Hospital, Imperial NHS Trust on 020 3312 6666 Secretary: 020 3312 6806**.**

Kind regards,
Patricia Richards BSc. MSc CSci MIBMS
Senior Biomedical Scientist /University of Westminster Doctoral Research Student

APPENDIX 14 – Interview Transcript samples

Coding the Qualitative Material.

These two tables provide an example of how the main themes were developed by combinations of the smaller codes elicited from the transcripts. Four transcripts then follow which are from younger and older patients whose words have been coded according to the themes shown in these tables. It is noteworthy that, generally, the second interviews were shorter and less full then the first as most of the personal information has already been discussed. Nevertheless, they provide valuable information about the patients coping strategies and responses to the change of medication.

Table one: The main themes and supporting codes elicited from the first interview at the time of the switch.

First patient interviews before switching

Main theme	Supporting codes
Managing complexity	• Coping with different illnesses and their impact on taking Warfarin correctly and feelings of wellbeing. • Findings ways to cope with so many different tablets to be taken throughout the day. • Organisation of domestic life, getting help with pill taking routine. • Juggling the dosage of medications to manage their side effects.
Stalwartness.	• A tendency to dismissing personal discomfort resulting from their other illnesses as normal, just to be tolerated. • A desire to make no fuss. • It's a normal part of aging – nothing to be done. • Pain and limitation of pain relief due to Warfarin.

Loss of control – the domino effect	• Social isolation leading to loneliness and anxiety about health. • Coping alone – even just the small things are hard. • One thing leads to another: the burden of food restriction due to medication and impact on exercise. • Fear of getting it wrong – errors with dosages can lead to an emergency admission to hospital. • One medication side effect leads to another problem.
Freedoms lost	• Family activates curtailed – sport for example. • Travel restricted to short trips as need to attend appointments. • The health care process as a Restriction - the time it takes to get to the clinic. • Pleasure denied - drinking alcohol - an educated risk.
Self-reliance - within a partnership	• Self- organize life or fail. • The importance of a good GP.

Appendix 14 Table 1
Main themes and supporting information colour coded before switching

First interview - at time of switch.

 **75 – 84 St Lucia**

15/04/2018

Patient 8 – SS, 82/F

Topic: Living with Warfarin

Q 1. You have been on Warfarin for some time now, can you tell me what that is like? For example, how does it impact your day?

SS: It's bleeding awful, I have problems swallowing pills, always have done. so, I hate it. 12 or 13 years ago, I had a stroke, 2 days after my 70th birthday! Can you believe it? Just my luck… if it were going to happen to anyone it would be me. I later found out that I had this AF condition and have done for years, but I had no idea. I kept telling the GP that I was lightheaded and faint and that my chest felt funny. It was never picked up. Now I have to take 2 tablets twice a day. Oh, just awful……. My health has gotten worst over the years, especially after my husband died 20 years ago… of a stroke and I don't have much help. I can't walk very far, I need help getting dressed and all my relatives live so far away, and we never had kids. I get really lonely sometimes. I looked after my husband for 24 years before he passed away. He was very ill towards the end.

Q 2. Does having a drug regimen interfere or enhance with your lifestyle in any way?

SS: Enhance? Enhance? I really wouldn't say so. I keep thinking, today is going to be the day I can be done with it, but It never ends. I don't mind coming to the clinics every few weeks to get tested. It is so hard to get a GP appointment in Ladbroke Grove. The bus is sometimes late to take me here though, I have complained. The driver said that he was new, then he said he not familiar with area and now he doesn't say much.

Q 3. How do you get on with self-medicating – giving the medicine to your-self?

SS: It's difficult, in the morning, I have the Warfarin, then the citalopram and then the insulin. I was on antibiotics back in December, but I finished that last course of amoxicillin in January. I get really fed up. I have asked about syrups or dissolvable tablets…... I did have some dissolvable pain killers, those were very strong, but they tasted so awful. I usually keep all my pills in the kitchen near the door, just in case. The last few times the ambulance came to my house, the box was right there at the kitchen door which was handy…… I come in and out and in and out, I may as well move into St Marys! I tell yah, I have not been very well.

Topic: Information provision. ***This section was not coded and themed in the same way because the information was generally factual. But a some key factors did emerge and are reported in Chapter Five.***

Q 4. Thinking back to when you first started on Warfarin, how much information were you given?

SS: ohhh, probably not much, everyone is so busy these days, everything is online, and I don't have a computer…….. I knew about it before the stroke because J*** was on it after his heart operation for years. I do know its rat poison; did you know that.... I does go through my mind sometimes. NO wonder patients who take it has all these problems.

4a How was the information provided? (leaflets/conversion/website).

SS: I can't really remember, probably a conversation. I think they waste so much paper these days printing things. Most young people these days don't even read.

4b Did you understand the information easily?

SS: I don't know. I was in hospital at the time. After the stroke, I was in ITU for 2 weeks, felt like there was an elephant sitting on my chest. Very painful and uncomfortable. Even if they had told me, I was probably not in a position at the time to take it all in.

