The **A**trial **F**ibrillation **A**nd **S**troke **T**hromboprophylaxis in h**E**art failu**R**e

(AFASTER) Study.

Patient-centered approaches to thromboprophylaxis in heart failure with atrial fibrillation.

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CERTIFICATE OF ORIGINAL AUTHORSHIP

I certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text.

I also certify that the thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

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7. **Ferguson C**, Inglis SC, Newton PJ, Middleton S & Davidson PM (2012) Atrial fibrillation and thromboprophylaxis: methods in risk assessment and addressing barriers to adherence: A review. Australasian Cardiovascular Nursing College. Coogee, Sydney, Feb 2012.

OTHER PUBLISHED WORKS RELATED TO THIS THESIS

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2. **Ferguson C** (2013) "Unhealthy Buzz" *U:Magazine*, June Edition. Available via http://newsroom.uts.edu.au/umag

3. **Ferguson C** & Davidson (2012) "Energy drink binge leaves teens with more than a hangover" *The Conversation.* April 2012. Available via: https://theconversation.edu.au/energy-drink-binge-leaves-teens-with-more-than-a-hangover-6165

4. **Ferguson C** & Davidson PM (2012) "Getting to the heart of the matter on stroke" *The Conversation*. May 2012 Available via: https://theconversation.edu.au/getting-to-the-heart-of-the-matter-on-stroke-7180

5. **Ferguson C**, DiGiacomo M, & Davidson PM (2012) "Lady Killer: the hidden dangers to women's health. *The Conversation*. July 2012. Available via: https://theconversation.edu.au/ladykiller-the-hidden-danger-to-womens-health-7591

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LIST OF ACRONYMS AND ABBREVIATIONS USED IN THIS THESIS

ACC: American College of Cardiology

ACNC: Australian Cardiovascular Nursing College

AF: Atrial Fibrillation

AFASTER: The Atrial Fibrillation And Stroke Thromboprophylaxis in hEart failure Study

AFFIRM: Atrial Fibrillation Follow-up Investigation of Rhythm Management trial

AHA: American Heart Association

ANZ: Australia and New Zealand

ARITOTLE: Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation trial

ATRIA: The AnTicoagulation and Risk Factors in Atrial Fibrillation Study

AVERROES: Apixaban versus Acetylsalicylic Acid to Prevent Strokes in Atrial Fibrillation Patients Who Have Failed or Are Unsuitable for Vitamin K Antagonist Treatment trial.

BAFTA: The Birmingham Atrial Fibrillation Treatment of the Aged Trial

CCI: Charlson Comorbidity Index

CCU: Coronary Care Unit

CHA_2DS_2VASc: (Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, Prior Stroke or TIA or Thromboembolism)

$CHADS_2$: (Congestive heart failure or left ventricular systolic dysfunction, Hypertension, Age ≥ 75 years, Diabetes mellitus, Prior Stroke or TIA or Thromboembolism, Vascular disease, Age 65-74, Sex category i.e. female sex)

CHARM: Candesartan in Heart Failure-Assessment of Reduction in Mortality and Morbidity Study

CHF STAT: The Congestive Heart Failure-Survival Trial of Antiarrhythmic Therapy trial

CHF: Chronic Heart Failure

CIBIS II: The Cardiac Insufficiency Bisoprolol Study II

CINAHL: Cumulative Index to Nursing and Allied Health Literature

COMET: Carvidilol Or Metoprolol European Trial

CONSENSUS: The Cooperative North Scandinavia Enalapril Survival Study

CPG: Clinical Practice Guideline

CrCl: Creatinine Clearance

CSANZ: Cardiac Society of Australia and New Zealand

DBP: Diastolic Blood Pressure

DCE: Discrete Choice Experiment

DIAMOND CHF: Danish Investigations of Arrhythmia and Mortality ON Dofetilide Study

DIG: The Digitalis Investigation Group Trial

ECG: Electro Cardio Graph

eGFR: Estimated Glomerular Filtration Rate

EHFScBS: European Heart Failure Self-care Behaviour Scale

ENGAGE: Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation – Thrombolysis in Myocardial Infarction 48 trial

GESICA: Grupo de Estudio de la Sobrevida en la Insuficien Cardiaca en Argentina Study

GP: General Practitioner/ Primary care physician

HAS-BLED: (Hypertension, Abnormal renal/ liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drug/ alcohol concomitantly).

HEMMORR$_2$HAGES: (Hepatic or renal disease, ethanol abuse, malignancy, older age, reduced platelet count, re-bleeding risk, anemia, genetic factors, excessive falls risk, stroke)

HF: Heart Failure

HRS: Heart Rhythm Society

INR: International Normalized Ratio

LAA: Left Atrial Appendage

LVEF: Left Ventricular Ejection Fraction

MERIT HF: Metoprolol CR/XL Randomized Intervention Trial in-Congestive Heart Failure

MMSE: Mini Mental State Examination

MOCA: Montreal Cognitive Assessment

MORISKY: 4 item medication adherence self-report questionnaire

NOAC: Novel Oral Anticoagulant

NSW: New South Wales

NT-Pro-BNP: N-terminal prohormone of brain natriuretic peptide

NYHA: New York Heart Association Classification

OPTIMAAL: Optimal Trial in Myocardial Infarction with the Angiotensin II Antagonist Losartan trial

OPTIME CHF: Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure Study.

PBS: Pharmaceutical Benefits Scheme

PCC: Patient Centered Care

PRIME: The Prospective Epidemiological Study of Myocardial Infarction Study

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PSM: Patient Self-Monitoring/ Patient Self-Management

PST: Patient Self-Testing

RE-LY: The Randomized Evaluation of Long-Term Anticoagulation Therapy trial

ROCKET AF: Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation trial.

SAFETY: Standard versus atrial fibrillation-specific management strategy to reduce recurrent admission and prolong survival: pragmatic, multicenter randomized controlled trial.

SBP: Systolic Blood Pressure

SDM: Shared Decision Making

SHARE-FI: Survey of Health, Ageing and Retirement in Europe Frailty Instrument

SOLVD: Studies of Left Ventricular Dysfunction Prevention Study

SPAF: Stroke Prevention in Atrial Fibrillation

SPORTIF: Stroke Prevention Using Oral Thrombin Inhibitor in Atrial Fibrillation Study

TGA: Therapeutic Goods Administration

TIA: Transient Ischaemic Attack

TTR: Time in Therapeutic Range

V-HeFT I and II: The Vasodilator Heart Failure Trial

VKA: Vitamin K Antagonist

WARCEF: The Warfarin and Aspirin in Patients with Heart Failure and Sinus Rhythm Study

WATCHMAN: A nickel-titanium umbrella implantable device

WHO: World Health Organisation

THESIS ABSTRACT

Background

Atrial fibrillation (AF) is a common arrhythmia in heart failure (HF) and presents a significant risk factor for thromboembolic stroke. Despite recommendations in best practice guidelines, implementation of risk stratification, therapeutic approaches for AF and thromboprophylaxis are not uniformly applied in practice.

Purpose

This study aims to identify both barriers and enablers to thromboprophylaxis in patients with HF and AF as a concomitant condition at the levels of the patient, provider and health system.

Methods

This was undertaken through a series of discrete studies, including: (1) a prospective cohort study of individuals with HF and AF at St Vincent's Hospital, Sydney; (2) bedside interviews with patients, and medical file note review; and (3) an electronic survey of cardiovascular nurses to explore their current knowledge and practice patterns.

Results

Patient level: Results of this research demonstrate that patient choice and preference were important factors in thromboprophylaxis decisions, including treatment burden, unfavorable or intolerable side effects and patient refusal. Facilitators to successful prescription and adherence were caregiver support, reminders and routine, self-testing and the use of technology. At a **health system level**, financial barriers included cost of travel; medication cost and reimbursement were important considerations.

Provider level: Survey findings revealed mixed levels of education on AF, stroke risk, anticoagulation and health behavior modification. The CHA_2DS_2VASc and HAS-BLED risk stratification tools were reported to be underused. Nurses reported key barriers to anticoagulation to include; fears of patients falling, fears of poor adherence to medication taking and routine monitoring. Additionally, patient self-monitoring and self-management were reported to be underutilized. Cardiovascular nurses reported their key role to be counselling and advising patients on therapy regimens. Anticoagulant-drug interaction knowledge was generally poor. From the medical file note review, clinician reticence included fear of falls, frailty, age, fear of bleeding and the challenges of multi-morbidity. Psychological factors included psychiatric illness, cognitive impairment and depression. Social barriers included homelessness and the absence of a caregiver or lack of caregiver assistance. The cohort study revealed that 66% of participants were prescribed an anticoagulant at discharge from hospital. Self-reported self-care behavior and 'not for CPR' were associated with not receiving anticoagulation at discharge. Whilst statistical significance was not achieved, those who were assessed as frail or having greater comorbidity, were less likely to receive anticoagulation at discharge from hospital.

Recommendations

1. Treatment decisions must be tailored to meet the needs of individuals, whilst balanced in the context of the best available evidence.

2. There is need to formalize the role of the caregiver in the management of AF and CHF.

3. Improved focus on AF within existing chronic care programs is warranted, given the aging population.

4. Developing quality patient education materials and self-management strategies are key priority areas for enhancing sustainable models of care.

5. There is scope for improvement in nurses' knowledge and practice in contemporary AF management.

6. Patient preference, choice and attributes must be considered when making complex thromboprophylaxis treatment decisions.

Conclusion

The findings of this thesis point to the need for patient-centered approaches to the management of AF in the setting of HF, as well as increased skills and competencies for nurses. This thesis demonstrates that although stroke and bleeding risk calculation are important there are other salient considerations in making clinical decisions for thromboprophylaxis including cognitive impairment, multimorbidity, self-care ability and frailty. These factors not only influence decision making on the part of provider and patient but also influence clinical outcomes. Shared decision making provides a framework for patients and providers to have quality communication, negotiate consensus and find agreements on treatment goals. These findings underscore the need for shared decision making when making complex treatment decisions around thromboprophylaxis.

CHAPTER 1: INTRODUCTION

1.1. BACKGROUND

Approximately one third of patients with heart failure (HF) are likely to have atrial fibrillation (AF) as a comorbid condition.[1] Epidemiological surveys and large clinical trials in HF provide strong evidence that AF is a marker of major acute cardiovascular events. Poor rate control, irregularity of ventricular response, and loss of atrial systolic activity can contribute adversely to health related quality of life.[2,3] There is strong evidence that ischaemic stroke patients with AF have substantially worse outcomes than patients without AF, which can be partly explained by advancing age and greater co-morbidities.[4] Therefore, treating the risk of stroke with definitive therapies, including antithrombotic therapies, is not only highly justified but recommended by international best practice guidelines.[5-8] Although there are numerous risk stratification tools to assist clinicians in allocating treatment,[9] commonly these do not consider factors such as frailty, poor adherence or self-care behavior which impact adversely on health outcomes. A recent study by Lee et al (2011) identified that in patients with AF, the use of anticoagulants prior to first stroke did not increase with increasing stroke risk.[10] This study highlighted the need for further improvement in risk factor reduction in high-risk patients with AF. Lip (2011) stresses that stroke risk assessments need to evolve to enable better identification of the truly low risk subjects who do not need antithrombotic therapy, whilst all other patients with ≥ 1 stroke risk factors should be considered for oral anticoagulants.[11]

1.2. CHRONIC HEART FAILURE

1.2.1. DEFINITION OF CHRONIC HEART FAILURE

There are many definitions of chronic heart failure (CHF). Given this study was conducted in the Australian healthcare setting; an Australian definition has been selected, as provided by the National Heart Foundation (NHF) and the Cardiac Society of Australia and New Zealand (CSANZ).

"CHF is a complex clinical syndrome with typical symptoms (e.g. dyspnea, fatigue) that can occur at rest or on effort, and is characterized by objective evidence of an underlying structural abnormality or cardiac dysfunction that impairs the ability of the ventricle to fill with or eject blood (particularly during physical activity). A diagnosis of CHF may be further strengthened by improvement in symptoms in response to treatment".[5]

In simplistic terms, CHF can be described as a syndrome whereby the heart is unable to meet the needs of the body. It is commonly characterized by fatigue, dyspnea, sleep disturbance, oedema, cognitive dysfunction and frailty. Chronic heart failure outcomes are generally very poor. Previous researchers have characterized heart failure as being 'more malignant than cancer',[12] with well-documented survival rates of at 1 year and 5 years of 57% and 25% for men, and 64% and 38% for women.[13] Refer to Table 1.1 below. Hospitalization is common and costly.[14] Frequently cause of hospitalization will relate to symptom management, and may be as a consequence of suboptimal self-care management in the home setting.[15]

TABLE 1.1 HEART FAILURE SURVIVAL RATES FROM FRAMINGHAM DATA

Survival	**1 year**	**2year**	**5 year**	**10 year**
Men	57%	46%	25%	11%
Women	64%	56%	38%	21%

1.2.2. *HEART FAILURE SEVERITY CLASSIFICATIONS*

There are two commonly used classification models used to grade chronic heart failure severity. The New York Heart Association (NHYA) functional classification system classifies individuals from Class I through to Class IV and is based on symptom severity.[16]

TABLE 1.2 NYHA FUNCTIONAL CLASSIFICATION SYSTEM

NYHA CLASS	CHARACTERISATION
Class I	No limitation on physical activity
Class II	Slight limitation of physical activity
Class III	Marked limitation of physical activity
Class IV	Symptoms at rest

The second classification system classifies individuals according to the structural abnormality of their heart. There are four stages A- D. This system was established by the American College of Cardiology/ American Heart Association (ACC/AHA).[17]

TABLE 1.3 ACC/ AHA CLASSIFICATION OF HEART FAILURE

STAGE	CHARACTERISATION
Stage A	No identified structural or functional abnormality. However, individuals are at high risk for developing heart failure
Stage B	Developed structural heart disease that is strongly associated with the development of heart failure
Stage C	Symptomatic heart failure associated with underlying structural heart disease
Stage D	Advanced structural heart disease and marked symptoms of heart failure at rest despite maximal medical therapy

Optimal Management of Chronic Heart Failure

There are five key components to optimal chronic heart failure management[18]

They include:

1) Multidisciplinary care coordination
2) Patient and caregiver education
3) Promoting self-management
4) Effective follow up
5) Optimizing medication use

This thesis focuses on the fifth component of chronic heart failure management, *'optimizing the use of medications'*, with particular focus on anticoagulation. The components of patient and caregiver education, and promoting self-management are essential to optimizing medication use, and are therefore key considerations in this thesis.

1.3. ATRIAL FIBRILLATION

1.3.1. DEFINITION OF ATRIAL FIBRILLATION

Atrial fibrillation (AF) is the most commonly occurring cardiac arrhythmia and is estimated to affect two million people in the United States.[19] AF occurs when structural and/or electrophysiological abnormalities alter atrial tissue to promote abnormal impulse formation and/or propagation. These abnormalities are caused by a range of pathophysiological mechanisms. The mechanisms of AF are not fully understood, however AF represents a final common phenotype for multiple disease pathways.[19]

The AHA/ ACC/ HRS provide a simplified scheme to define and classify AF.[19]

TABLE 1.4 CLASSIFICATION OF AF

Term	Definition
Paroxysmal AF	• AF that terminates spontaneously or with intervention within 7 days of onset. • Episodes may recur with variable frequency.
Persistent AF	• Continuous AF that is sustained >7 days
Longstanding persistent AF	• Continuous AF of >12 months duration.
Permanent AF	• Permanent AF is used when there has been a joint decision by the patient and clinician to cease further attempts to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of the AF • Acceptance of AF may change as symptoms, the efficacy of therapeutic interventions, and patient and clinician preferences evolve.
Non-valvular AF	• AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve or mitral valve repair.

Selected risk factors for the development of AF and a more comprehensive overview of AF are provided in the literature review in Chapter 2. Importantly, CHF is a well-established independent risk factor for the development of AF.[20,21] AF begets HF and HF begets AF, in a highly complex relationship.

1.3.2. INCIDENCE AND PREVALENCE

Internationally, population prevalence of AF ranges 2.3-3.4%.[22] There are upward trends of AF incidence, with a life-time risk of AF estimated to be 1 in 4.[22] There is increased incidence for those over 85 years (6-12%).[22] Hospitalization for AF is a common occurrence, and the burden of AF related hospitalization is increasing.[22] However, this is likely due to increase in technology and treatment procedures to treat AF.[22] There is a paucity of Australian data and epidemiological studies to estimate Australian prevalence.[23] To date, there are only two previously published studies on the prevalence of AF in Australia. Both studies are dated, published in 1989 and 2002. The first study originated from Western Australia, and included 1,770 community participants aged 60 years and over, which assessed relative mortality in people with and without AF. Recruitment for this study was from 1966 to 1981.[24] The second study included 16,148 participants' aged 30 years and older attending general practices across Australia during 2000, where researchers examined the prevalence of stroke risk factors including AF. The authors report an overall AF prevalence rate of 4% in people aged 30 years and older (6% among 5,801 men, and 4% among 8,393 women). A very low prevalence of AF in people was noted in participants aged less than 50 years.[25]

A more recent report by Deloitte conducted in 2011, estimates that 506,045 Australians have AF including 101,209 undiagnosed and 404,836 diagnosed cases.[23] The average age of a patient with AF is between 75 and 85 years.[7] There is a clear increased risk in the development of AF with advancing age.[7] Several studies have demonstrated that up to 50% of individuals with a diagnosis of CHF will also have concomitant AF.[26-28] (Refer to Figure 1.2).