4c Were you give any more information after that time?

SS: The GP and the clinic has always been good and telling me any new bits that I need to know. You don't know what you don't know, so I probably don't know enough, or should know more than I do but how would I know what I don't know?

Topic: Current health self-assessment and expectations

Q 5. How much do you know about the condition (AF) that Warfarin helps you with?

SS: I know that it is a very dangerous condition and that it is very serious. I worry all the time about AF episodes coming on, they can be quite distressing. I worry about the long-term effects. I worry about serious heart damage because of it. It's been a constant worry, I could have a cardiac arrest, stroke. Every time I have the slighted murmur or chest pain, I think, is this it? Am I having a heart attack or a stroke? It never leaves your mind. It's like a constant that I'm going to die. You only get one heart you know. Sometimes I worry that my other medication is working because of the Warfarin, or even the Warfarin not working because of the other tablets…... absolute constant torture. I feel anxious right now.

Q 6. How many other medications do you take? Do you think you can name them?

SS: 3 – citalopram, insulin, and Warfarin…...sometimes ibuprofen for my pain, some vitamin c and sometimes I have a bit of cod liver oil. But mostly just the 3.

Q 7. Do you know why your medicine is being changed?

SS: Well, I am not doing very well. I hear this new one… Apixaban is better than the Warfarin, we will have to wait and see. When I spoke to my cardiologist last week, I told him that I was so worried about the whole thing. I think I will still phone the Warfarin clinic to speak to the ladies here……yes, I know they are not testing anymore, but just in case I have any questions; I think I will call here (clinic).

Q 8. Do you think that switching to drug (DOAC) will change anything for you?

SS: It can't get much worse, so it can only get better.

Q 9. What benefits are you expecting from the new drug, if any?

SS: Hopefully, I won't always be lightheaded and get lots of nose bleeds and bleeding gums. I really hope that I can have some normality really. Day to day life on Warfarin can be really unpredictable, I'm getting old now. I don't want to have all these worries about fainting on the stairs…. I would love a Stena stair lift, but they are so expensive, so in the meantime, I really don't want to fall off the stairs again, that was painful last time.

Q 10. Do you have any concerns about taking the new drug?

SS: Lots, I don't really know how it works or if it works, well I assume it works or they wouldn't give it to me, but I thought that with Warfarin and that was bloody awful. I think that because I have had such a tough time with the other meds, I really don't have much hope for this new one.

Q 11. Have you had any unexpected experiences or events since using Warfarin?

SS: Oh, do we have enough time? So many, as I said, I've had bleeding gums, headaches, dizziness, nose bleeds, fainting spells, palpitations, you name it.

And finally

Q 12. Is there anything else you would like to tell me about being on Warfarin or your feelings about the change to a different medicine.

SS: I know it's odd, but as bad as it is being on Warfarin, I don't really want to change. Better the devil you know. I am very worried about the change.

First interview

 **65 - 74 England**

05/03/18

Patient 10 – MC, 65/M

Topic: Living with Warfarin

Q 1. You have been on Warfarin for some time now, can you tell me what that is like? For example, how does it impact your day?

MC: 15 years now. It is very difficult to plan trips away, I have struggled for years to keep within range - but it's always something (to go wrong). I take a few other medications, which affects it, and my diet affects it, even if I have a drink at the local it affects it.

Q 2. Does having a drug regimen interfere or enhance with your lifestyle in any way?

MC: I wouldn't say enhance but definitely interfere. I mean, touch wood I haven't had a stroke, (this is good) but no I don't think Warfarin enhances my lifestyle it's a hinderance if anything.

Q 3. How do you get on with self-medicating – giving the medicine to your-self?

MC: I am pretty good, unless I have had a good night out. If I am travelling then the time difference tends to throw me off, but I am generally quite good.

Topic: Information provision. Not colour themed - see Chapter five paragraph?? for analysis.

Q 4. Thinking back to when you first started on Warfarin, how much information were you given?

MC: Aaahh…… not much to be honest. I have had heart problems since I was young and take one medication or the other all the time, so I know quite a bit now. But I think back then the condition was explained, and the medication or 'fix' was given - I was told it was life long, but I really don't think I had a lengthy conversation about Warfarin.

4a How was the information provided? (leaflets/conversion/website).

MC: at a consultation with the cardiac consultant, I can't remember when.

4b Did you understand the information easily?

MC: Yeah

4c Were you give any more information after that time?

MC: Oh of course, several papers and articles and conversations with my GP. The nurses in the clinic are pretty good, here and at Hammersmith.

Topic: Current health self-assessment and expectations

Q 5. How much do you know about the condition (AF) that Warfarin helps you with?

MC: Quite a bit, I am in a support group with the AF association, they put on events and things and they send out information packs from time to time.

Q 6. How many other medications do you take? Do you think you can name them?

MC: 4 or 5, a lot's going on, but I take it in my stride.

Q 7. Do you know why your medicine is being changed?

MC: Yes, it was my TTR, it was in the time range? Basically, it means that my INR is not within range sufficiently, it's really poorly managed not because I don't take the

blessed thing, because I do, it's just so unpredictable and it stops me from having a tipple.

Q 8. Do you think that switching to drug (DOAC) will change anything for you?

MC: Well no more clinics for a start. I am here sometimes every week or every other week. Very tiresome. I was told there is better control and less interactions but no antidote - that's concerning.

Q 9. What benefits are you expecting from the new drug, if any?

MC: Better control of my INR, well it's not INR anymore, but better blood thinner control. I went to Cornwall last week; I hadn't been in a long time.

Q 10. Do you have any concerns about taking the new drug?

MC: Just the reversal issue. Sometimes my INR is 10 or 11, very high, not sure what happens if the Apixaban is very high.

Q 11. Have you had any unexpected experiences or events since using Warfarin?

MC: I have had several bleeds, sometimes I get really bad headaches and joint pains, hence why I take all these other pills, but I'm generally ok.

Q 12. Is there anything else you would like to tell me about being on Warfarin or your feelings about the change to a different medicine.

MC: No, just want to get on with the switch and see what happens.

Table two: the main themes and supporting codes from the second interviw held at 90 days.

Table two: The main themes and supporting codes elicited from the first interview at 90 days post switch.

Themes	Supporting codes
Stalwartness – a continuing theme	• All is well on the face of it. • Not always a good thing, patients tend to mask difficulties from healthcare staff. • The system can be frustrating not the people who run it.
A leap of faith - increased patient responsibility	• How will I know if the new medication works? • Total trust in the medical staff's decision that they can cope alone. • Increased responsibility for own health. Up to the patient to keep a check.
Liberation – reigning control	• No more clinic - more time to self • Freedom to travel longer distances and for longer periods of time. • Medical freedoms - reduction in pain due to better pain relief. • Wider choice of food stuffs so better health
Fewer Tablets – Simpler regime	• Less tablets taken per day • Fewer regimens to remember (i.e. to be taken before/after food)
New beginnings	• The switch enabling a life review. • Virtuous circles begin – one thing leads to another

Liberation – but a loss for some	• Missing the clinic visit and the reassurance it brought. • Missing the company of other patients at the clinic. • Raised anxiety for some.

Appendix 14 Table 2
Main themes and supporting information colour coded at 90 days post switch

Day 90 **75 – 84 St Lucia**

16/07/2018

Patient 8 – SS, 82/F

Topic: The switch over.

Q 1. How was the switch over for you at the time?
SS: I was very worried about the change. I still am.

Q 2. Did you understand the reason for it?
SS: I know that my INR was always wrong, I could have had a stroke at any time, so I had no choice but to change. The Warfarin was just not working.

Q 3. How long did it take to get used to taking the new medicine?
SS: I'm still getting used to it now. Really happy that its less tablets to take and on the whole, I do feel better, I just think it's too soon to tell.

Topic: Living with the new medication.

Q 4. Now that you have been on your new medication for three months, how are things going for you?
SS: it's been going ok; I only take 1 tablet a day for the AF now instead of 4 Warfarin ones. So, I feel good about that, I really struggled to swallow all them pills.

Q 5. How are you getting on with the routine of self-medicating?
SS: I still take a few other tablets and I can't crush up this new tablet but apart from that, I am doing ok.

Q 6. How do you think switching to drug (DOAC) has impacted on your life?
SS: It's still too soon to say, but I am already noticing small things like – I haven't had a headache or a nosebleed in a while. My gums still bleed from time to time when I'm brushing my teeth, but that maybe because of my toothbrush. I feel like I do nothing all day. I have no kids and I'm widowed, so I don't really have much to do, or people to visit. It can get very lonely, this clinic has been a God send, I will miss it.

Q 7. Have you had any unexpected experiences or events have you had since switching to DOAC?
SS: like what? I suppose as this is a new experience everything is unexpected, so I really don't know how to answer that.

Q 8. Are you glad you switched?
SS: the jury is still out, I do feel better, there are small things that I have noticed, but it's probably mind over matter, I will have to wait and see…… If I had to choose between this one and the Warfarin, I would say this new one.

Topic: Expectations

Q 9. Are there any expectations that you had initially that have/haven't been met? If so, what are they?

SS: I was hoping to take less tablets per day really and to have less day to day issues. I still worry about the future, I still worry about dying from a stroke, I don't get tested anymore, so it's a worry. Big concern. Perhaps I need time to get used to the change.

Topic: Overall Satisfaction

Q 10. In broad terms, how happy are you that you made the switch to this new medication.
Very unhappy. 1 2 3 4 5 6 7 Very happy
SS:4 or 5

Q 11. Is there any way the hospital could make your medication regimen better for you or others with the same condition?
SS: they should carry on testing my INR, just to see what it is and to give me some peace of mind.

Day 90  **65 - 74 England**

28/06/18

Patient 10 – MC, 65/M

Topic: The switch over.