Chapter 2 provides a more detailed overview of the epidemiology and risk factors for the development of HF and AF. Comorbid conditions and significant risk factors for the development of AF and HF include; genetic predisposition; advancing age; hypertension; diabetes; valvular disease; coronary artery disease; ischaemic and non ischaemic cardiomyopathy; obesity, metabolic syndrome; inflammation; thyroid dysfunction, sleep apnoea; pulmonary disease; alcohol use; and smoking. As outlined in Figure 1.1, the aforementioned factors contribute to structural, functional, electrical, and neurohormonal changes which increase the propensity for the development of AF-HF complex.29

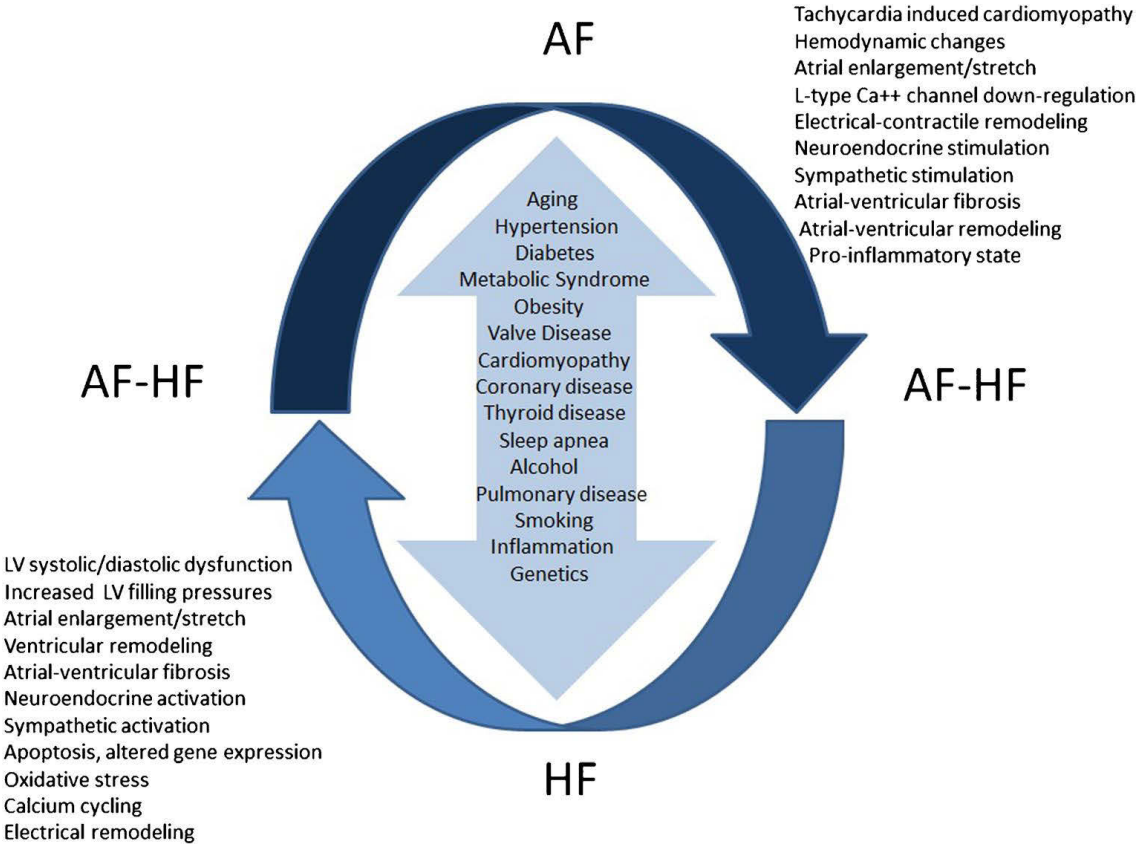

FIGURE 1.1 AF AND HF BOTH AS CAUSES AND EFFECTS OF THE AF-HF COMPLEX: A VICIOUS CYCLE AND BIDIRECTIONAL MODEL.

Permissions: Luong et al (2014)[29]

It is estimated that AF increases the risk of CHF 3-fold, and 42% of AF patients develop CHF at some time during their life.[2,21]

1.4. AF AND CHF COMORBIDITY IN CLINICAL TRIALS

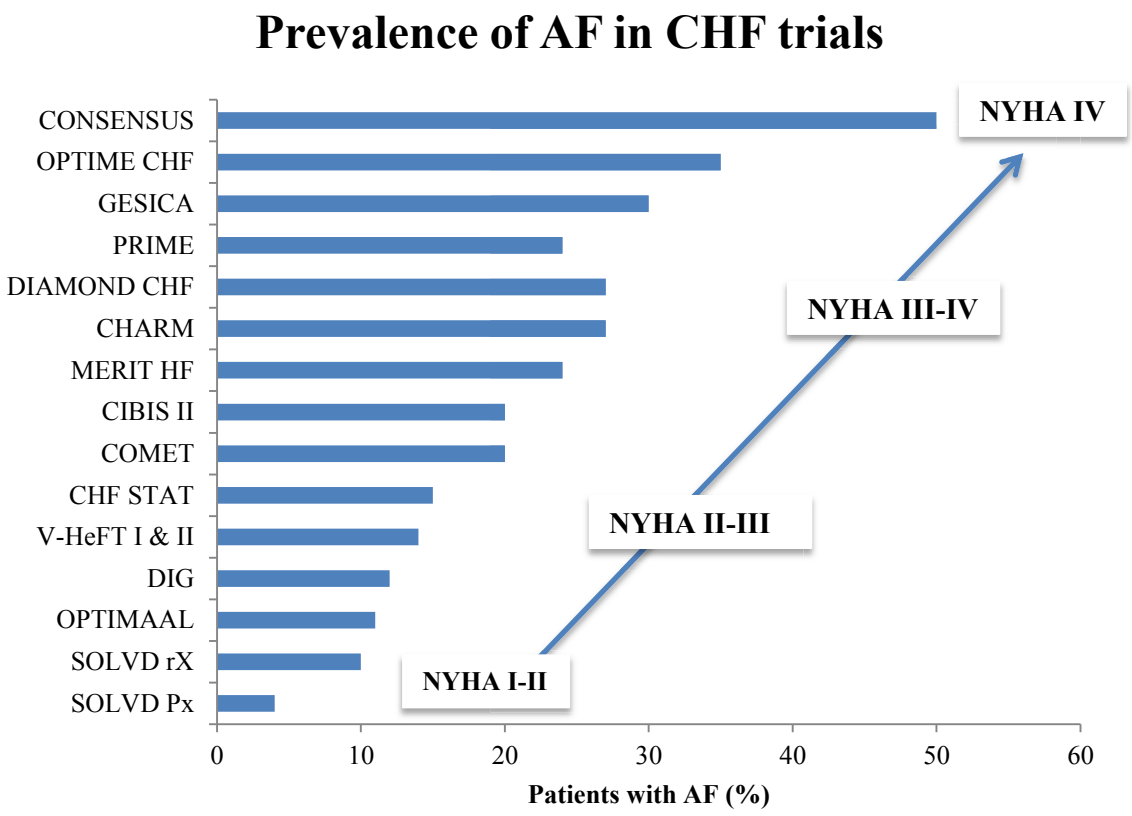

FIGURE 1.2 PREVALENCE OF AF IN CHF CLINICAL TRIALS

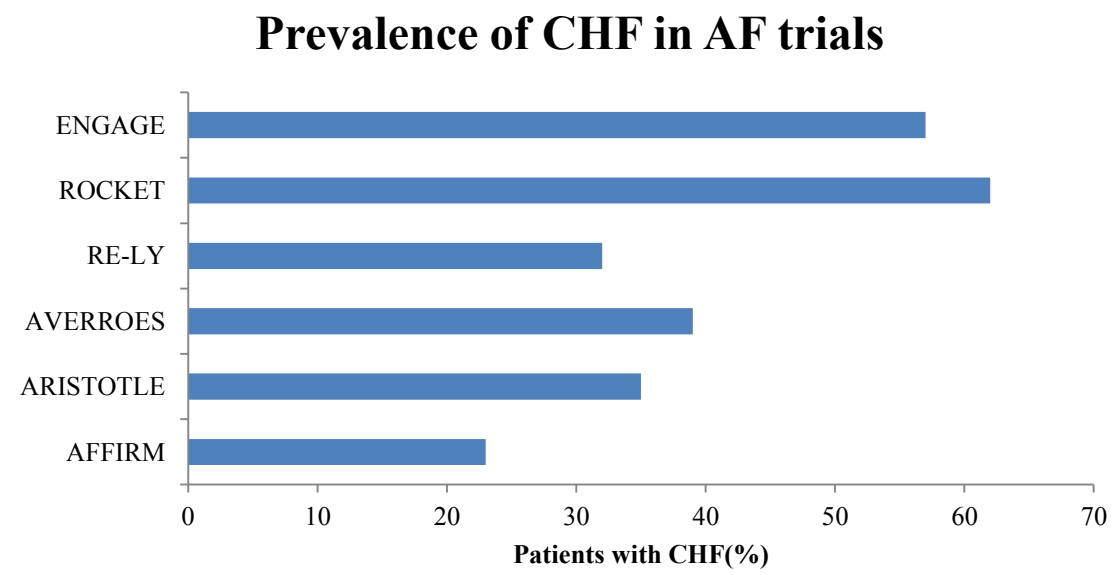

FIGURE 1.3 PREVALENCE OF CHF IN AF CLINICAL TRIALS

Figure 1.2 and 1.3 highlight the prevalence of AF in CHF trials, and the prevalence of CHF in AF trials. Figure 1.2 illustrates that with the increase in NYHA classification, there is likely to be an increase in the prevalence of AF in CHF.

1.5. EVIDENCE-BASED PRACTICE AND KNOWLEDGE TRANSLATION

Evidence-based care ought to be positioned in the context of the best available evidence, recognizing the clinicians own experience, whilst tailored to an individual's needs.[30] Yet, translating evidence into practice remains a major challenge in healthcare.[31] Knowledge translation is an approach for improving healthcare delivery by interacting with patients and their caregivers and clinicians to identify needs and barriers, to develop and apply individually tailored approaches, to promote the adoption of evidence-based care.[32] There is evidence to support that informed, educated and supported patients who are engage in their own healthcare have improved outcomes.[32] Engaging patients with complex chronic conditions can be challenging. However, patient and caregiver involvement is critical to develop and maintain a healthcare system that meets the needs of patients.[32]

1.6. PATIENT-CENTERED CARE

Patient-centered care can be defined as *"care that is respectful of and responsive to individual patient preferences, needs and values"* and that ensures *"the patient values guide all clinical decisions"*. This definition highlights the importance of clinician and patient partnerships to work together to optimize patient outcome. [33,34]

Patient-centered care is a model of care, where patients are individuals and positioned at the center of care, and should not be reduced to their condition alone. Their interactions with the environment, strengths, future plans and rights also must be central to care assessment and planning. [35] There is a focus on sharing the management of an individual's condition between

the clinician and the patient. Patient-centered care can improve adherence, reduce morbidity and improve quality of life.[36] The idea of patient-centered care is not new. Origins of the concept date back to the Florence Nightingale period. Nursing can be distinguished from medicine by its focus on the individual rather than the condition.[37] Patient-centered care may positively impact adherence to treatment regimens and outcomes for individuals living with heart failure and atrial fibrillation.

1.6.1. SHARED DECISION MAKING

Shared decision making (SDM) is described as the pinnacle of patient-centered care. It provides a framework for communicating with individuals about healthcare choices, aimed to improve the quality of conversation. It can also provide a mechanism for applying evidence with an individual through personalizing treatment decisions and overall care.[38] There are four key characteristics of SDM. They include; 1) that at minimum the individual and the clinician be involved; 2) both partners share information i.e. bidirectional conversation; 3) both parties take actions to build consensus to preferred treatment option; 4) An agreed care pathway of action is reached.[39]

1.6.2. ADHERENCE

Adherence is defined as the '*active, voluntary and collaborative involvement of the patient in a mutually acceptable course of behavior to produce a therapeutic result*'.[40] Adherence and compliance can be used synonymously. The WHO estimates that adherence to long-term therapies for the treatment of chronic conditions is approximately 50% in the developed world.[41] Sub-optimal adherence to long-term therapies can negatively impact treatment effect. This can have deleterious impact, given the complex nature of thromboprophylaxis. Given the more-often-than-not life-time duration of treatment, adherence may be an important factor to consider in decision making around suitable treatment. However, adherence is often improved with once daily dosing schedules.[42] Shared decision making has shown to be beneficial in other chronic conditions, and demonstrated improved adherence and clinical outcomes.[43] There is scope to improve patients and caregivers knowledge about their condition and treatment through SDM. Exploration is warranted in the setting of CHF and AF. The aggregate cost of hospital admissions related to medication non-adherence is estimated to be $100 billion per year.[44] It is estimated that 33-69% of all medication-related hospital admissions in the US are due to poor medication adherence.[42] Improving medication adherence in the CHF population is likely beneficial to prevent potentially avoidable rehospitalisations.[44]

1.6.3. MULTIMORBIDITY

Multimorbidity is defined as the coexistence of two or more chronic conditions in an individual, and is increasingly being normalized as a common occurrence in individuals with advancing age. [45,46] Both CHF and AF are frequently associated with multiple comorbidity. It is of rare occasion that they exist in the absence of other comorbidity.[47] A recent study by Wong and colleagues evaluated multimorbidity in association with adherence to cardiovascular medication.[46] This study demonstrated that multimorbidity was associated with poorer medication adherence. From this study, factors associated with multimorbidity included advanced age, smoking, family history of hypertension, and poor or fair self-perceived health status. Factors associated with poor medication adherence included; younger age, lower income, alcohol consumption and poor or fair self-perceived health status. A hypothesized rational for the association between multimorbidity and poor adherence is the inability to comply with medication-taking schedules, higher possibility of poly-pharmacy.[46] An additional factor is thought to be most models of care only catering for single diseases, and this leading to *'silo-ing'* of care for individuals with multiple chronic conditions. This eventuating to chaotic, episodic and fragmented care provision.[48] This may be a limitation of models of care such as 'AF clinics'. Further, this strengthens the argument to increase AF management components in other chronic disease management programs.

There has been recent criticism of singular disease specific clinical practice guidelines.[49] Despite the fact that multimorbidity if a frequent occurrence in individuals with cardiovascular disease, current guidelines do not consider cumulative impact of treatment recommendations. Whilst clinical guidelines play a vital role in informing evidence based care, there is need to consider individuals with multimorbidity and the impact of treatment related burden.[49]

1.6.4. FRAILTY

Frailty is a multidimensional physiological syndrome, more frequently occurring in people with advanced age. Fried defined frailty is *'a state of high vulnerability for adverse health outcomes, including disability, dependency, falls, need for long term care, and mortality'.*[50] It occurs more commonly in individuals with chronic heart failure than those of the general population.[51] Table 1.5 presents the prevalence rates of frailty in HF across 6 studies. Rates are estimated from 15 to 45%. Frailty is associated with poor prescription of anticoagulant medications.[52] This is primarily due to clinician apprehension, related to fear of falls and intracranial haemorrhage,[53] associated with increased morbidity and mortality. [54,55] The Fried Frailty Index was originally developed from data used in the Cardiovascular Health Study (CHS).[56] There are five components to the Fried Frailty Index: unintentional weight loss, weakness, poor endurance or exhaustion, slowness/ slow gait, and low physical activity. The Fried Frailty Index has been validated and compared against other frailty indices using independent data sources in the MOBILIZE Boston Study, where is demonstrated good ability to distinguish relevant geriatric conditions, functional and cognitive impairments and predictive ability of adverse outcomes by the level of frailty.[56] Frailty is an established predictor of increased visits to the emergency department, hospitalisation and mortality. Further, it is associated with decreased mobility, increased tendency to fall, polypharmacy, increased comorbidity, cognitive dysfunction and nutritional impairment.[51]

TABLE 1.5 PREVALENCE OF FRAILTY IN HEART FAILURE.

Authors	CHF Patients (n)	Frailty (%)
Newman et al	181	23 (intermediate frailty 54)
Carriatore et al	120	15
Woods et al	509	45 (intermediate frailty 28)
Altimir et al	360	41
Lupon et al	622	39.9
McNallan et al	448	19 (intermediate frailty 55)

Adapted; Uchmanowicz et al, 2014.[51]

1.7. HEART FAILURE SELF CARE BEHAVIOUR

Optimizing individual's self-care is important as CHF is a chronic, progressive condition and most care is undertaken in the primary care setting.[57] Self-care is a fundamental component of effective clinical management.[15] It refers to strategies adopted by the individuals to optimize their health and overall well-being. There are three key components of self-care in CHF. They include:[58]

1. Optimizing medication management (including dosage and adherence).
2. Lifestyle and behavior management.
3. Symptom recognition and response, with appropriate utilization of health services.

The European Heart Failure Self Care Behaviour Scale (EHFScBS) was originally designed for evaluation of CHF management with a focus on self-care behavior in the chronic heart failure population.[59] This questionnaire is widely used in chronic heart failure research and is well validated. The global score ranges from 12 (best self-care) to 60 (worst self-care), where a lower score indicates better self-care behavior and a high score indicates poor self-care behavior.[59] Assessment of self-care behavior should form the part of a comprehensive patient assessment for individuals with CHF. However, the EHFScBS is limited in its approach to self-care in the context of AF, and to date there has been limited attention to self-care behavior in AF.

1.8. CONTRAST BETWEEN RISK STRATIFICATION AND A PATIENT CENTERED ASSESSMENT

To date, most international AF management guidelines recommend risk stratification for stroke and bleeding using the validated and widely available tools including CHA_2DS_2VASc and HAS-BLED. Whilst these tools are useful for use in the clinical setting, it is important to distinguish between a risk prediction score (estimation of risk/ year of stroke and bleeding) versus a patient centered consultation. Complex statistics may be overwhelming for patients and their caregivers to digest. The use of apps in the clinical setting is increasing, to enhance consultation and provide recommendations for treatment. Novel smartphone applications including risk assessments such as the ACC endorsed Anticoag Evaluator™ application[60] fail to consider other important factors in clinical decision making. Therefore, it is important that clinicians use these appropriately, and with caution. It is vital to consider a wide range of factors when considering thromboprophylaxis for stroke prevention.

1.9. SIGNIFICANCE AND INNOVATION

Despite evidence demonstrating benefit of anticoagulation therapy in AF, adherence to these recommendations is far from optimal. Decision making in this area of practice is problematic and highly complex. Reluctance to anticoagulate patients is based upon fear of adverse effects and poor adherence with monitoring, particularly in the elderly. This is likely due to the complexity of warfarin therapy.[11] Although the use of novel agents including direct thrombin inhibitors show particular promise,[61] concerns regarding adherence, adverse events and the lack of a reversal agent remain.[62] Despite some Australian data describing the barriers and facilitators to warfarin therapy in older Australians, there has been a lesser focus on individuals with HF.[52,63-65] Understanding local factors, particularly patterns of care provision, are integral to achieving adherence with evidence-based therapies.[64] Failure to adhere to evidence-based recommendations is associated with additional costs and adverse events.[66]

In a study undertaken by Perera *et al,* frail patients were less likely to receive warfarin than non-frail patients on hospital admission ($p = 0.002$) and discharge ($p < 0.001$).[52] During hospitalisation, the proportion of frail participants prescribed warfarin decreased by 10.7% and that of non-frail increased by 6.3%. Compared to non-frail, frail participants were significantly more likely to experience adverse events.[52] Best-practice management of CHF involves multidisciplinary care, commonly involving nurses, cardiologists and pharmacists, along with other allied health professionals.[67] There is convincing evidence that, among people who have been hospitalised with CHF, those who receive multidisciplinary care have better health outcomes than those who do not. Many patients in these programs have AF. In fact, recently in the WHICH? Trial (an Australian multi-center RCT of CHF patients examining home versus clinic based intervention), 172/280 (61%) participants had AF as comorbidity.[26] Therefore, increasing focus on AF management in these programs is justified.

1.10. STUDY OBJECTIVES

Translating knowledge into practice is a major challenge. Optimizing adherence to evidence based recommendations requires an understanding of diverse factors moderating implementation.[68] This study seeks to address barriers and enablers to antithrombotic therapy in individuals aged 18 years and older with documented CHF and AF, from the perspective of the patient, provider and health system.

For the purpose of this thesis the following definitions will be used: **Patient** relates to the multidimensional facets of individuals- including physical, social, psychological factors. **Providers** denote health professionals providing formal care; and **System** pertains to factors relating to the organisation and funding of health care systems.[69]

1.10.1. STUDY AIMS

1. Explore the barriers and enablers to thromboprophylaxis in individuals with HF and AF from the perspective of the patient, provider and health system.
2. Summarize the caregiver role with attention to enabling attributes that specifically promote adherence to thromboprophylaxis.
3. Examine knowledge and practice patterns of AF in cardiovascular nursing.
4. Describe the rate and type of thromboprophylaxis in a prospective cohort of individuals aged 18 years and older with AF with a confirmed diagnosis of HF of any aetiology.
5. Determine the predictors of all-cause mortality and rehospitalisation in individuals with HF and coexistent AF.

1.10.2. RESEARCH QUESTIONS

1. What are the barriers and enablers to thromboprophylaxis from the perspective of health care system, providers, and patients?
2. What is the role of the caregiver in supporting and enabling adherence to thromboprophylaxis?
3. What are the knowledge and practice gaps related to AF for cardiovascular nurses in Australia and New Zealand?
4. What is the rate and type of thromboprophylaxis in patients with chronic heart failure and atrial fibrillation as a co morbid condition?
5. What are the predictors of adverse events attributed to thromboprophylaxis in patients with AF and HF?

1.11. Outline of this thesis

This thesis presents a series of discrete, but interconnected studies to address the study questions. With an overarching focus of patient -centered approaches to thromboprophylaxis in individuals with HF and concomitant AF. This thesis is presented in eight chapters. Six of these chapters are presented in the form of peer reviewed journal articles (published and submitted currently undergoing peer review). Each chapter is presented as a stand-alone report in the style of a journal article. This is aimed to enhance readability; however it is hoped this does not cause too much repetition for the reader. To meet journal requirements for manuscript submission, spelling may vary between US English and British English for chapters 2-7. Chapters 1 and 8 are written in Australian English. It is hoped this does not cause concern for the reader.

Chapter one provides contextual background information, including the purpose of this thesis. The rationale and methods for each discrete study is also provided within this chapter. This provides an overview of the thesis structure, including a summary of acronyms and abbreviations used.

Chapter two presents a review of the epidemiology of AF and stroke, stroke and bleeding risk assessment tools and evidence-based treatment options for the prevention of stroke in AF, including the use of novel anti-thrombin agents. A review was conducted of key electronic data bases from 2002 – 2012 using the key search terms '*atrial fibrillation*' *'anticoagulation' 'risk assessment'* and *'clinical management'*. The following electronic databases were searched: CINAHL, Medline, Scopus, the Cochrane Library and Google Scholar. Reference lists were manually hand searched. Key clinical guidelines from National Institute for Clinical Excellence (NICE, UK), American Heart Association (AHA, USA), American College of Cardiology (ACC, USA) and the European Society of Cardiology (ESC) and key government policy documents were also included. Articles were included in the review if they addressed nursing

management with a focus on Australia. This paper was published in *Australian Critical Care* in 2014.

Chapter three presents an overview of current validated risk assessment tools for AF, however, with an emphasis on the importance of addressing both tailoring individual risk for stroke and weighing the benefits of treatment. Further, this review provides details of innovative and patient-centered methods for optimising adherence to prescribed therapy. This paper was published in *Vascular Health & Risk Management* in 2013.

Chapter four examines enablers to thromboprophylaxis in additional detail. It provides a review of available information on the caregiver role in AF, specifically in promoting adherence to thromboprophylaxis and evidence for strategies to support and enable the caregiver. A review of electronic databases and search engines were undertaken including Medline, Scopus and CINAHL. The search terms '*atrial fibrillation*' '*anticoagulation*' *'carer'* '*caregiver*' '*family support'* were used. Dates searched from Jan 1990 – Nov 2012. This review was published in the *European Journal of Cardiovascular Nursing* in 2014.

Chapter five is a qualitative primary research paper. The purpose of this study was to elucidate the barriers and enablers to thromboprophylaxis in individuals with CHF with concomitant AF from the perspective of patients, providers and health systems. Data from face to face individual interviews with patients and information retrieved from healthcare file note review documented the clinician perspective. This study is a synthesis of the two data sources, obtained during patient clinical assessments as part of the AFASTER cohort study. Patient choice and preference were important factors in thromboprophylaxis decisions, including treatment burden, unfavourable or intolerable side effects and patient refusal. Financial barriers included cost of travel, medication cost and reimbursement. Psychological factors included psychiatric illness, cognitive impairment and depression. Social barriers included homelessness and the absence of a caregiver or lack of caregiver assistance. Clinician reticence included fear of falls, frailty, age,

fear of bleeding and the challenges of multimorbidity. Facilitators to successful prescription and adherence were caregiver support, reminders and routine, self-testing and the use of technology. Many complex barriers remain to patients receiving thromboprophylaxis.

Chapter six presents findings from a survey of cardiovascular nurses on current knowledge and practice patterns of anticoagulation and AF in the Australian and New Zealand context. This study aimed to; 1) Explore the nurse's role in clinical decision making in anticoagulation in the setting of AF; 2) Describe perceived barriers and enablers to anticoagulation in AF; 3) Investigate practice patterns in the management of anticoagulation in the Australian and New Zealand setting; 4) Assess cardiovascular nurses' knowledge of anticoagulation. A paper-based survey on current practices and knowledge of AF and anticoagulation was distributed during the Australasian Cardiovascular Nursing College (ACNC) Annual Scientific Meeting, February 2014. This survey was also emailed to nursing members of the Cardiac Society of Australia and New Zealand (CSANZ) and Cardiovascular Trials Nurses throughout New South Wales, Australia. This chapter presents the results of this survey.

Chapter seven presents findings from the AFASTER cohort study. This study was conducted in an academic medical center during 2013, and completed 12-month outcome data collection during 2014. This study addressed the aims to 1) Describe the clinical characteristics of a cohort of individuals hospitalised with CHF and concomitant AF; 2) Describe the rate and type of thromboprophylaxis; 3) Examine practice patterns of therapy prescription; 4) Compare the overall quality of AF and CHF care in this cohort, when benchmarked against recommendations of international guidelines; 5) Determine the predictors of adverse events including all-cause rehospitalisation and mortality.

This was achieved through a 6-month prospective cohort study with 12-month outcomes. Prospective consecutive participants with CHF and concomitant AF of any type and aetiology admitted to a cardiology ward were enrolled in the cohort study during April – October 2013.

Socio-demographic and clinical characteristics including medical history, frailty, medication adherence, self-care behaviour and thromboprophylaxis prescription were assessed at index hospitalisation. Participants were followed by telephone at 12 months. Endpoints were assessed including, stroke or TIA, bleeding, all –cause rehospitalisation and mortality. Baseline and outcome findings are described in this chapter.

Chapter eight details the implications for practice, policy and research. This chapter includes details of contemporary clinical management issues related to individuals with CHF and AF within the modern healthcare system in Australia. It provides an overview of the implications of this program of research.

Appendices including copies of Human Research Ethics Committee clearance, participant information and consent forms, case report forms, copies of published works, and copyright permissions are included at the end of this thesis. A summary of acronyms and abbreviations used throughout this thesis is included at the beginning of this thesis.

1.12. STRUCTURE OF THIS THESIS

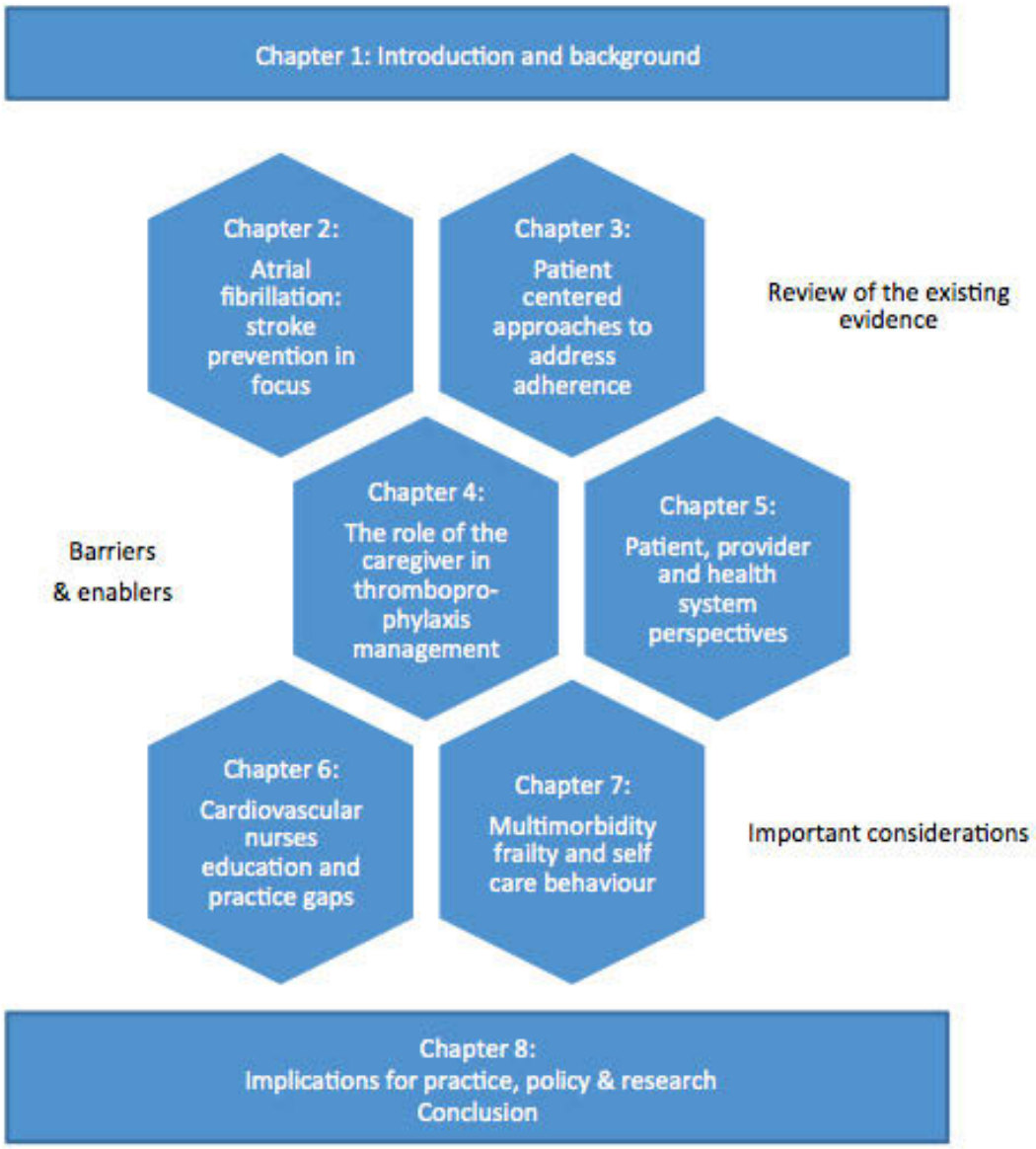

FIGURE 1.4 STRUCTURE OF THIS THESIS

1.13. REFERENCES

1. Teng THK, Hung J, Finn JC, Knuiman M, Stewart S, Arnolda L. Long-term Mortality and Morbidity Trends in Men and Women with Heart Failure of Ischemic versus Non-ischemic Etiology in Western Australia between 1990 and 2005. *Circulation.* 2010;122.

2. Stewart S, Hart CL, Hole DJ, McMurray JJV. A population-based study of the long-term risks association with atrial fibrillation: 20 year follow-up of the Renfrew/ Paisley study. *Am J Med.* 2002;113:359-364.

3. Teng THK, Hung J, Finn JC, Knuiman M, Stewart S, Arnolda L. Long-term Mortality and Morbidity Trends in Men and Women with Heart Failure of Ischemic versus Non-ischemic Etiology in Western Australia between 1990 and 2005. *Circulation.* 2010;122.

4. Gattellari M, Goumas C, Aitken R, Worthington JM. Outcomes for patients with Ischameic Stroke and Atrial Fibrillation: The PRIMS Study (A Program of Research Informing Stroke Management). *Cerebrovascular Diseases.* 2011;32(370-382).

5. Krum H, Jelinek MV, Stewart S, Sindone A, Atherton JJ. 2011 Update to National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand. Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006. *Medical Journal of Australia.* 2011;194(8):405-409.

6. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Updating the 2006 Guideline): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation..*2011;123(1):104-123.

7. Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. *European Heart Journal.* 2012;33:2719-2747.

8. National Institute for Health Care Excellence. *Atrial fibrillation: the management of atrial fibrillation.* UK: NICE; June, 2014 2014.

9. Lip GYH, Nieuwlatt R, Pisters R, Lane DA, Crijns HJGM. Refining clinical risk stratification for predicted stroke and thromboembolism in atrial fibrillation using a novel risk factor- based approach: The Euro Heart Survey on Atrial Fibrillation. *Chest.* 2010;137:263-272.

10. Lee S, Shafe ACE, Cowie MR. UK stroke incidence, mortality and cardiovascular risk management 1999- 2008: time-trend analysis from the General Practice Research Database. *BMJOpen.* 2011;2:1-8.

11. Lip GYH. Stroke in atrial fibrillation: epidemiology and thromboprophylaxis. *Journal of Thrombosis and Haemostasis.* 2011;9:S1 344-351.