Q 1. How was the switch over for you at the time?
MC: Pretty straight forward.

Q 2. Did you understand the reason for it?
MC: oh yes

Q 3. How long did it take to get used to taking the new medicine?
MC: about a day or two, I felt a bit funny at first…...lightheaded, but all good now.

Topic: Living with the new medication.

Q 4. Now that you have been on your new medication for three months, how are things going for you?
MC: Pretty good, no real issues.

Q 5. How are you getting on with the routine of self-medicating?
MC: It's been much easier than I thought it would be, definitely a lot easier than the Warfarin. I was told that there are possible side effects, but so far I haven't had any.

Q 6. How do you think switching to drug (DOAC) has impacted on your life?
MC: At first, I was sceptical, but I am definitely a convert. The new medication really doesn't bother my other pills, for some reason my joints don't hurt as much, and I feel much better in myself.

Q 7. Have you had any unexpected experiences or events have you had since switching to DOAC?
MC: No, just the initial dizziness

Q 8. Are you glad you switched?
MC: Absolutely, I have a little control back, not much but a little.

Topic: Expectations

Q 9. Are there any expectations that you had initially that have/haven't been met? If so, what are they?

MC: I was hoping to have better coagulation control, my INR was all over the shop which made you feel sick all the time, and now, I feel much better – new lease on life.

Topic: Overall Satisfaction

Q 10. In broad terms, how happy are you that you made the switch to this new medication.

Very unhappy. 1 2 3 4 5 6 7 Very happy

MC: 10! So very happy

Q 11. Is there any way the hospital could make your medication regimen better for you or others with the same condition?

MC: I still have some concerns about the reversal, so perhaps there should be some form of testing, I mean I feel better, but how do I know it's working? Will I still be able to come to the clinic if I have questions?

APPENDIX 15 - Statistics underpinning the scale data analysis.

Table 1 – PSS ANOVA DATA Statistics unperpinning Figure 7.1

Anova: Single Factor

SUMMARY

Groups	Count	Sum	Average	Variance		
Time Point 1	3	56.19	18.73	0.50		
Time Point 2	3	42.08	14.03	0.46		
Time Point 3	3	39.60	13.20	0.94		
ANOVA						
Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	53.37	2	26.68	42.24	0	5.14
Within Groups	3.79	6	0.63			
Total	57.16	8				

Anova: Single Factor

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Time Point 1	3	56.19	18.73	0.50
Time Point 2	3	42.08	14.03	0.46
Time Point 3	3	39.60	13.20	0.94

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	53.37	2	26.68	42.24	0	5.14
Within Groups	3.79	6	0.63			
Total	57.16	8				

Table 2 – Age groups average PSS Scores Statistics underpinning Figure 7.1

Row Labels	Average of PSS Total Scores T1	Average of PSS Total Scores T2	Average of PSS Total Scores T3
65-74	19.53	14.11	14.00
75-84	18.48	14.67	13.48
85-94	18.19	13.31	12.13
Grand Total	**18.75**	**14.09**	**13.27**

Table 3 – Mean PSS Scores by age and sex Statistics underpinning Figure 7.2 and 7.3

Row Labels	Mean of PSS Total Scores T1	Mean of PSS Total Scores T2	Mean of PSS Total Scores T3
65-74	**19.53**	**14.11**	**14**
F	19.75	13.92	13.33
M	19.14	14.43	15.14
75-84	**18.48**	**14.67**	**13.48**
F	17.17	14.83	13.17
M	19.00	14.6	13.6
85-94	**18.19**	**13.31**	**12.13**
F	17.89	15.00	11.56
M	18.57	11.14	12.86
Grand Total	**18.75**	**14.09**	**13.27**

Table 4 – Total PSS Scores by age and sex Statistics underpinning Figure 7.3

UPN	Age	Sex	PSS Total Scores T1	PSS Total Scores T2	PSS Total Scores T3
1	91	F	19	21	14
2	84	F	24	25	16
3	84	M	14	11	15
4	84	F	12	19	9
5	91	M	16	2	9
6	65	M	16	23	28
7	73	F	22	14	14
8	75	F	10	6	17
9	84	M	21	22	15
10	65	M	19	15	17
11	92	M	18	13	16
12	65	M	21	18	14
13	76	M	18	15	17
14	65	F	23	17	17
15	73	F	17	14	19
16	75	M	21	12	12
17	85	M	17	15	19
18	81	M	19	16	19
19	80	M	22	15	13
20	92	M	17	15	12
21	83	M	17	18	12
22	65	F	19	14	10
23	83	M	17	18	11
24	65	F	19	14	14
25	83	M	20	18	13
26	68	F	19	14	12
27	69	M	20	14	13
28	66	M	22	14	6
29	89	F	20	17	12
30	67	F	19	13	6
31	65	F	22	12	17
32	78	M	19	12	16
33	69	F	16	16	12
34	76	F	22	13	9
35	89	F	16	14	12
36	91	F	21	10	13
37	82	M	16	11	9
38	94	F	14	18	7
39	84	M	22	7	14
40	75	M	20	16	12
41	65	F	22	10	19
42	85	M	19	13	9
43	84	M	19	14	14
44	82	M	20	14	12
45	81	F	15	14	17
46	86	F	17	13	10
47	90	F	22	20	14
48	66	M	16	7	12
49	85	M	22	10	13
50	69	M	20	10	16
51	68	F	22	15	10
52	71	F	17	14	10
53	85	M	21	10	12
54	85	F	15	9	9
55	86	F	17	13	13
56	82	F	20	12	11

Table 5 - Average PCS and MCS by age underpinning Figure 7.4

Row Labels	Average of PCS	Average of MCS	Sum of Age
Time 1	**38.37**	**39.01**	**4390.00**
Group1	**39.33**	**39.58**	**1278.00**
64	48.23	28.81	64.00
66	38.72	42.45	132.00
67	41.37	35.33	67.00
68	42.19	35.72	136.00
69	36.47	40.76	207.00
71	41.27	37.59	71.00
73	27.63	49.25	146.00
Group2	**37.68**	**39.58**	**1696.00**
75	43.88	38.52	225.00
76	36.59	39.22	152.00
78	37.84	36.42	78.00
80	30.80	38.80	80.00
81	40.87	39.34	162.00
82	35.69	39.96	246.00
83	38.67	39.92	249.00
84	35.50	40.59	504.00
Group3	**38.12**	**37.60**	**1416.00**
85	41.16	34.67	425.00
86	35.89	34.88	172.00
89	39.30	38.94	178.00
90	40.15	37.90	90.00
91	35.80	41.83	273.00
92	34.59	40.26	184.00
94	36.96	36.66	94.00

Table 6 – Participants response by average SF-36 scores underpinning Figure 7.5

Row Labels	SF-36 Scores
Moderate	2412
Excellent	966
Poor	356
Not stated	238
Grand Total	**3972.5**

Table 7 - Average MCS by sex underpinning Figure 7.6

Row Labels	Mean of PCS	Mean of MCS
F	40.84	37.65
M	39.94	36.51
Grand Total	**40.36**	**37.04**

Table 8 - All domains at 3 timepoints of the SPSS data, underpinning Figure 7.7

Substituting Warfarin with Direct Oral Antico - SF Comparison for Total Sample - --- All Timepoint Values --- **Report Date: 28/04/2019**

Report Type: SF Comparison for Total Sample

Survey: SF-36v2® Health Survey

Report Criteria	
Date Range	26/01/2018 - 31/10/2018
Timepoint	All

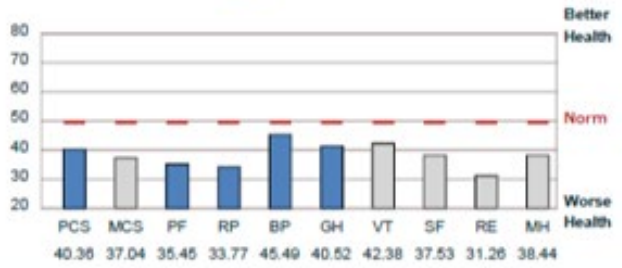
Demographic Profile	
Sample Size	168
Male (*)	54% (90)
Female (*)	46% (78)
Mean Age	76
Age Range	57 - 91

*Of those reporting gender (n=168)

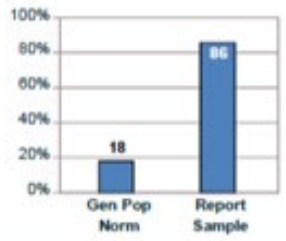
Comments

Print this report Instructional Guide

Scores for Total Sample — Physical Health Scores — Mental Health Scores

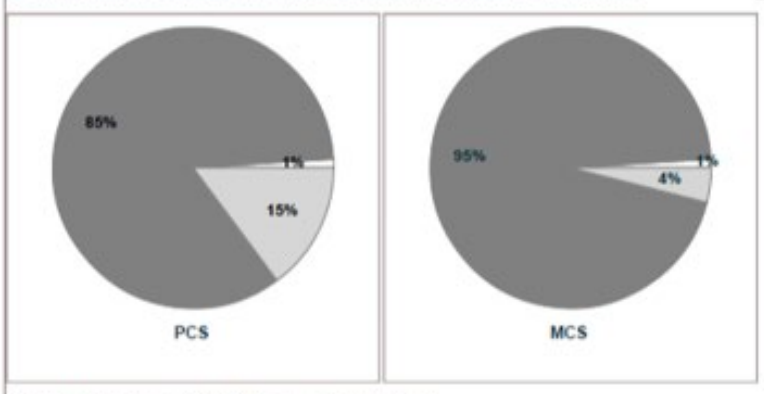


First Stage Positive Depression Screening: % at Risk



Abbreviation
PCS = Physical Component Summary
MCS = Mental Component Summary
GH = General Health
PF = Physical Functioning
RP = Role Physical
BP = Bodily Pain
VT = Vitality
SF = Social Functioning
RE = Role Emotional

% Sample whose Scores are Above, At or Below the General Population Norm — % Above — % At — % Below



PCS Scale Scores:

MCS Scale Scores:

Note: Totals may not equal 100%, due to statistical rounding.