12. Stewart S, MacIntyre K, Hole DJ, Capewell S, McMurray JJV. More 'malignant' than cancer? Five-year survival following a first admission for heart failure. *European Journal of Heart Failure.* 2001;3(3):315-322.

13. Ho KK, Anderson KM, Kannel WB, Grossman W, Levy D. Survival after the onset of congestive heart failure in Framingham Heart Study subjects. *Circulation.* July 1, 1993 1993;88(1):107-115.

14. Ahmed A, Allman RM, Fonarow GC, et al. Incident heart failure hospitalization and subsequent mortality in chronic heart failure: a propensity-matched study. *J Card Fail.* Apr 2008;14(3):211-218.

15. Jaarsma T, Abu-Saad HH, Dracup K, Halfens R. Self-care Behaviour of Patients with Heart Failure. *Scandinavian Journal of Caring Sciences.* 2000;14(2):112-119.

16. The Criteria Committee of the NEw York Heart Association. *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels.* Massachusetts: Little, Brown & Co; 1994.

17. Jessup M, Abraham W, Casey D, et al. ACCF/ AHA Guideline Update for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;119:1977-2016.

18. Rich MW. Management of Heart Failure in the Elderly. *Heart Failure Reviews.* 2002;7(1):89-97.

19. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive SummaryA Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Journal of the American College of Cardiology.* 2014.

20. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. *JAMA.* 1994;271(11):840-844.

21. Wang TJ, Larson MG, Levy D, et al. Temporal Relations of Atrial Fibrillation and Congestive Heart Failure and Their Joint Influence on Mortality: The Framingham Heart Study. *Circulation.* 2003;107(23):2920-2925.

22. Ball J, Carrington M, McMurray JJV, Stewart S. Atrial fibrillation: Profile and burden of an evolving epidemic in the 21st century. *International Journal of Cardiology.* 2013;167(5):1807-1824.

23. Deloitte Access Economics Pty Ltd. Off beat: Atrial fibrillation and the cost of preventable strokes. 2011.

24. Lake FR, Cullen KJ, de Klerk NH, McCall MG, Rosman DL. Atrial fibrillation and mortality in an elderly population *Australian and New Zealand Journal of Medicine.* 1989;19(4):321-326.

25. Sturm JW, Donnan GA, Davis SM, O'Sullivan JG, Vedadhaghi ME. The Avoid Stroke as Soon as Possible (ASAP) general practice stroke audit. *Medical Journal of Australia.* 2002;176(7):312-316.

26. Stewart S, Carrington MJ, Marwick TH, et al. Impact of home versus clinic-based management of chronic heart failure: the WHICH? (Which Heart Failure Intervention Is Most Cost-Effective & Consumer Friendly in Reducing Hospital Care) multicenter, randomized trial. *J Am Coll Cardiol.* 2012;60(14):1239-1248.

27. The Consensus Trial Study Group. Effects of Enalapril on Mortality in Severe Congestive Heart Failure. *New England Journal of Medicine.* 1987;316(23):1429-1435.

28. Felker GM, Benza RL, Chandler AB, et al. Heart failure etiology and response tomilrinone in decompensated heart failureResults from the OPTIME-CHF study. *Journal of the American College of Cardiology.* 2003;41(6):997-1003.

29. Luong C, Barnes M, Tsang TM. Atrial Fibrillation and Heart Failure: Cause or Effect? *Curr Heart Fail Rep.* 2014/09/26 2014:1-8.

30. Sackett DL, Rosenberg WM, Gray JAM, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *British Medical Journal.* 1996;312:71-72.

31. Greenhalgh T. *How to read a paper: The basics of evidence-based medicine.* 4th ed. Oxford, UK: Wiley-Blackwell; 2010.

32. Gagliardi AR, Legare F, Brouwers MC, et al. Protocol: developing a conceptual framework of patient medicated knowledge translation, systematic review using a realist approach. *Implementation Science.* 2011;6(25).

33. Barry MJ, Edgman-Levitan S. Shared Decision Making — The Pinnacle of Patient-Centered Care. *New England Journal of Medicine.* 2012;366(9):780-781.

34. National Research Council. *Crossing the quality chasm: a new health system for the 21st century.* Washington DC,2001.

35. Ekman I, Swedberg K, Taft C, et al. Person-Centered Care — Ready for Prime Time. *European Journal of Cardiovascular Nursing.* 2011;10(4):248-251.

36. Bauman AE, Fardy HJ, Harris PG. Getting it right: why bother with patient-centred care? *Med J Aust.* 2003;179(5):253-256.

37. Morgan S, Yoder LH. A Concept Analysis of Person-Centered Care. *Journal of Holistic Nursing.* 2012;30(1):6-15.

38. Hoffmann TC, Legare F, Simmons MB, et al. Shared decision making: what do clinicians need to know and why should they bother. *Medical Journal of Australia.* 2014;201(1):35-39.

39. Charles C, Gafni A, Whelan T. Shared decision-making in the medical encounter: What does it mean? (Or it takes at least two to tango). *Soc. Sci. Med.* 1997;44(5):681-692.

40. Ho P, Bryson C, Rumsfeld J. Medication Adherence. *Circulation.* 2009 2009;119(23):3028-3035.

41. World Health Organisation. *Adherence to Long Term Therapies: Evidence for Action.* Geneva, Switzerland: World Health Organisation;2003.

42. Osterberg L, Blaschke T. Adherence to Medication. *New England Journal of Medicine.* 2005;353(5):487-497.

43. Wilson SR, Strub P, Buist AS, et al. Shared Treatment Decision Making Improves Adherence and Outcomes in Poorly Controlled Asthma. *American Journal of Respiratory and Critical Care Medicine.* 2010;181(6):566-577.

44. Hubbard T, McNeill N. *Thinking outside the pillbox: Improving medication adherence and reducing readmissions.* NEHI;2012.

45. Guralnik JM. Assessing the impact of comorbidity in the older population. *Annals of Epidemiology.*6(5):376-380.

46. Wong MCS, Liu J, Zhou S, et al. The association between multimorbidity and poor adherence with cardiovascular medications. *International Journal of Cardiology.*INPRESS

47. Marengoni A, Rizzuto D, Wang H-X, Winblad B, Fratiglioni L. Patterns of Chronic Multimorbidity in the Elderly Population. *Journal of the American Geriatrics Society.* 2009;57(2):225-230.

48. Mangin D, Heath I, Jamoulle M. Beyond diagnosis: rising to the multimorbidity challenge. *BMJ.* 2012;344.

49. Hughes LD, McMurdo MET, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. *Age and Ageing.* 2013;42(1):62-69.

50. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the Concepts of Disability, Frailty, and Comorbidity: Implications for Improved Targeting and Care. *The Journals of Gerontology.* 2004;59A(3):255-263.

51. Uchmanowicz I, Łoboz-Rudnicka M, Szeląg P, Jankowska-Polańska B, Łoboz-Grudzień K. Frailty in Heart Failure. *Curr Heart Fail Rep.* 2014/09/01 2014;11(3):266-273.

52. Perera V, Bajorek BV, Matthews S, Hilmer SN. The impact of frailty on the utilisation of antithrombotic therapy in older patients with atrial fibrillation. *Age and Ageing.* 2009;38:156-162.

53. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GYH. Underuse of Oral Anticoagulants in Atrial Fibrillation: A Systematic Review. *The American Journal of Medicine.* 2010;123:638-645.

54. Appelboam R, Thomas EO. Warfarin and intracranial haemmorhage. *Blood Rev.* 2009;23:1-9.

55. Sjoblom L, Hardemark HG, Lindgren A, et al. Management and prognostic features of intracerebral hemmorhage during anticoagulant therapy: a Swedish multicentre study. *Stroke.* 2001;32:2567-2574.

56. Kiely DK, Adrienne LA, Lipsitz LA. Validation and comparison of 2 frailty indexes: The MOBILIZE Boston Study. *J Am Geriatr Soc.* 2009;57(9):1532-1539.

57. Oosterom-Calo R, van Ballegooijen A, Terwee C, et al. Determinants of adherence to heart failure medication: a systematic literature review. *Heart Failure Reviews.* 2012;18(4):409-427.

58. Davidson PM, Ferguson C. Chapter 25: Management of Patients with Complications for Heart Disease. In: Farrell M, Dempsey J, eds. *Smeltzer and Bare's textbook of medical-surgical nursing. (3rd Australian and New Zealand edition)*. 3rd ed. Sydney: Lippincott Williams & Wilkins; 2014:686-710.

59. Jaarsma T, Strömberg A, Mårtensson J, Dracup K. Development and testing of the European Heart Failure Self-Care Behaviour Scale. *European Journal of Heart Failure.* June 1, 2003 2003;5(3):363-370.

60. Misra S. ACC Anticoag Evaluator app is a great resource for improving AFib care. 2014; http://www.imedicalapps.com/2014/11/acc-anticoag-evaluator-app-great-resource-improving-afib-care/. Accessed 17th Nov, 2014.

61. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus Warfarin in patients with atrial fibrillation. *The New England Journal of Medicine.* 2009;361(12):1139-1151.

62. Department of Health & Ageing. *Issues and Options Paper: Review of Anticoagulation Therapies in Atrial Fibrillation.* Australian Government;2012.

63. Bajorek BV, Krass I, Ogle SJ, Duguid MJ, Shenfield GM. Optimizing the use of antithrombotic therapy for atrial fibrillation in older people: A pharmacist-led multidisciplinary intervention. *Journal of the American Geriatrics Society* 2005;53(11):1912-1920.

64. Bajorek BV, Ogle SJ, Duguid MJ, Shenfield GM, Krass I. Management of warfarin in atrial fibrillation: views of health professionals, older patienst and their carers. *MJA*. 2007;186(4):175-180.

65. Castelino RL, Bajorek BV, Chen TF. Targeting suboptimal prescribing in the elderly: A review of the impact of pharmacy services. *The Annals of Pharmacotherapy*. 2009;43:1096-1106.

66. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Medical Care.* 2005;43:521-530.

67. Krum H, Jelinek MV, Stewart S, Sindone A, Atherton JJ. 2011 Update to National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand. Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006. *MJA*. 2011;194(8):405-409.

68. Grimshaw JM, Russell IT. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *The Lancet.* 1993;342:1317-1322.

69. McEntee M, Cuomo L, Dennison C. Patient-, provider-, and system-level barriers to heart failure care. *Journal of Cardiovascular Nursing.* 2009;24(4):290.

CHAPTER 2: ATRIAL FIBRILLATION: STROKE PREVENTION IN FOCUS

2.1. CHAPTER PREFACE

Publication Reference:

Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. Atrial fibrillation: stroke prevention in focus. *Aust Crit Care.* 2014;27(2):92-98.

Chapter 1 provided a summary of healthcare context and definitions of key concepts. Further, it provided an outline of this thesis, including the study aims, questions design, significance and innovation.

This chapter presents an article in its original form, published in *Australian Critical Care* (2014) Volume 27, Issue 2, Pages 92-98. This article is provided in its published form as an appendix. This review was aimed at the audience of nurses working in the acute care setting. Australian Critical Care is the official journal of the Australian College of Critical Care Nurses.

Background:

Atrial fibrillation (AF) is a common arrhythmia and a risk factor for stroke and other adverse events. Internationally, there have been recent advancements in the therapies available for stroke prevention in AF**.** Nurses will care for individuals with AF across a variety of primary and acute care settings and should be familiar with evidence based therapies.

Aim of the study:

This paper provides a review of the epidemiology of AF and stroke, risk assessment tools and evidence based treatments for the prevention of stroke in AF including the use of novel anti-thrombin agents.

A review of key databases was conducted from 2002 – 2012 using the key search terms '*atrial fibrillation*' *'anticoagulation' 'risk assessment'* and *'clinical management'*. The following electronic databases were searched: CINAHL, Medline, Scopus, the Cochrane Library and Google Scholar. Reference lists were manually hand searched. Key clinical guidelines from National Institute for Clinical Excellence (NICE, UK), American Heart Association (AHA, USA), American College of Cardiology (ACC, USA) and the European Society of Cardiology (ESC) and key government policy documents were also included. Articles were included in the review if they addressed nursing management with a focus on Australia.

Summary of the results:

Many treatment options exist for AF. Best practice guidelines make a variety of recommendations which include cardioversion, ablation, pulmonary vein isolation, pharmacological agents for rate or rhythm control approaches, and antithrombotic therapy (including anticoagulation and antiplatelet therapy). Treatment should be patient-centered and individualised based upon persistency of the rhythm, causal nature, risk and co-morbid conditions.

AF is a common and burdensome condition where treatment is complex and not without risk. Nurses will encounter individuals with AF across a variety of primary and acute care areas understanding the risk of AF and appropriate therapies is important across all care settings. Treatment must be individually tailored to the needs of the patient and balanced with the best available evidence

Implications:

This paper provided a summary of evidence based therapies to prevent stroke in AF. Further, it highlights the need for more holistic approaches to anticoagulation, the need for newer patient-centered, cross-condition models of care, and the lack of a comprehensive multidisciplinary AF management guideline in Australia and New Zealand.

2.2. INTRODUCTION

Atrial fibrillation (AF) is an emergent health concern,[1] described by some as an evolving epidemic.[2] AF is the most commonly occurring cardiac arrhythmia and is a risk factor for stroke. Factors contributing to thrombus formation, include abnormalities of the heart wall, abnormal blood stasis and blood constituents, are described as Virchow's Triad.[3] In AF structural heart disease, stasis of blood within the left appendage and atrium, and abnormalities of coagulation contribute to stroke risk.[3] A patient's stroke risk can be minimised through timely identification and diagnosis of AF and application of evidence-based treatment. Internationally, there have been recent advancements in therapies aimed at reducing stroke. These include novel anticoagulants, surgical procedures and implantable devices.[4-8] These innovative therapies are becoming more common in the Australian healthcare system. Therefore, it is imperative that nurses remain knowledgeable of the available therapies and risk factors for the prevention of stroke in AF.

2.3. AIMS & OBJECTIVES

This paper outlines stroke prediction and bleeding risk assessment tools and provides a review of evidence-based therapies to manage stroke risk in AF.

2.4. METHODS

A review of key databases was conducted from 2002 – 2012 using the key search terms '*atrial fibrillation*' *'anticoagulation' 'risk assessment'* and *'clinical management'*. The following electronic databases were searched: CINAHL, Medline, Scopus and the Cochrane Library. Google Scholar was used to augment the search. Policy documents and clinical evidence based guidelines were also included. Reference lists were manually hand searched. Results were limited to English language and full text documents. Clinical guidelines from National Institute for Clinical Excellence (NICE, UK), American Heart Association (AHA, USA), American College of Cardiology (ACC, USA) and the European Society of Cardiology (ESC) along with key government reports were also included. Articles were included in the review, if they addressed clinical management with a focus on Australia.

2.5. ATRIAL FIBRILLATION

AF is distinguished by chaotic electrical atrial activation and ineffective contraction. It is commonly observed on ECG by the substitution of regular P waves with rapid oscillations or fibrillatory waves that vary in amplitude, shape, and timing, associated with an irregular frequent ventricular response when AV conduction is intact.[9] Cardiac and non-cardiac risk factors for the development of AF including emergent risk factors are summarised in Table 2.1 overleaf.

TABLE 2.1 CARDIAC AND NON-CARDIAC RISK FACTORS FOR THE DEVELOPMENT OF AF

CARDIAC	NON-CARDIAC
• Hypertension • Heart Failure • Valve Disease • Ischaemic Heart Disease • Cardiomyopathy • Cardiac Surgery • Atrial Septal Defects • Ion Channel Disorders • Myocarditis • Pericarditis • Left atrial enlargement • Left ventricular hypertrophy • Congenital defects	• Age • Gender: male • Diabetes • Electrolyte abnormalities • Excessive alcohol intake • Obesity • Smoking • Obstructive sleep apnoea • COPD • Pulmonary embolism • Thyroid dysfunction • Altered metabolism • Autonomic changes • Environmental influences • Excessive caffeine consumption
NOVEL & EMERGENT RISK FACTORS	
• Genetic Influences & Familial History	• Parental history of AF doubled risk of AF in offspring[10]
• Ethnic and Socio-demographic differences	• Blacks appear to be at a lower risk of AF than whites.[11] • European ancestry in African Americans at an increased risk[12] • Increased probability if Caucasian • Increased probability if from a lower socio-economic background
• Excessive endurance sports training[13]	• Athletes may experience any arrhythmia during rest of exercise,[14] however AF is the most common cause of palpitations in athletes.[15] • Possible association between anabolic steroid use and development of AF.[16,17]
• Pericardial Fat	• Pericardial fat is associated with the prevalence of AF.[18]
• Chronic Kidney Disease	• Reduced kidney function and the presence of albumin-urea are strongly associated with the incidence of AF.[19]
• Rheumatoid arthritis	• Increased risk of developing AF.[20]
• Coeliac disease	• Increased risk of developing AF.[21]

2.5.1. DEFINITION AND CLASSIFICATION

AF can be classified as paroxysmal, *recurrent episodes that self-terminate, usually within 48 hours*, persistent, *recurrent episodes that last more than one week*, or permanent, *ongoing AF*. The normal progression of AF is from short, rare episodes increasing in duration to more frequent events and over time, most patients develop sustained episodes of AF.[22] Classification systems aim to provide an easier description of types of AF. The ACC/ AHA/ ESC Guidelines recommend a simplistic scheme for clinical relevance, as detailed in Figure 2.1.

- Paroxysmal AF: Self terminating within 7 days[23]
- Persistent: requiring termination by pharmacological or electrical cardioversion[23]
- Permanent: restoration to normal sinus rhythm is either impossible or unadvisable[23]

Stroke risk is similar with paroxysmal, persistent or permanent AF. Therefore, the selection of antithrombotic prophylaxis should be independent of the rate/ rhythm control strategy.[24]

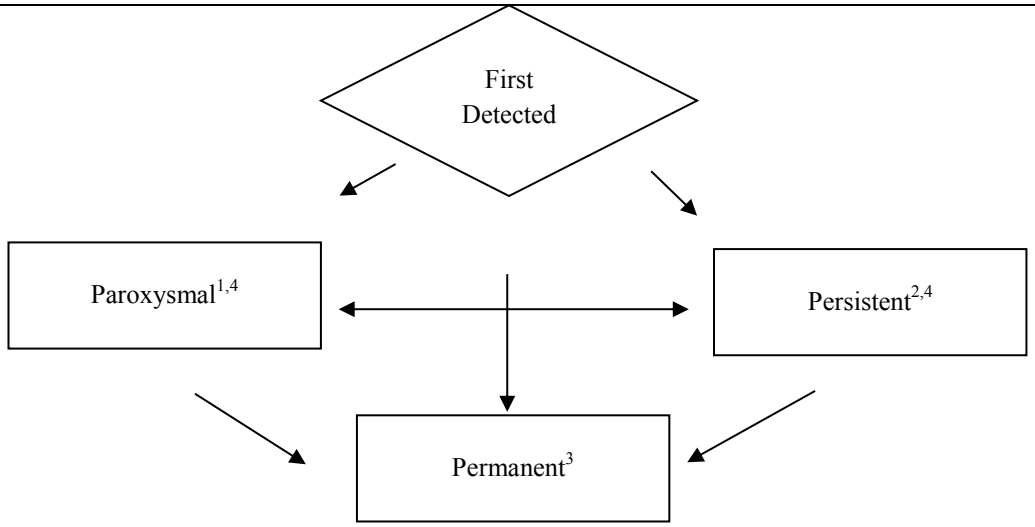

Figure 2.1 - Patterns of AF: (1) Episodes that generally last 7 days or less (most less than 24 hours) (2) episodes that usually last longer than 7 days (3) cardioversion failed or not attempted (4) both paroxysmal and persistent AF may be recurrent.

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Circulation. 2006; 114: e257-e354

FIGURE 2.1 PATTERNS OF AF

2.5.2. *SCREENING AND DIAGNOSIS*

The screening and diagnosis of AF can be problematic. This is due to fluctuations in the presence of signs, particularly in paroxysmal AF many of which can be subtle and silent in nature. Signs and symptoms of AF are summarised in Table 2.2. An opportunistic manual palpation of a patient's radial pulse remains one of the most effective, feasible, and valid ways of checking for heart rate and rhythm irregularity.[25] An ECG recording is gold standard in the diagnosis of AF. Any arrhythmia that has the hallmark characteristics of AF and is 30 seconds in duration on a rhythm strip or long enough to be captured on a 12 lead ECG is considered to be AF.[26]

TABLE 2.2 GENERAL SIGNS AND SYMPTOMS OF AF

General signs and symptoms[27]
• Palpitations • Dyspnoea • Chest pain • Worsening angina • Hypotension • Reduced capacity to exercise • Fatigue • General malaise • Dizziness and light-headedness • Polyuria • Panic attacks • Syncope

2.6. Epidemiology of Atrial Fibrillation and Stroke in Australia

AF affects 1 – 2% of the Australian population (equivalent to 240,000 – 400,000 Australians).[22] It is more commonly seen in the elderly with an estimated prevalence of 8% in people over the age of 80 years.[28] AF reduces an individual's capacity to exercise, and may lead to cognitive dysfunction and reduced quality of life.[29,30] Stroke is a major cause of death and disability and accounts for 9% of all-cause mortality worldwide. 20% of stroke survivors require institutional care after 3 months and 15% to 30% will be permanently disabled.[31,32] This highlights the need for a strong focus on primary stroke prevention.[33] A gradual reduction in mortality from stroke is attributed to the better control of modifiable risk factors, such as AF.[34]

2.7. Stroke Prevention

It is estimated that 20 – 35% of all patients with ischaemic strokes have AF.[35] It is thought to be an aetiological factor in as many as 30% of strokes in the elderly.[36] This equates to 5% of all AF patients developing an embolic stroke every year.[37,38] Patients who experience an ischaemic stroke with AF as an existing condition are known to have substantially worse outcomes than patients without AF.[35] This may be due to increasing age and the greater likelihood of other co-morbidities.[35] The risk of stroke was 5.6 times greater in patients with AF than that in comparably aged patients in sinus rhythm in the Framingham Cohort Study.[39] Predicting and treating the risk of stroke with definitive therapies, including antithrombotic therapies, is highly justified and recommended by best practice guidelines[33,40,41] and should be individually tailored, based on comorbidities and contraindications.[9,42-44]

2.8. HOSPITALISATIONS

The burden of AF-related hospitalisation is set to increase rapidly over the next decade with the growing ageing population.[23,45] The prevalence of cardiovascular disease is likely to increase at least three-fold by 2050.[46] A large proportion of hospitalisations for arrhythmia are due to AF.[47] Wong and colleagues reported a 203% increase in the number of AF related hospitalisations in Australia between 1993 to 2007.[1] This may be largely due to technological advances and the increased availability and utilisation of hospital based therapies, such as electrical cardioversion, ablation and insertion of left atrial appendage closure devices.[48]

2.9. STROKE AND BLEEDING RISK ASSESSMENT TOOLS

Risk assessment tools are intended to guide clinical decision making in the allocation of thromboprophylactic therapies and are based on the evidence that certain risk factors increase the likelihood of clinical events.[49] Several risk stratification schemes have been established with the aim to quantify the risk of stroke in individual patients with AF and are summarised in Table 2.3.[38,50-53] The tool known as the Congestive heart failure, Hypertension, Age > 75 years, Diabetes and prior Stroke or TIA ($CHADS_2$) is a simple and well-validated tool. It allocates 1 point for a history of congestive heart failure, hypertension, age >75, or diabetes and 2 points for a history of stroke or TIA. Patients with 2 or more points on this scheme are predicted to have an annual stroke risk of over 4%, while those with no points have a predicted annual risk of less than 1 to 2%.[50] A score of 0 identifies patients at low stroke risk, a score of 1 to 2 identified patients at moderate stroke risk, and a score greater than 2 identified patients at high stroke risk.[50,54] It uses well-established independent stroke risk factors to assess patient risk.[55] The CHA_2DS_2-VASc scheme includes scoring categories for vascular disease, age between 65 – 74 years and sex, and provides greater sensitivity to predict thromboembolism than the original $CHADS_2$ score.[56]

Risk scores are used to estimate the absolute risk of an adverse event, which is helpful when advising patients and making complex treatment decisions.[57] However, these are limited within the context of complex cardiogeriatric syndromes as such models fail to consider frailty, cognitive and functional decline or non-adherence to therapy.[44] There is need to expand such risk prediction models to include a combination of these factors.[44] As part of a comprehensive patient assessment and prior to the commencement of oral anticoagulation it is important to undertake a bleeding risk assessment.[49] The HAS-BLED (Hypertension, Abnormal renal/ liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly (>65), Drugs/ alcohol concomitantly) bleeding risk score is a simple yet well-validated risk assessment tool, where a score of more than or equal to 3 indicates 'high risk'.[58] (Refer to Table 2.4). Treatment should be balanced within the context of the patient's individual circumstances, best available evidence, and clinical expertise.[59]

2.10. TREATMENT AND MANAGEMENT OF ATRIAL FIBRILLATION

Therapeutic recommendations include pharmacological management, electrical cardioversion, ablation, pulmonary vein isolation, pharmacological agents for rate or rhythm control approaches, and antithrombotic therapy including anticoagulation and antiplatelet therapy.[9,40] Treatment is dependent upon persistency of the rhythm, causal nature, risk and co-morbid conditions.[40] A range of pharmacotherapies used to prevent stroke in AF are summarised in Table 2.5.

TABLE 2.3 STROKE RISK STRATIFICATION SCHEMATA

SPAF (Stroke Prevention in Atrial Fibrillation) Acronym			
Age, female sex, diabetes, previous stroke or TIA, hypertension, or elevated systolic BP			
Framingham Tool			
Age, gender, systolic blood pressure, diabetes and prior stroke or TIA			
$CHADS_2$ Acronym [50]	**Score**	**$CHADS_2$ Score**	**Adjusted Stroke Rate (%/year)**[49]
Congestive heart failure	1	0	1.9%
Hypertension	1	1	2.8%
Aged ≥75 yrs	1	2	4.0%
Diabetes mellitus	1	3	5.9%
Stroke/ TIA	2	4	8.5%
Max Score	6	5	12.5%
		6	18.2%
CHA_2DS_2-VASc Acronym [60]	**Score**	**CHA_2DS_2-VASc Score**	**Adjusted Stroke Rate (%/year)** [49]
Congestive heart failure/ LV dysfunction	1	0	0%
Hypertension	1	1	0.7%
Aged ≥75years	2	2	1.9%
Diabetes mellitus	1	3	4.7%
Stroke/ TIA/ TE	2	4	2.3%
Vascular disease (prior to MI, PAD or aortic plaque)	1	5	3.9%
Aged 65-74 years	1	6	4.5%
Sex **c**ategory (ie. Female gender)	1	7	10.1%
Max Score	10	8	14.2%
		9	100%

Reference: Lip YHG (2011) Implications of the CHA2DS2-VASc and HAS-BLED Scores for Thromboprophylaxis in Atrial Fibrillation [49]

TABLE 2.4 THE HAS-BLED SCORE

ACRONYM	SCORING
Hypertension	1 point
Abnormal liver or kidney function	1 point each
Stroke	1 point
Bleeding	1 point
Labile INRs	1 point
Elderly	1 point
Drugs or alcohol	1 point each

Notes:
Hypertension = Systolic Blood Pressure > 160mmHg
Abnormal renal function = dialysis/ renal transplantion/ serum creatinine >200mmol/L
Abnormal liver function = chronic hepatic dysfunction (eg cirrhosis) or biochemical evidence of significant hepatic derangement (eg bilirubin 2 x upper limit of normal in association with aspartate aminotransferase/ alanine aminotransferase/ alkaline phosphatase 3 x upper limit normal etc)
Bleeding = history of bleeding or a bleeding diathesis
Drugs = concomitant use of antiplatelet or non-steroidal anti-inflammatory agent

TABLE 2.5 RECOMMENDED PHARMACOLOGICAL AGENTS FOR STROKE PREVENTION IN AF

DRUG	CLASS	INDICATION(S)	PHARMACOKINETICS ACTION	CONSIDERATIONS
Warfarin	Anticoagulant Vitamin K antagonist	Prevention and management of thromboembolism in AF for high risk patients	Suppresses the vitamin-k dependent synthesis of prothrombin and factors VII, IX and X in the liver Narrow therapeutic range	Requires frequent checking of INR to maintain time within therapeutic range Use can be burdensome
Dabigatran	Anticoagulant Direct thrombin inhibitor	Prevention of stroke or systemic embolism in patients with non valvular AF at moderate to high risk of stroke	Novel anticoagulant A potent direct competitive inhibitor of thrombin. Excreted by the kidneys. Serum half life is 14 – 17 hours.	Requires less invasive and close serum coagulation level monitoring than warfarin Concerns regarding a lack of an effective reversal agent
Rivaroxaban	Anticoagulant direct oral activated factor Xa inhibitor	Prevention of stroke or systemic embolism in patients with non valvular AF at moderate to high risk of stroke	Novel anticoagulant Oral factor Xa inhibitor Serum half life is 5 to 9 hours	Requires less invasive and close serum coagulation level monitoring than warfarin Concerns regarding a lack of an effective reversal agent
Apixaban	Anticoagulant direct oral activated factor Xa inhibitors	Prevention of stroke or systemic embolism in patients with non valvular AF at moderate to high risk of stroke	Novel anticoagulant Oral factor Xa inhibitor	Not yet licensed in Australia for stroke prevention in AF
Clopidogrel	Antiplatelet	Prevention of vascular ischaemic associated with atherothrombotic events Prevention and management of thromboembolism in AF for low risk patients or those deemed unsuitable for traditional warfarin therapy	Inhibits platelet aggregation by irreversibly binding to ADP platelet receptors	May alter metabolism of warfarin Caution if administered with warfarin as may increase risk of bleeding
Aspirin	Antiplatelet	Prevention and management of thromboembolism in AF for low risk patients or those deemed unsuitable for traditional warfarin therapy	Inhibits thrombus formation by decreased platelet aggregation Antiplatelet due to the non-competitive inhibition of cyclo-oxygenase, which is needed for thromboxane synthesis	Advise to take with food Risk of GI complications with long term usage

2.10.1. PHARMACOLOGICAL INTERVENTIONS TO PREVENT STROKE IN AF

Warfarin

Warfarin is the first line pharmacotherapy for thromboprophylaxis[61] and reduces relative risk of recurrent stroke in patients with TIA or minor stroke by approximately 70% (hazard ratio 0.34, 95% CI 0.20–0.57)[62] Bleeding is a common risk with warfarin therapy. Poor treatment adherence, drug or diet interactions or the inconvenience of INR monitoring are causal factors of adverse events including haemorrhage and stroke. Warfarin requirements may be different according to a range of factors, such as; genetic factors, ethnicity, and cultural differences including food preferences.[63] The major concerns with warfarin therapy are the potential for catastrophic haemorrhage, predominantly intracranial haemorrhage which may lead to increased morbidity and mortality.[64-66] The optimal target therapeutic range for INR is between 2 and 3 for stroke prevention in AF.[67] A higher therapeutic range may be aimed for in patients with prosthetic heart valves or mitral heart disease.[68] Patients should maximise their time spent in their target range INR.[69,70] The relative contraindications to warfarin therapy include a past medical history of peptic ulcer disease, concomitant use of non-steroidal anti-inflammatory drugs, or advanced age (>85 years). Absolute contraindications to therapy include recent intracranial haemorrhage, cirrhotic liver disease, or advanced malignancy.[71] The burden of monitoring, and unpredictable pharmacokinetics of warfarin have prompted the search for more efficacious agents. [61]

Novel Oral Anticoagulants

Dabigatran is a novel oral direct thrombin inhibitor. Clinical trials have demonstrated that when given at a dose of 110mg, it leads to lower rates of stroke when compared with warfarin.[4] Dabigatran was successfully listed on the Pharmaceutical Benefits Scheme in 2011 for stroke prevention in AF. However, considerable fears still exist amongst clinicians pertaining to the risk of bleeding.[72] The Therapeutic Goods Administration has announced a safety advisory notice regarding risk of bleeding with associated use.[73] Apixaban and rivaroxaban are both direct oral factor Xa inhibitors that are superior to warfarin in preventing strokes. Rivaroxaban is noted to have less frequent intracranial and fatal bleeding occurrence, whilst apixaban causes less bleeding and results in a lower mortality.[5,6] Apixaban is not yet licensed for use in stroke prevention for AF patients in Australia. Rivaroxaban was registered with the TGA in April 2012 in Australia for use in the prevention of stroke in patients with non-valvular AF and at least one additional risk factor for stroke.[74] The advantages these novel anticoagulants have over warfarin is that they have predictable pharmacokinetics and eliminate the burden of routine anticoagulation monitoring. A recent meta-analysis comparing the efficacy of new anticoagulants, including apixaban, dabigatran and rivaroxaban to warfarin therapy established that treatment with all three new anticoagulants was associated with lower risks of intracranial haemorrhage (RR 0.49, 95% CI 0.36 to 0.66) and appear to have a favourable safety profile.[75] Yet clinicians remain apprehensive prescribing novel anticoagulants due to the unavailability of any clinically proven reversal agent.[72] Recombinant factor VIIa, invasive renal dialysis or charcoal haemofiltration are highlighted as possible reversal strategies.[76] However such measures are expensive and may not be readily available.[72]

Rate and Rhythm Control

Ventricular rate control is a key aim in the management of AF. The aim is to maintain a ventricular rate within a haemodynamically acceptable range even though the atria continue to fibrillate. Ventricular rate is often controlled by treatment with betablockers, non-dihydropyridine calcium channel antagonists or digoxin. The selection of any rate control therapy should consider the pharmacological impact on any pre-existing comorbidities including hypertension, ischaemic heart disease and chronic heart failure.[77] Rhythm control aims to restore and maintain normal sinus rhythm. This process is referred to as cardioversion and there are 2 treatment types; pharmacological and non-pharmacological. Pharmacological therapies include amiodarone, sotalol, flecainide and dronedarone.