Note: This report utilizes normative data from the QualityMetric 2009 General Population Sample.

Table 9a

Row Labels	Count of Warfarin/ DOAC Difference
F	**24**
Better ac control and QoL. Able to cook/eat a woder varirety of meals and foods..	1
Better ac control, feels better	1
Better ac control, no dosage issues	1
Better ac control, no dosage issues, no more interactions	6
Contacts the clinic/GP to ask questions.	1
Easier to take regularly	2
Has to take the tablet at the same time each day which may not always be practical	1
Misses clinic, No pain meds, Had wait 2 weeks for GP appointment.	1
Misses the health professional contact.	1
No difference. Travels more	1
No dosage issues, feels better	3
No more interactions. Clinic visits. Feek better	2
None stated	2
Prefers warfarin	1
M	**27**
Better ac control and QoL	1
Better ac control, less calcification post 90 days. Reduced risk of stroke.	1
Better ac control, no dosage issues	1
Better ac control, no dosage issues, no more interactions	3
Can now eat chick peas, greens and drink alcohol	1
Can stop DOAC on the day of op. Not worried about forming clots. DOAC easier to take than warfarin	2
Does not miss the clinic. Now has time for other things. No ill effects from DOAC	1
Has nerve damage in his back, unable to exercise, drinks a lot as he is in a lot of pain and is overweight.	1
No difference	1
No difference.	1
No difference. Travels more	1
No dosage issues, feels better	6
No longer has increased heartrate. Does not need to stop his meds 5 days before his op. No longer dizzy.	1
Not sure if drop in BP was caused by switching to DOAC.	1
Now has a better diet and is able to eat Kale etc which he wasn't able to before. No more interactions.	1
Parties	1
Sill contacts the clinic regularly. No dosage issues	1
Still in a lot of pain, but no more night sweats and is now on medication for ADHD.	1
Takes the tablet at the same dose and time everyday. Much easier than warfarin. Has had a reduction in kidney function since DOAC. Being monitored.	1
Grand Total	**51**

Table 9b

Count of Warfarin/ DOAC Difference	Col		
Row Labels	F	M	Grand Total
Better ac control and QoL		1	1
Better ac control and QoL. Able to cook/eat a woder varirety of meals and foods..	1		1
Better ac control, feels better	1		1
Better ac control, less calcification post 90 days. Reduced risk of stroke.		1	1
Better ac control, no dosage issues	1	1	2
Better ac control, no dosage issues, no more interactions	6	3	9
Can now eat chick peas, greens and drink alcohol		1	1
Can stop DOAC on the day of op. Not worried about forming clots. DOAC easier to take than warfarin		2	2
Contacts the clinic/GP to ask questions.	1		1
Does not miss the clinic. Now has time for other things. No ill effects from DOAC		1	1
Easier to take regularly	2		2
Has nerve damage in his back, unable to exercise, drinks a lot as he is in a lot of pain and is overweight.		1	1
Has to take the tablet at the same time each day which may not always be practical	1		1
Misses clinic, No pain meds, Had wait 2 weeks for GP appointment.	1		1
Misses the health professional contact.	1		1
No difference		1	1
No difference.		1	1
No difference. Travels more	1	1	2
No dosage issues, feels better	3	6	9
No longer has increased heartrate. Does not need to stop his meds 5 days before his op. No longer dizzy.		1	1
No more interactions. Clinic visits. Feek better	2		2
None stated	2		2
Not sure if drop in BP was caused by switching to DOAC.		1	1
Now has a better diet and is able to eat Kale etc which he wasn't able to before. No more interactions.		1	1
Parties		1	1
Prefers warfarin	1		1
Sill contacts the clinic regularly. No dosage issues		1	1
Still in a lot of pain, but no more night sweats and is now on medication for ADHD.		1	1
Takes the tablet at the same dose and time everyday. Much easier than warfarin. Has had a reduction in kidney function since DOAC. Being monitored.		1	1
Grand Total	**24**	**27**	**51**