The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial was a large multicentre RCT that compared cardioversion and adjunct use of anti-arrhythmic drugs verses rate controlling drugs. The investigators found that there was an increased risk of stroke in the rhythm control group. In addition, the rhythm control group were significantly at an increased risk of being hospitalised and developing adverse drug effects than those in the rate control group.[78]

2.10.2. NON PHARMACOLOGICAL INTERVENTIONS TO TREAT AF

Electrical cardioversion

Cardioversion aims to revert the arrhythmia back to normal sinus rhythm and therefore increase cardiac performance and lower the risk of stroke and should be considered as a first line treatment in all patients with AF.[79] Cardioversion is performed through a synchronous direct electric current discharge via an external cardioversion with a goal to repolarise the errant atrial conduction and to restore ordered conduction.[79] Success rates are influenced by any underlying aetiologies and vary between 20 - 90%.

Catheter ablation

Catheter ablation is routinely performed for patients with symptomatic AF.[7] It is normally reserved for those patients who are symptomatic despite treatment for both rate and rhythm control.[26] The procedure involves electrical isolation of the pulmonary veins through the application of radiofrequency ablation.[80] Success rates are dependent on variables, such as duration of AF, the presence of comorbidities including obesity and sleep apnoea and the duration of follow-up.[7] Ablation is primarily effective in reducing the recurrences of AF,[81] however multiple attempts of the procedure may be required for success in treatment.[82] The evidence demonstrates that catheter ablation is more effective than anti-arrhythmic drug therapy in controlling AF and may lead to improved quality of life.[7] The equipment and technical procedures used to perform ablation continues to rapidly evolve.[7]

Left atrial appendage (LAA) closure

Embolic stroke in patients with non-valvular AF is often associated with left atrial appendage thrombi.[8] It is estimated that up to 90% of thrombi in patients with non-valvular AF originate from the LAA.[83] Percutaneous closure devices are non-inferior to treatment with oral warfarin therapy and that it may be an effective alternative to anticoagulation.[8] The WATCHMAN© device is a self-expanding nickel titanium frame structure with fixation barbs and a permeable polyester fabric cover. It is implanted via a trans-septal approach by use of a catheter-based delivery system to seal the ostium of the LAA.[8] The main benefit to implantation is the cessation of any oral anticoagulant therapy shortly after implant thus eliminating the need for burdensome monitoring and associated coagulopathic complications. Whilst this device shows particular promise in clinical trials and practice overseas, it is not yet available on PBS in Australia and not yet registered as a prosthetic implant with many private health insurance companies.[84] It is important to highlight that such devices are in the very early stages of implantation in Australia and further investigation into the long-term efficacy and safety is warranted.

2.11. LIFESTYLE ADVICE AND PATIENT EDUCATION

Patient education is essential to ensure optimal adherence to any prescribed pharmacological therapy. A patient's knowledge of therapy is often a determinant of adherence, and has consequential effects to anticoagulant control and a lack of perception of the importance of medications.[85] A lack of awareness of risk-to-benefit threshold may cause altered coagulation and ultimately lead to adverse events.[85] Patient education is challenging due to AF primarily affecting the older population, where functional and cognitive impairment are common. Educational interventions must take account of this complexity and be individualised to meet the patient's needs.

2.12. FUTURE RESEARCH

Additional research is required in Australia to advance healthcare that is available for AF patients in the 21st century. The burden of AF is set to increase with the burgeoning ageing population. AF often coexists with concomitant cardiovascular conditions and future research needs to take account of such complexity. Attention should be drawn to the need for newer cross-condition models of AF care, and the need for more holistic approaches to stroke risk assessment. Of considerable note is Australia's lack of a comprehensive accessible multi-disciplinary evidence based guideline for the management of AF. Such evidence based guidelines that are similar to that of the European Society of Cardiology in Europe, the American Heart Association in the US and the National Institute of Clinical Excellence in the UK are well overdue to assist health professionals with bedside decision-making.

2.13. CONCLUSION

AF is a common and burdensome condition where treatment is complex and not without risk. Nurses will encounter individuals with AF across a variety of primary and acute care areas. Therefore understanding the risk of AF and appropriate therapies is important across all care settings. Treatment must be individually tailored to the needs of the patient and balanced with the best available evidence.

2.14. REFERENCES

1. Wong CX, Brooks AG, Leong DP, Roberts-Thomson KC, Sanders P. The increasing burden of atrial fibrillation compared with heart failure and myocardial infarction: A 15 year study of all hospitalisations in Australia. *Archives of Internal Medicine.* 2012;172(9):739-740.

2. Ball J, Carrington M, McMurray JJV, Stewart S. Atrial fibrillation: Profile and burden of an evolving epidemic in the 21st century. *International Journal of Cardiology.* 2013;IN PRESS(XX):XX

3. Lip GYH, Lim HS. Atrial fibrillation and stroke prevention. *Lancet.* 2007;6:981-993.

4. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus Warfarin in patients with atrial fibrillation. *The New England Journal of Medicine.* 2009;361(12):1139-1151.

5. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *The New England Journal of Medicine.* 2011;365(10):883-891.

6. Granger CB, Alexander JH, McMurray JJV, et al. Apixaban versus Warfarin in patients with Atrial Fibrillation. *The New England Journal of Medicine.* 2011;365(11):981-992.

7. Calkins H. Catheter ablation to maintain sinus rhythm *Circulation.* 2012;125:1439-1445.

8. Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. *The Lancet.* 2009;374(9689):534-542.

9. Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation. *Circulation.* 2006;114(7):e257-e354.

10. Lubitz SA, Yin X, Fontes JD, et al. Association Between Familial Atrial Fibrillation and Risk of New-Onset Atrial Fibrillation. *JAMA.* 2010;304(20):2263-2269.

11. Borzecki A, Bridgers D, Liebscutz J, Kader B, Kazis L, Berlowitz D. Racial differences in the prevalence of atrial fibrillation among males. *J Natl Med Assoc.* 2008;100:237-245.

12. Marcus G, Alonso A, Peralta C, et al. European ancestry as a risk factor for atrial fibrillation in African Americans. *Circulation.* 2010;122:2009-2015.

13. Schoonderwoerd BA, Smit MD, Pen L, Van Gelder IC. New risk factors for atrial fibrillation: causes of 'not-so-lone atrial fibrillation'. *Europace.* 2008;10(6):668-673.

14. Coelho A, Palileo E, Ashley A, Swiryn S, Petropoulos A, Welch W. Tachyarrythmias in young athletes. *J Am Coll Cardiol.* 1986;7:237-243.

15. Furanello F, Bertoldi A, Dallago M, et al. Atrial fibrillation in elite athletes. *J Cardiovasc Electophysiol.* 1998;9.

16. Sullivan M, Martinez C, Gallagher E. Atrial fibrillation and anabolic steriods. *J Emerg Med.* 1999;17:851-857.

17. Lau D, Stiles M, John B, Shahidhar, Young G, Sanders P. Atrial filbrillation and anabolic steriod use. *Int J Cardiol.* 2007;117.

18. Thanassoulis G, Massaro J, O'Donnell C, et al. Pericardial fat is associated with prevalent atrial fibrillation. *Circ Arrhthm Electrophysiol.* 2010;3:345-350.

19. Baber U, Howard V, Halperin J, et al. Association of chronic kidmey disease with atrial fibrillation among adults in the United States: reasons for geopraphic and racial differences in stroke (REGARDS) study. *Circ Arrhthm Electrophysiol.* 2011;4:26-32.

20. Lindhardsen J, Ahlehoff O, Gislason G, et al. Risk of atrial fibrillation and stroke in rheumatoid arthritis: Danish nationawide cohort study. *BMJ.* 2012;344.

21. Emilsson L, Smith J, West J, Melander O, Ludvigsson J. Increased risk of atrial fibrillation in patients with coeliac disease: a nationwide cohort study. *European Heart Journal.* 2011;32(19):2340-2437.

22. Department of Health and Ageing. *Review of Anticoagulation Therapies in Atrial Fibrillation* Canberra, Australia: Australian Government;2012.

23. Iwasaki Y, Nishida K, Kato T, Nattel S. Atrial Fibrillation Pathophysioloy: Implications for Management. *Circulation.* 2011;124:2264-2274.

24. Medi C, Hankey GJ, Freedman SB. Stroke risk and antithrombotic strategies in atrial fibrillation. *Stroke.* 2010;41:2705-2713.

25. Lip GYH, Tse H. Management of atrial fibrillation. *Lancet.* 2007;370:604-618.

26. Camm AJ, Kirchhof P, Lip G, et al. Guidelines for the management of atrial fibrillation: the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC). *European Heart Journal.* 2010;31(19):2369-2429.

27. Bloe C. Atrial fibrillation and primary stroke prevention. *Nursing Standard.* 2011;26(6):49-57.

28. Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). *The American Journal of Cardiology.* 1994;74(3):236-241.

29. Smit MD, VanGelder IC. New treatment options for atrial fibrillation: towards patient tailored therapy. *Heart.* 2011;97:1796-1802.

30. Marzona I, O'Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with atrial fibrillation: results of the ONTARGET and TRANSCEND studies. *Canadian Medical Association Journal.* 2012.

31. Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S. Guidelines for the primary prevention of stroke: A guidelines for healthcare professionals from the American Heart Association/ American Stroke Association. *Stroke* 2011;42:517-584.

32. Lloyd-Jones D, Adams J, Brown TM. Heart Disease and Stroke Statistics – 2010 Update. *Circulation.* 2010;121(e46-215).

33. National Stroke Foundation Australia. Clinical Guidelines for Acute Stroke Management. *National Stroke Foundation.* 2007.

34. Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. *Lancet.* 2008;371:1612-1623.

35. Gattellari M, Goumas C, Aitken R, Worthington JM. Outcomes for patients with Ischameic Stroke and Atrial Fibrillation: The PRIMS Study (A Program of Research Informing Stroke Management). *Cerebrovascular Diseases.* 2011;32(370-382).

36. Kannel WB, Wolf PA, McGee DL, Dawber TR, McNamara P, Castelli WP. Systolic Blood Pressure, Arterial Rigidity, and Risk of Stroke: The Framingham Study. *JAMA.* 1981;245(12):1225-1229.

37. Go AS, Hylek EM, Phillips JA. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: The AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA.* 2001;285:2370-2375.

38. Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation: analysis of pooled data from five randomized controlled trials. *Archives of Internal Medicine* 1994;154(13):1449-1457.

39. Ezekowitz MD, Levine JA. Preventing stroke in patients with atrial fibrillation. *JAMA.* 1999;281:1830-1835.

40. National Institute for Clinical Excellence. Atrial Fibrillation. The management of atrial fibrillation. *National Institute for Clinical Excellence.* 2006.

41. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/ AHA/ HRS Focused Update on the Management of Patients with Atrial Fibrillation: A report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;1234:104-123.

42. VanStaa TP, Setakis E, DiTanna GL, Lane DA, Lip GYH. A comparison of risk stratification schemes for stroke in 79844 atrial fibrillation patients in general practice. *Journal of Thrombosis and Haemostasis.* 2011;9:39-48.

43. Singer DE, Albers GW, Dalen JE, et al. Antithrombotic therapy in Atrial Fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Ed). *Chest.* 2008;133:546S-592S.

44. Ferguson C, Inglis S, Newton P, Middleton S, Macdonald P, Davidson P. Atrial fibrillation and thromboprophylaxis in heart failure: the need for patient-centrered approaches to address adherence. *Vascular Health & Risk Management.* 2013;9:1-9.

45. Stewart S. Epidemiology and Economic Impact of Atrial Fibrillation. *Journal of Cardiovascular Nursing.* 2004;19(2):94-102.

46. Savelieva I, Camm J. Update on Atrial Fibrillation: Part I. *Clinical Cardiology.* 2008;31(2):55-62.

47. Bialy D, Lehmann M, Schumacher D, Steinman R, Meisser M. Hospitalization for arrhythmias in the United States: importance of atrial fibrillation. *J Am Coll Cardiol.* 1992;19.

48. Miyasaka Y, Barnes M, Gersh B, et al. Changing trends of hospital utilisation in patients after their first episode of atrial fibrillation. *Am J Cardiology.* 2008;102:568-572.

49. Lip GYH. Implications of the CHA2DS2-VASc and HAS-BLED scores for thromboprophylaxis in atrial fibrillation. *The American Journal of Medicine.* 2011;124:111-114.

50. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke. *The Journal of the American Medical Association.* 2001;285(22):2864-2870.

51. Albers GW, Dalen JE, Laupacis A, Manning WJ, Petersen P, Singer DE. Antithrombotic therapy in atrial fibrillation *Chest.* 2001;119(1):s194-206.

52. Stroke Prevention In Atrial Fibrillation Investigators. Risk factors for thromboembolism during aspirin therapy in patients with atrial fibrillation: The Stroke Prevention in Atrial Fibrillation Study. *J Stroke Cerebrovasc Dis.* 1995;5:147-157.

53. Healey JS, Hart RG, Pogue J, et al. Risks and benefits of oral anticoagulation compared with clopidogrel plus aspirin in patients with atrial fibrillation according to stroke risk: The Atrial fibrillation Clopidogrel Trial with Irbestartan for preventiong of Vascular Events (ACTIVE-W). *Stroke.* 2008;39:1482-1486.

54. Lip GYH, Halperin JL. Improving stroke risk stratification in atrial fibrillation. *The American Journal of Medicine.* 2010;123:484-488.

55. Waldo AL. Anticoagulation: Stroke prevention in patients with atrial fibrillation. *Cardiology Clinics.* 2009;27:125-135.

56. Boriani G, Botto GL, Padeletti L, et al. Improving Stroke Risk Stratification Using the CHADS2 and CHA2DS2VASc Risk Scores in Patients With Paroxysmal Atrial Fibrillation by Continuous Arrhythmia Burden Monitoring. *Stroke* 2011;42:1768-1770.

57. Wang TJ, Massaro JM, Levy D, et al. A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community. *The Journal of the American Medical Association* 2003;290(8):1049-1056.

58. Lip GYH, Banerjee A, Lagrenade I, Lane DA, Taillandier S, Fauchier L. Assessing the Risk of Bleeding in Patients With Atrial Fibrillation / Clinical Perspective. *Circulation: Arrhythmia and Electrophysiology.* 2012;5(5):941-948.

59. Sackett DL, Rosenberg WM, J A Muir Gray, Haynes RB, W Scott Richardson. Evidence based medicine: what it is and what it isn't *British Medical Journal* 1996;312:71-72.

60. Lip GYH, Nieuwlatt R, Pisters R, Lane DA, Crijns HJGM. Refining clinical risk stratification for predicted stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: The Euro Heart Survey on Atrial Fibrillation. *Chest.* 2010;137:263-272.

61. Chaudhari D, Bhuriya R, Arora R. Newer Anticoagulants as an Alternate to Warfarin in Atrial Fibrillation: A Changing Paradigm. *American Journal of Therapeautics.* 2011;18:e1-e11.

62. EAFT Study Group. Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. *Lancet.* 1993;342(8882):1255-1262.

63. Lee BH, Park JS, Park JH, et al. The effect and safety of the antithrombotic therapies in patients with atrial fibrillation and CHADS2 score 1. *Journal of Cardiovascular Electrophysiology.* 2010;21(5):501-507.

64. Appelboam R, Thomas EO. Warfarin and intracranial haemmorhage. *Blood Reviews* 2009;23:1-9.

65. Sjoblom L, Hardemark HG, Lindgren A, et al. Management and prognostic features of intracerebral hemmorhage during anticoagulant therapy: a Swedish multicentre study. *Stroke.* 2001;32:2567-2574.

66. Gattellari M, Worthington J, Zwar N, Middleton S. Barriers to the use of anticoagulation for nonvalvular atrial fibrillation. *Stroke.* 2008;39:227-230.

67. Hylek EM, Singer DE. Risk Factors for Intracranial Hemorrhage in Outpatients Taking Warfarin. *Annals of Internal Medicine.* 1994;120:897-902.

68. Samardhi H, Santos M, Denman R, Walters DL, Bett N. Current management of atrial fibrillation. *Australian Prescriber.* 2011;34(4):100-104.

69. Stroke Prevention In Atrial Fibrillation Investigators. Bleeding During Antithrombotic Therapy in Patients With Atrial Fibrillation. *Archives of Internal Medicine.* 1996;156(4):409-416.

70. Connolly SJ, Laupacis A, Gent M, Roberts RS, Cairns JA, Joyner C. Canadian atrial fibrillation anticoagulation (CAFA) study. *Journal of the American College of Cardiology.* 1991;18(2):349-355.

71. Kistler PM, Habersberger J. Managment of atrial fibrillation. *Australian Family Physician.* 2007;36(7):506-511.

72. Department of Health & Ageing. *Issues and Options Paper: Review of Anticoagulation Therapies in Atrial Fibrillation.* Australian Government;2012.

73. Department of Health & Ageing. Dabigatran (Paradaxa): risk of bleeding related to use. November 2011; 14th Feb 2012. Available at: http://www.tga.gov.au/safety/alerts-medicine-dabigatran-111005.htm. Accessed 9th March 2012,.

74. Department of Health & Ageing. Public Summary Document by Meeting: Rivaroxaban 2012; http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-psd-rivaroxaban-march12.

75. Miller CS, Grandi SM, Shimony A, Filion KB, Eisenberg MJ. Meta-analysis of efficacy and safety of new oral anticoagulants (dabigatran, rivaroxaban, apixaban) versus warfarin in patients with atrial fibrillation. *The American Journal of Cardiology.* 2012;IN PRESS(xx):xx.

76. vanRyn J, Stangier J, Haertter S, et al. Dabigatran etexilate - a novel reversible, oral direct thrombin inhibitor: Interpretation of coagulation assays and reversal of anticoagulant activity. *Thromb Haemost.* 2010;103:1116-1127.

77. Eagle KA, Cannom DS, Garcia DA. Management of atrial fibrillation: translating clinical trial data into clinical practice. *The American Journal of Medicine.* 2011;124:4-14.

78. Wyse D, Waldo A, DiMarco J, et al, For the AFFIRM Study Investigators. A comparision of rate control and rhythm control in patients with atrial fibrillation. *New England Journal of Medicine.* 2002;347(23):1825-1833.

79. Lip GY. Cardioversion of atrial fibrillation. *Postgraduate Medical Journal.* 1995;71(838):457-465.

80. Medi C, Hankey GJ, Freedman SB. Atrial Fibrillation: Clinical Update *MJA.* 2007;186(4):197-202.

81. Calkins H, Reynolds M, Spector P, et al. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. *Circ Arrhthm Electrophysiol.* 2009;2:349-361.

82. Cappato R, Calkins H, Chen S-A, et al. Worldwide Survey on the Methods, Efficacy, and Safety of Catheter Ablation for Human Atrial Fibrillation. *Circulation.* 2005;111(9):1100-1105.

83. Blackshear J, Odell J. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. *Ann Thorac Surg.* 1996;61:755-759.

84. Department of Health & Ageing. Private Health Insurance - Prostheses List 2012; http://www.health.gov.au/internet/main/publishing.nsf/content/health-privatehealth-prostheseslist.htm. Accessed 30th April 2012.

85. Brophy MT, Snyder KE, Gaehde S, Ives C, Gagnon D, Fiore LD. Anticoagulant Use for Atrial Fibrillation in the Elderly. *Journal of the American Geriatrics Society.* 2004;52(7):1151-1156.

CHAPTER 3: ATRIAL FIBRILLATION AND THROMBOPROPHYLAXIS IN HEART FAILURE: THE NEED FOR PATIENT-CENTERED APPROACHES TO ADDRESS ADHERENCE

3.1. CHAPTER PREFACE

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Ferguson C, Inglis S, Newton P, Middleton S, Macdonald P, Davidson P. Atrial fibrillation and thromboprophylaxis in heart failure: the need for patient-centrered approaches to address adherence. *Vascular Health & Risk Management.* 2013;9:3-11.

Chapter 2 provided an overview of the epidemiology, risk stratification schemata, and pharmacological and non-pharmacological treatment options for the prevention of stroke in AF. This chapter reports on patient centered approaches to thromboprophylaxis to optimise adherence to prescribed regimes.

This chapter presents an article in its original form, published in *Vascular Health & Risk Management* (2013) Volume 9, Pages 3 – 11. This article is provided in its published form as an appendix.

Background:

Atrial fibrillation is a common arrhythmia in chronic heart failure and a risk factor for stroke. Risk assessment tools can assist clinicians with decision making in the allocation of thromboprophylaxis.

Aim of the study:

This review provides an overview of current validated risk assessment tools for atrial fibrillation and emphasizes the importance of addressing both tailoring individual risk for stroke and weighing the benefits of treatment. Further, this review provides details of innovative and patient-centered methods for ensuring optimal adherence to prescribed therapy.

Summary of the results:

This paper adopts a solution focused approach, framed within the WHOs Multidimensional Adherence Model.[28] It provides potential solutions to barriers including; health system related; treatment-related; socio-economic; patient-related; and condition related factors. There is a strong focus on patient-centered interventions and approaches to optimise adherence with an anticoagulation treatment regime. Prior to initiating oral anticoagulant therapy, a comprehensive risk assessment should include evaluation of associated cardiogeriatric conditions, potential for adherence to prescribed therapy, frailty, and functional and cognitive ability.

Implications:

This paper emphasizes that whilst stroke and prediction tools (such as the CHA_2DS_2VASc and HAS-BLED) are highly useful in practice, these should be used with caution by clinicians and not in isolation to guide treatment decisions. Secondly, this paper emphasizes the need for a patient-centered approach to address potential barriers to anticoagulation for stroke prevention. Lastly, it advocates a solution focused approach to address potential barriers may be helpful in improving adherence.

3.2. INTRODUCTION

Heart failure (HF) is a complex and primarily cardiogeriatric syndrome.[1] One-third of patients with HF are likely to have atrial fibrillation (AF) as a concomitant condition.[2] AF is a predictor of stroke in patients with HF.[3] Therefore, predicting and treating the risk of stroke with definitive therapies, including antithrombotics, is highly justified and recommended by best practice guidelines.[4–6] Yet, commonly these therapies are not applied in practice.[7] Under 70% of estimated eligible patients receive anticoagulation therapy.[7]

Although the use of anticoagulants has increased in the past two decades,[8] those individuals considered to be at an increased risk of bleeding are less likely to be prescribed anticoagulation therapy.[8] As a consequence, patients may not be receiving therapy based purely upon their predicted stroke risk alone. Many factors contribute to clinical decision making amongst physicians that influence prescription.[9,10] Factors such as cognitive impairment and frailty are common reasons for clinicians choosing not to prescribe thromboprophylaxis.[11,12]

This is a clinical conundrum for health professionals in prescribing evidence-based therapy and deciding if the risk of treatment outweighs the risk of nontreatment.[13] The Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) trial compared dose-adjusted warfarin with 75 mg aspirin in elderly patients over 75 years. The investigators found that warfarin was associated with a significant reduction in stroke with no difference in the risk of significant hemorrhage.[14] However, the Warfarin and Aspirin in Patients with Heart Failure and Sinus Rhythm (WARCEF) study,[15] although conducted in people in sinus rhythm and not AF, showed that the benefit of warfarin in reducing ischemic stroke was offset by an increased risk of major hemorrhage.[15] Underpinning the choice to prescribe thromboprophylaxis should be one that is individualised to the risk of the patient.

This review provides a critique of current risk assessment tools for the evaluation of stroke and bleeding risk in AF. Further, it identifies the need to extend these assessments to factors that impact treatment adherence and to consider risks for adverse events, particularly bleeding. Strategies for promoting adherence to prescribed therapy are also included.

3.3. STROKE AND BLEEDING RISK ASSESSMENT SCHEMATA IN AF

Risk classification schemata are intended to guide treatment decisions in AF by defining the likelihood of future clinical events based on independent risk factors.[13] Risk scores can be used to estimate the absolute risk of an adverse event. This may be helpful in counseling patients and informing treatment decisions.[16] These metrics do not consider the balance of risk of adverse events and potential nonadherence. The $CHADS_2$ (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke, transient ischemic attack, or thromboembolism) score (Table 3.1) was derived from the Atrial Fibrillation Investigators' and Stroke Prevention in Atrial Fibrillation Investigators' schemata. This was validated in a retrospective cohort of hospitalised patients with AF. A score of zero identified patients at low stroke risk. A score of one to two identified patients at moderate stroke risk. A score greater than two identified patients at high stroke risk.[17,18] Patients with two or more points are predicted to have an annual stroke risk of over 4%, whereas those scoring no points have a predicted annual risk of less than 1%–2%.[18]

The Stroke Prevention in Atrial Fibrillation (SPAF) scheme estimates risk based upon the presence of the following risk factors alone or in combination: age, female sex, diabetes, previous stroke or transient ischemic attack, hypertension, or elevated systolic blood pressure.[19,20] Similarly, the Framingham scheme can be used to risk assess stroke risk through the assignment of values to each of the following well-established independent risk factors: age, gender, systolic blood pressure, diabetes, and prior stroke or transient ischemic attack.[16,20] The $CHADS_2$, SPAF, and Framingham schemes have demonstrated greater predictive accuracy than

chance.[20] This predictive ability may allow clinicians to target high-risk patients for more aggressive therapeutic intervention.[20] The CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke, transient ischemic attack, or thromboembolism, vascular disease, age 65–74 years, sex category) score, provides the highest sensitivity of all schemes to predict thromboembolism (Table 3.1).[21]

A number of bleeding risk stratification tools exist. Amongst these are the $HEMORR_2HAGES$ (hepatic or renal disease, ethanol abuse, malignancy, older age, reduced platelet count, rebleeding risk, anemia, genetic factors, excessive falls risk, stroke)[22] and the HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio [INR], elderly, drug/alcohol concomitantly)[23] tools, yet these are not often used in clinical practice and use is cumbersome. Many use complex scoring systems, and few have been validated in patients with AF and HF. The HAS-BLED bleeding risk tool originated in 2011 and was validated in a European cohort of 3978 participants with AF (Table 3.2). In a comparative validation, the HAS-BLED tool displayed an increased predictive ability than four other bleeding risk stratification methods[22,24–26] among patients in the combined Stroke Prevention Using Oral Thrombin Inhibitor in Atrial Fibrillation (SPORTIF) III and V cohort.[23] Following validation, the HAS-BLED tool was suggested as a simple, yet easy to calculate tool that can be used to assess bleeding risk in AF patients within everyday clinical practice.[13] A HAS-BLED score of at least three indicates high risk and the developers of the tool suggest the need for regular review and some caution following the initiation of oral anticoagulant or aspirin therapy.[13]

TABLE 3.1 STROKE RISK STRATIFICATION WITH CHADS2 AND CHA2DS2-VASC ASSESSMENT TOOLS

$CHADS_2$ acronym	**Score**	**$CHADS_2$ score**	**Adjusted stroke rate (%/year)**
Congestive heart failure	1	0	1.9%
Hypertension	1	1	2.8%
Aged ≥75 years	1	2	4.0%
Diabetes mellitus	1	3	5.9%
Stroke/TIA	2	4	8.5%
Max score	6	5	12.5%
		6	18.2%
CHA_2DS_2-VASc acronym	**Score**	**CHA_2DS_2-VASc score**	**Adjusted stroke rate (%/year)**
Congestive heart failure/LV dysfunction	1	0	0%
Hypertension	1	1	0.7%
Aged ≥75 years	2	2	1.9%
Diabetes mellitus	1	3	4.7%
Stroke/TIA/TE	2	4	2.3%
Vascular disease (prior to MI, PAD, or aortic plaque)	1	5	3.9%
Aged 65–74 years	1	6	4.5%
Sex **c**ategory (ie, female gender)	1	7	10.1%
Max score	10	8	14.2%
		9	100%

Abbreviations: LV, left ventricular; MI, myocardial infarction; PAD, peripheral artery disease; TE, thromboembolism; TIA, transient ischemic attack.

TABLE 3.2 THE HAS-BLED SCORE

Clinical characteristic	Score	HAS-BLED score	Bleeds per 100 patient-years
Hypertension	1 point	0	1.13
Abnormal liver or kidney function	1 point each (1 or 2)	1	1.02
Stroke	1 point	2	1.88
Bleeding	1 point	3	3.74
Liable international normalized ratios	1 point	4	8.70
Elderly	1 point		
Drugs or alcohol	1 point each (1 or 2); max 9 points		

Notes: Hypertension = systolic blood pressure >160 mmHg; abnormal renal function = dialysis/renal transplantation/serum creatinine >200 mmol/L; abnormal liver function = chronic hepatic dysfunction (eg, cirrhosis) or biochemical evidence of significant hepatic derangement (eg, bilirubin twice the upper limit of normal in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase three times the upper limit of normal); bleeding = history of bleeding or a bleeding diathesis; drugs = concomitant use of antiplatelet or nonsteroidal anti-inflammatory drugs.

3.4. ADHERENCE

Failing to adhere to recommendations is a major reason for adverse events.[27] Adherence is a multidimensional phenomenon determined by the relationship of five series of factors or dimensions. There are five dimensions within the World Health Organisation's multidimensional adherence model which incorporate socioeconomic-, health care system-, condition-, treatment-, and patient-related factors.[28] The World Health Organisation's multidimensional adherence model assists in providing a framework for the organisation of barriers to anticoagulant therapy (Table 3.3). Implications for practice including strategies that may be employed to improve adherence are also provided.

TABLE 3.3 BARRIERS TO THROMBOPROPHYLAXIS

Health system-related factors	Clinician apprehension Fear of intracranial haemorrhage and falls Lack of multidisciplinary approach Urban versus rural resource barriers
Treatment-related factors	International normalized ratio monitoring Dietary restrictions Risk of haemorrhage
Socioeconomic-related factors	Cost of medication Cost of visiting clinics Ability to attend clinics
Patient-related factors	Level of cognition Medication and condition knowledge Language difficulties Inadequate patient education
Condition-related factors	Polypharmacy Frailty Cognitive and functional impairment Stress and depression

Once the need for oral anticoagulation is identified, several additional factors must be considered. Despite the evidence demonstrating the benefits of anticoagulation therapy in AF and HF, adherence to these recommendations is far from optimal.[10,29,30] The hesitation to anticoagulate patients is often based upon fear of adverse effects and poor adherence with

monitoring, and this is most pronounced in the elderly.[12] The need for monitoring and titration as well as the adverse effect profile likely contributes to this reticence.[31] Although the use of newer agents such as oral direct thrombin inhibitors (eg, dabigatran) and oral factor Xa inhibitors (eg, rivaroxaban and apixaban) show particular promise in decreasing monitoring, concerns regarding adherence and adverse events remain high.[13] Despite data describing the barriers and facilitators to thromboprophylaxis in the elderly, there has been a lesser focus on individuals with HF who are at high risk.[12] New approaches, that are patient centered, are required to enhance evidence-based use of therapy to prevent thromboembolism and identify risk of bleeding.[32]

3.5. HEALTH SYSTEM-RELATED FACTORS

Clinical trials and meta-analyses have demonstrated the effect of anticoagulation in reducing the risk of ischemic stroke in patients with AF.[33–37] Yet, a large proportion of patients with AF are not treated with anticoagulant therapy. Despite the well-recognised association between AF and prevention of ischemic stroke and the benefits of therapy, anticoagulant therapy remains underused in AF patients.[7] There are numerous reasons why anticoagulant therapy is not initiated, but it is largely due to clinician and patient concerns about the risk of falls and hemorrhagic complications.[7] Clinicians may be apprehensive about initially prescribing oral anticoagulants to elderly patients given the concerns about a higher risk of oral anticoagulant-associated hemorrhage.[38] Of 4188 patients in the Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study with AF who were newly commenced on warfarin therapy, more than one-quarter of patients had discontinued treatment after 1 year.[39] The study authors hypothesized that this may have been due to difficulty in INR control or concerns from clinicians or patients about bleeding risk.[39] More recently, in a Swedish atrial fibrillation cohort study, in almost all patients within a large cohort of 182,678 patients with AF, the risk of ischemic stroke without anticoagulant treatment was higher than the risk of intracranial bleeding with anticoagulant treatment.[40]

3.6. SOLUTION TO HEALTH SYSTEM-RELATED FACTORS

Clinician apprehension may be reduced through providing training and education and practical clinical practice guidelines that provide support for clinical decision making.[41–43] The additional use of a bleeding prediction tool (eg, HAS-BLED) with the stroke risk prediction tool (eg, CHA_2DS_2-VASc) may also assist in clinical decision making.[13] Undertaking chart reviews and clinical audits and excluding patients with documented contraindications to therapy may assist in the identification of patients who are eligible for oral anticoagulant therapy; however, this is not prescribed as a method to increase uptake.[44] From a wider health systems perspective, having access to a state or national surveillance system or the development of a national AF and anticoagulation registry is advocated.[41,45] Clinician adherence to guidelines is a complex issue.[46] Cabana et al offer a range of barriers why clinicians don't follow guidelines. They include barriers affected by clinician knowledge (eg, lack of awareness or lack of familiarity), attitudes (lack of agreement, lack of self-efficacy, lack of outcome expectancy, or the inertia of previous practice), or behavior.[47] A way to improve clinician adherence to guidelines may include developing specialized anticoagulation clinics with expert nurses and doctors as a way to reduce clinician apprehension when commencing patients on oral anticoagulant therapy.[48] This warrants further exploration.