Appendix 15 table 16 - SPSS Statistics

UPN	Age	Sex	PSS Total Scores T1	PSS Total Scores T2	PSS Total Scores T3
1	91	F	19	21	14
2	84	F	24	25	16
3	84	M	14	11	15
4	84	F	12	19	9
5	91	M	16	2	9
6	65	M	16	23	28
7	73	F	22	14	14
8	75	F	10	6	17
9	84	M	21	22	15
10	65	M	19	15	17
11	92	M	18	13	16
12	65	M	21	18	14
13	76	M	18	15	17
14	65	F	23	17	17
15	73	F	17	14	19
16	75	M	21	12	12
17	85	M	17	15	19
18	81	M	19	16	19
19	80	M	22	15	13
20	92	M	17	15	12
21	83	M	17	18	12
22	65	F	19	14	10
23	83	M	17	18	11
24	65	F	19	14	14
25	83	M	20	18	13
26	68	F	19	14	12
27	69	M	20	14	13
28	66	M	22	14	6
29	89	F	20	17	12
30	67	F	19	13	6
31	65	F	22	12	17
32	78	M	19	12	16
33	69	F	16	16	12
34	76	F	22	13	9
35	89	F	16	14	12
36	91	F	21	10	13
37	82	M	16	11	9
38	94	F	14	18	7
39	84	M	22	7	14
40	75	M	20	16	12
41	65	F	22	10	19
42	85	M	19	13	9
43	84	M	19	14	14
44	82	M	20	14	12
45	81	F	15	14	17
46	86	F	17	13	10
47	90	F	22	20	14
48	66	M	16	7	12
49	85	M	22	10	13
50	69	M	20	10	16
51	68	F	22	15	10
52	71	F	17	14	10
53	85	M	21	10	12
54	85	F	15	9	9
55	86	F	17	13	13
56	82	F	20	12	11

Appendix 16 – Critical Appraisal Skills Programme (CASP) Checklist

CASP
Critical Appraisal Skills Programme

www.casp-uk.net
info@casp-uk.net
Summertown Pavilion, Middle Way Oxford OX2 7LG

CASP Checklist: 10 questions to help you make sense of a Systematic Review

How to use this appraisal tool: Three broad issues need to be considered when appraising a systematic review study:

- Are the results of the study valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

The 10 questions on the following pages are designed to help you think about these issues systematically. The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions. There is some degree of overlap between the questions, you are asked to record a "yes", "no" or "can't tell" to most of the questions. A number of italicised prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

About: These checklists were designed to be used as educational pedagogic tools, as part of a workshop setting, therefore we do not suggest a scoring system. The core CASP checklists (randomised controlled trial & systematic review) were based on JAMA 'Users' guides to the medical literature 1994 (adapted from Guyatt GH, Sackett DL, and Cook DJ), and piloted with health care practitioners.

For each new checklist, a group of experts were assembled to develop and pilot the checklist and the workshop format with which it would be used. Over the years overall adjustments have been made to the format, but a recent survey of checklist users reiterated that the basic format continues to be useful and appropriate.

Referencing: we recommend using the Harvard style citation, i.e.: *Critical Appraisal Skills Programme (2018). CASP (insert name of checklist i.e. Systematic Review) Checklist. [online] Available at: URL. Accessed: Date Accessed.*

CASP
Critical Appraisal Skills Programme

Paper for appraisal and reference:.....

Section A: Are the results of the review valid?

1. Did the review address a clearly focused question?

Yes ☐
Can't Tell ☐
No ☐

HINT: An issue can be 'focused' In terms of
- the population studied
- the intervention given
- the outcome considered

Comments:

2. Did the authors look for the right type of papers?

Yes ☐
Can't Tell ☐
No ☐

HINT: 'The best sort of studies' would
- address the review's question
- have an appropriate study design (usually RCTs for papers evaluating interventions)

Comments:

Is it worth continuing?

3. Do you think all the important, relevant studies were included?

Yes ☐
Can't Tell ☐
No ☐

HINT: Look for
- which bibliographic databases were used
- follow up from reference lists
- personal contact with experts
- unpublished as well as published studies
- non-English language studies

Comments:

CASP
Critical Appraisal Skills Programme

4. Did the review's authors do enough to assess quality of the included studies?

Yes ☐
Can't Tell ☐
No ☐

HINT: The authors need to consider the rigour of the studies they have identified. Lack of rigour may affect the studies' results ("All that glisters is not gold" Merchant of Venice – Act II Scene 7)

Comments:

5. If the results of the review have been combined, was it reasonable to do so?

Yes ☐
Can't Tell ☐
No ☐

HINT: Consider whether
- results were similar from study to study
- results of all the included studies are clearly displayed
- results of different studies are similar
- reasons for any variations in results are discussed

Comments:

Section B: What are the results?

6. What are the overall results of the review?

HINT: Consider
- If you are clear about the review's 'bottom line' results
- what these are (numerically if appropriate)
- how were the results expressed (NNT, odds ratio etc.)

Comments:

NHS
Health Research Authority

Dr Patricia Maitland
Copland Building
University Of Westminster
115 New Cavendish Street
W1W 6XH

Email: hra.approval@nhs.net

13 November 2017

Dear Dr Maitland

Letter of HRA Approval

Study title:	**A study of the impact of substituting Warfarin with Direct Oral Anticoagulants (DOAC), in Atrial Fibrillation (AF) patients over 65 years old:– the Patients' and Clinicians' Perspectives.**
IRAS project ID:	**196397**
REC reference:	**17/LO/0290**
Sponsor	**University of Westminster**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from the HRA website.

Appendices

The HRA Approval letter contains the following appendices:

- A – List of documents reviewed during HRA assessment
- B – Summary of HRA assessment

After HRA Approval

The document *"After Ethical Review – guidance for sponsors and investigators"*, issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website.

Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found through IRAS.

IRAS project ID	196397

HRA Training

We are pleased to welcome researchers and research management staff at our training days – see details on the HRA website.

Your IRAS project ID is **196397**. Please quote this on all correspondence.

Yours sincerely

Catherine Adams

Senior Assessor

Email: hra.approval@nhs.net

Copy to: *Ms Huzma Kelly, Sponsor Representative*
Ms Ruth Nicholson, Imperial College

IRAS project ID	196397

Appendix A - List of Documents

The final document set assessed and approved by HRA Approval is listed below.

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance Verification Documents]	1	01 August 2016
HRA Schedule of Events	1	09 November 2017
HRA Statement of Activities	1	13 November 2017
Interview schedules or topic guides for participants [Question guide for first patient interview]	1	23 March 2017
Interview schedules or topic guides for participants [Question guide for the second patient interview]	2	23 March 2017
Interview schedules or topic guides for participants [Question guide for clinicians and biomedical scientists interview]	1	23 March 2017
IRAS Application Form [IRAS_Form_16062017]		16 June 2017
Other [Questionnaire]		
Participant consent form [Patient Participant Consent form]	3	25 September 2017
Participant consent form [Staff Participant Consent Form]	3	25 September 2017
Participant information sheet (PIS) [Information sheet for Staff Participants]	3	25 September 2017
Participant information sheet (PIS)	4	09 November 2017
Research protocol or project proposal [A study of the impact of substituting Warfarin with Direct Oral Anticoagulants (DOAC), in Atrial Fibrillation (AF) patients over 65 years old: the Patients' and Clinicians' Perspectives.]	7	14 March 2017
Summary CV for Chief Investigator (CI) [Patricia Maitland's CV]	1	23 March 2017
Summary CV for student [Patricia Richards' CV]	1	04 October 2016
Summary CV for supervisor (student research) [Patricia Maitland's CV]	1	27 March 2017
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Gantt chart]	1	14 March 2017
Validated questionnaire [Short-Form 36 (SF-36) Questionnaire]	1	23 March 2017
Validated questionnaire [Percieved Stress Scale]	1	23 March 2017

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	No comments
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	A statement of activities will act as agreement of an NHS organisation to participate. The sponsor is not requesting and does not expect any other site agreement.
4.2	Insurance/indemnity arrangements assessed	Yes	Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the activities expected of them for this research study
Section	**HRA Assessment Criteria**	**Compliant with Standards**	**Comments**
4.3	Financial arrangements assessed	Yes	No funding is to be provided as confirmed in the Statement of Activities Refer to source of information (e.g. Statement of Activities).
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments

Section	HRA Assessment Criteria	Compliant with Standards	Comments
4.3	Financial arrangements assessed	Yes	No funding is to be provided as confirmed in the Statement of Activities Refer to source of information (e.g. Statement of Activities).
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.
There is one participating organisation and therefore only one 'site-type' undertaking activities detailed in the protocol. The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. For NIHR CRN Portfolio studies, the Local LCRN contact should also be copied into this correspondence. For further guidance on working with

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participating NHS organisations please see the HRA website.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net. The HRA will work with these organisations to achieve a consistent approach to information provision.

Confirmation of Capacity and Capability

This describes whether formal confirmation of capacity and capability is expected from participating NHS organisations in England.

The HRA has determined that participating NHS organisations in England **are not expected to formally confirm their capacity and capability to host this research,** because the Principal Investigator retains responsibility for the study at the participating organisation.

The HRA has informed the relevant research management offices that you intend to undertake the research at their organisation. However, you should still support and liaise with these organisations as necessary.

- Following issue of the HRA Approval letter, and subject to the two conditions below, it is expected that these organisations will become participating NHS organisations 35 days after issue of this Letter of HRA Approval (no later than 18th December 2017):
  - You may not include the NHS organisation if they provide justification to the sponsor and the HRA as to why the organisation cannot participate
  - You may not include the NHS organisation if they request additional time to confirm, until they notify you that the considerations have been satisfactorily completed..
- You may include NHS organisations in this study in advance of the deadline above where the organisation confirms by email to the CI and sponsor that the research may proceed.
- The document "Collaborative working between sponsors and NHS organisations in England for HRA Approval studies, where no formal confirmation of capacity and capability is expected" provides further information for the sponsor and NHS organisations on working with NHS organisations in England where no formal confirmation of capacity and capability is expectations, and the processes involved in adding new organisations. Further study specific details are provided the *Participating NHS Organisations* and *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections of this Appendix.

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and the minimum expectations for education, training and experience that PIs should meet (where applicable).

The researcher is the Principal Investigator at the participating organisation. No additional investigators or collaborators are required.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England to aid study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

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