3.7. TREATMENT-RELATED FACTORS

Both the efficacy and safety of warfarin therapy are strongly correlated with therapeutic dosages.[49] An INR of 2.0–3.0 is well established as a therapeutic target range for stroke prevention in AF.[50,51] Therefore, time that a patient spends within their range of target INR should be maximized.[50,52] A major concern is intracranial hemorrhage, which is associated with high morbidity and mortality.[53,54] Novel anticoagulants appear to have a more favourable safety profile than warfarin, as evident through large clinical trials.[55–57] One of the foremost attractions of such novel agents including oral direct thrombin inhibitors and factor Xa inhibitors over

warfarin is that they have predictable pharmacokinetics, therefore reducing or eliminating the burden of routine anticoagulation monitoring. Nevertheless, reversal of such newer agents can be complex and problematic.[58]

3.8. SOLUTIONS TO TREATMENT-RELATED FACTORS

In patients with normal kidney function and an estimated glomerular filtration rate >30 mL/minute, thromboprophylaxis should be selected accordingly after a comprehensive clinical assessment. Dabigatran and rivaroxaban are excreted by the kidneys (dabigatran 80% and rivaroxaban 66%), therefore dosage may require adjustment according to estimated glomerular filtration rate.[59]

Many patients continue to be prescribed warfarin therapy, requiring them to have their INR monitored, which can be burdensome.[7] Health infrastructure must be supportive and enabling of this need for surveillance. Ensuring regular INR monitoring to maintain therapeutic targets and avoid adverse events is critical.[38] Rural outreach or metropolitan hospital liaison services and dedicated anticoagulation clinics are one such approach to achieve these goals.[41] INR self-check kits are an effective strategy to encourage patients with self-care.[60] However, patients must be able, well-informed, and be supplied with a coagulometer.[60] Although providing financial incentives to patients to attend clinics or visit clinicians to increase attendance rates is novel, uptake is low.[61]

3.9. SOCIOECONOMIC-RELATED FACTORS

The annual cost of anticoagulation with warfarin is estimated to be £207.30 in comparison to £1573.50 with the novel anticoagulant dabigatran (per patient; excluding the cost of INR monitoring).[62] The high cost of medication can prohibit initial purchase and continuation of therapy. In some instances this may lead to doses skipped in order to save money.[63] Costs associated with visiting a primary care physician or other member of the multidisciplinary health care team may discourage essential follow-up visits. It is essential to monitor the effectiveness of therapy. These factors may prohibit optimal care and outcomes of oral anticoagulation therapy.

3.10. SOLUTIONS TO SOCIOECONOMIC-RELATED FACTORS

Several suggested solutions have been offered to deal with such barriers. These include the use of innovative technologies like self-check INR kits to undertake self-care at home. This limits the need for frequent visits to primary care, though this may be an expensive appliance which the patient may have to purchase and maintain.[60] A level of cognitive capacity and knowledge is required to interpret results and respond to these in an appropriate manner.[64] Point of care and health rebate systems and monitoring pharmacy refill records may assist in the uptake and maintenance of therapy.[41]

3.11. PATIENT-RELATED FACTORS

Medication adherence in HF is a poorly understood yet fundamental aspect of patient care.[65] Medication adherence rates within the HF population vary widely.[66] Patients are required to balance the need for prescribed medication against any perceived adverse drug event, which may lead to nonadherence or permanent discontinuation of use of oral anticoagulant medications.[67] Such suboptimal drug use is associated with an increase in unplanned hospital admissions, increased mortality and morbidity rates, and accompanied by additional health care-related costs.[68] It has been estimated that patients who do not take their medications as prescribed costs the US health care system $290 billion in avoidable health-related spending every year.[69]

3.12. SOLUTIONS TO PATIENT-RELATED BARRIERS

The World Health Organisation emphasizes that despite the vast amount of knowledge that exists around adherence issues, efforts to address the problems have been divided and – with a few exceptions – have failed to encapsulate the potential contributions of the diverse health disciplines.[28] The World Health Organisation advocates that a stronger buy-in and commitment to a multidisciplinary model is required in order to make progress in the area of poor adherence.[28]

Poor patient education is a commonly cited problem contributing to poor adherence.[43] Patient knowledge is a determinant of anticoagulation control.[43] A lack of the perception of medication importance, risk of adverse events, irregular monitoring of serum INR, or a lack of the perception of risk-to-benefit threshold may lead to adverse events.[43] Inadequate self-management counseling and language difficulties also contribute to this multifaceted issue.[70] Bajorek et al advocate that a pharmacist-led multidisciplinary process within the hospital setting may increase overall antithrombolytic therapy use.[71] Simplified drug regimens and improved

case management comprising of patient education and discharge counseling may be of value.[71] This must address the behaviors and preferences of individual patients. Interventions that target the elderly and those with poor literacy are vital.[72] Such strategies may include providing pamphlets and printed materials with colors, pictures, and visual aids, the enlargement of materials, compact disc read-only memory (CD-ROM) or spoken materials, structured educational programs, the mailing of educational materials, or even online resources and social media patient education interventions.[41] Explicit instructions to primary care providers at patient discharge from acute care, patient reminder cards, and patient forums that provide peer support may be of help.[41] Telemonitoring may prove an effective method to improve medication adherence for HF patients at home. It was recently reported that HF patients using structured telephone support and telemonitoring experienced improvement in the use of evidence-based pharmacotherapy.[73]

3.13. CONDITION-RELATED FACTORS

Polypharmacy and falls

Polypharmacy and comorbidity are fundamental factors that affect medication adherence. Patients with HF and AF may be using antiplatelet therapy[74] or are likely to have concurrent use of multiple medications with antihypertensive properties that predispose patients to symptomatic orthostatic hypotension, syncope, or falls.[75] Being at an increased risk of falling may inevitably lead to an increased risk of hemorrhage, particularly intracranial if a head injury is sustained during a fall due to syncope. There are many explanations for an increased risk of falling. This may only be perceived by the clinician because of age.[75] However, this may be attributable to gait,[76] cognitive impairment, or dementia.[43] Anticoagulant therapy should not be denied based on age alone.[75]

Dietary restrictions

Patients may have dietary restrictions or preferences. This may affect pharmacokinetics and may lead to suboptimal coagulation and impact time spent in a therapeutic range.[67]

Associated condition burden

Frailty,[12] cognitive and functional impairment,[11] stress,[70] and depression[77] are all conditions associated with HF and AF. These conditions may lead to failure to adhere to appropriate INR monitoring or reduced adherence through the cognitive or physical inability to self-administer oral medications. Comparable to patients with cognitive decline, there is evidence that patients with mental health conditions and AF are less likely than those without mental health conditions to have adequate AF management.[78] Depression has been identified as a moderately common condition in HF,[79] and was associated with poor medication compliance in the Heart and Soul Study.[77]

3.14. SOLUTIONS TO CONDITION-RELATED FACTORS

Polypharmacy and falls

Clinicians ought to assess the risk of falls using reliable and valid methods. Planning fall minimization interventions should be in collaboration with the multidisciplinary team.[44] Assessment of any underlying conditions including neuropathy, frailty, and cognitive concerns should be investigated.[80] Cognitive ability can be evaluated using reliable and validated and readily accessible measures such as the Mini Mental State Examination or The Montreal Cognitive Assessment.[81]

The use of once-daily medication formulations or polypills may aid improved adherence.[82] Whilst this may be achievable with HF treatments where doses of many medications remain consistent once up-titrated, this may present difficulties in AF with varying dosages of certain anticoagulants and the need to regularly adjust dosage according to the INR.

Dietary restrictions

Clinicians must ensure that a dietician consultation with specific dietary advice regarding vitamin K intake occurs. This may occur via telephone consultations or clinic visits. This is a simple yet imperative strategy that may reduce the risk of inadequate anticoagulation. Patients altering their dietary intake of green leafy vegetables should be encouraged to notify their clinician as their dosage of warfarin may require adjustment.[83]

Monitoring adherence

Patient self-reporting is a useful method of assessing medication adherence. Self-reporting offers reliable predictors of a broad array of cardiovascular health outcomes – including blood pressure control, hospitalization for HF, and serum drug concentrations – that are highly applicable to this group of patients.[77] There are a number of tools available to measure self-reported adherence. The Morisky Scale provides good predictive ability and can be easily integrated as part of a comprehensive patient assessment prior to the commencement of any oral anticoagulant therapy.[84]

Associated condition burden

Although there are numerous risk stratification tools available to assist clinicians in allocating treatments, they do not consider frailty, which impacts adversely on health outcomes.[12] Cognitive and functional decline are significant consequences of both HF and AF.[85] Undertaking a formal frailty assessment may assist in the guidance of prescribing of oral anticoagulants and may help clinicians identify patients who are at increased risk of adverse events from anticoagulant therapy.[12] Further investigation is warranted to examine the causal relationship between depression and adherence particularly in the HF and AF patient population. Where depression exists, the inclusion of a mental health clinician in the multidisciplinary care model providing care to the patient may be of benefit.[74]

Enhanced models for stratifying bleeding risk particularly in the frail population are required.[45] Frailty assessment tools that currently exist could be used as an adjunct to any stroke risk prediction tool. Any new models or frailty assessment criteria should additionally be incorporated into clinical practice guidelines.[45] Strategies that aim to reduce or manage falls including assistance from family, relatives, informal caregivers, or the provision of home help should not be overlooked.

3.15. IMPLICATIONS FOR CLINICAL PRACTICE

Further research is required to examine the issue of anticoagulant therapy in patients with HF and AF. This is driven by population growth in the elderly and the increasing burden of the cardiogeriatric population.[86,87] Available data suggest it may be useful to include a risk assessment of other aspects of a patient's life as opposed to the restrictive tools that currently exist. Non-adherence with medication and other lifestyle recommendations is a major problem in patients with HF and has severe consequences for individual patients as well as for the health care system.[88] Treatment and care should take into account patients' individual needs and preferences. However, most people with AF should be considered for treatment with oral anticoagulants based on their risk of stroke, ability to tolerate anticoagulation without bleeding, and access to adequate anticoagulation monitoring.

Although there are robust stroke prediction tools, they cannot be considered external to a cardiogeriatric assessment. Extending and developing these tools to consider the risk of non-adherence to prescribed therapy and poor adherence are warranted. Currently, there is no comprehensive risk assessment tool that includes criteria that assesses or addresses the psychosocial aspects of a patient's ability to comply with anticoagulant therapy as well as the risk of stroke. Although novel agents offer promise, they still confer risk and do not negate the importance of individual monitoring.

3.16. CONCLUSION

Current stroke risk prediction tools are useful, yet limited, within the context of complex cardiogeriatric syndromes. Expanding these to consider frailty, cognitive and functional decline, or non-adherence to therapy is warranted. Although avoiding stroke is an important consideration, the potential adverse effects of treatment needs to be balanced within the context of best available evidence, clinical expertise, and the individual patient's circumstances.[89] Developing metrics that consider the combination of these factors are likely to shed light on the issues of adherence in this population.

3.17. REFERENCES

1. Krum H, Jelinek MV, Stewart S, Sindone A, Atherton JJ. 2011 Update to National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006. *Med J Aust*. 2011;194(8):405–409.

2. Gheorghiade M, Filippatos G. Reassessing treatment of acute heart failure syndromes: the ADHERE Registry. *Eur Heart J Suppl*. 2005;7(Suppl B):B13–B19.

3. Pullicino P, Homma S. Stroke in heart failure: atrial fibrillation revisited? *J Stroke Cerebrovasc Dis*. 2010;19(1):1–2.

4. National Institute for Clinical Excellence. Atrial fibrillation (CG36): the management of atrial fibrillation. 2006. Available from: http://www.nice.org.uk/cg36. Accessed December 17, 2012.

5. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011;123(1):104–123.

6. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines. *Circulation*. 2006;114(7):e257–e354.

7. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GY. Underuse of oral anticoagulants in atrial fibrillation: a systematic review. *Am J Med*. 2010;123(7):638–645.

8. Singer DE, Albers GW, Dalen JE, et al. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). *Chest*. 2008;133(6 Suppl):546S–592S.

9. Gattellari M, Worthington J, Zwar N, Middleton S. Barriers to the use of anticoagulation for nonvalvular atrial fibrillation: a representative survey of Australian family physicians. *Stroke*. 2008;39(1):227–230.

10. Baczek VTL, Chen WT, Kluger J, Coleman CI. Predictors of warfarin use in atrial fibrillation in the United States: a systematic review and meta-analysis. *BMC Fam Pract*. 2012;13(1):5.

11. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. 2008;(2):CD000011.

12. Perera V, Bajorek BV, Matthews S, Hilmer SN. The impact of frailty on the utilisation of antithrombotic therapy in older patients with atrial fibrillation. *Age Ageing*. 2009;38(2):156–162.

13. Lip GY. Implications of the CHA_2DS_2-VASc and HAS-BLED scores for thromboprophylaxis in atrial fibrillation. *Am J Med*. 2011;124(2):111–114.

14. Mant J, Hobbs FD, Fletcher K, et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet*. 2007;370(9586):493–503.

15. Homma S, Thompson JLP, Pullicino PM, et al. Warfarin and aspirin in patients with heart failure and sinus rhythm. *New Engl J Med*. 2012; May 2. [Epub ahead of print].

16. Wang TJ, Massaro JM, Levy D, et al. A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community: the Framingham Heart Study. *JAMA*. 2003;290(8):1049–1056.

17. Lip GY, Halperin JL. Improving stroke risk stratification in atrial fibrillation. *Am J Med*. 2010;123(6):484–488.

18. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA*. 2001;285(22):2864–2870.

19. Hart RG, Pearce LA, McBride R, Rothbart RM, Asinger RW. Factors associated with ischemic stroke during aspirin therapy in atrial fibrillation: analysis of 2012 participants in the SPAF I–III clinical trials. *Stroke*. 1999;30(6):1223–1229.

20. Baruch L, Gage BF, Horrow J, et al. Can patients at elevated risk of stroke treated with anticoagulants be further risk stratified? *Stroke*. 2007;38(9):2459–2463.

21. Boriani G, Botto GL, Padeletti L, et al. Improving stroke risk stratification using the $CHADS_2$ and CHA_2DS_2VASc risk scores in patients with paroxysmal atrial fibrillation by continuous arrhythmia burden monitoring. *Stroke*. 2011;42(6):1768–1770.

22. Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF). *Am Heart J*. 2006;151(3):713–719.

23. Lip GY, Frison L, Halperin JL, Lane DA. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. *J Am Coll Cardiol*. 2011;57(2):173–180.

24. Shireman TI, Howard PA, Kresowik TF, Ellerbeck EF. Combined anticoagulant–antiplatelet use and major bleeding events in elderly atrial fibrillation patients. *Stroke*. 2004;35(10):2362–2367.

25. Beyth RJ, Quinn LM, Landefeld CS. Prospective evaluation of an index for predicting the risk of major bleeding in outpatients treated with warfarin. *Am J Med*. 1998;105(2):91–99.

26. Kuijer PM, Hutten BA, Prins MH, Buller HR. Prediction of the risk of bleeding during anticoagulant treatment for venous thromboembolism. *Arch Intern Med*. 1999;159(5):457–460.

27. Komajda M, Lapuerta P, Hermans N, et al. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey. *Eur Heart J*. 2005;26(16):1653–1659.

28. World Health Organisation. *Adherence to Long Term Therapies: Evidence for Action*. Geneva: World Health Organisation; 2003. Available from: http://whqlibdoc.who.int/publications/2003/9241545992.pdf. Accessed December 17, 2012.

29. Piccini JP, Hernandez AF, Zhao X, et al. Quality of care for atrial fibrillation among patients hospitalised for heart failure. *J Am Coll Cardiol*. 2009;54(14):1280–1289.

30. Nieuwlaat R, Eurlings LW, Cleland JG, et al. Atrial fibrillation and heart failure in cardiology practice: reciprocal impact and combined management from the perspective of atrial fibrillation: results of the Euro Heart Survey on atrial fibrillation. *J Am Coll Cardiol*. 2009;53(18):1690–1698.

31. Lip GY. Stroke in atrial fibrillation: epidemiology and thromboprophylaxis. *J Thromb Haemost*. 2011;9(Suppl 1):S344–S351.

32. Go AS. Efficacy of anticoagulation for stroke prevention and risk stratification in atrial fibrillation: translating trials into clinical practice. *Am J Manag Care*. 2004;10(3 Suppl):S58–S65.

33. Ezekowitz M, Bridgers SL, James KE, et al; Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Investigators. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. *New Engl J Med*. 1992;327(20):1406–1412.

34. Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. *Arch Intern Med*. 1994;154(13):1449–1457.

35. Stroke Prevention In Atrial Fibrillation Investigators. Stroke prevention in atrial fibrillation trial. Final results. *Circulation*. 1991;84(2):527–539.

36. Miller CS, Grandi SM, Shimony A, Filion KB, Eisenberg MJ. Meta-analysis of efficacy and safety of new oral anticoagulants (dabigatran, rivaroxaban, apixaban) versus warfarin in patients with atrial fibrillation. *Am J Cardiol*. 2012;110(3):453–460.

37. Agarwal S, Hachamovitch R, Menon V. Current trial-associated outcomes with warfarin in prevention of stroke in patients with nonvalvular atrial fibrillation: a meta-analysis. *Arch Intern Med*. 2012;172(8):623–631.

38. Marinigh R, Lip GY, Fiotti N, Giansante C, Lane DA. Age as a risk factor for stroke in atrial fibrillation patients: implications for thrombophrophylaxis. *J Am Coll Cardiol*. 2010;56(11):827–837.

39. Fang MC, Go AS, Chang Y, et al. Warfarin discontinuation after starting warfarin for atrial fibrillation. *Circ Cardiovasc Qual Outcomes*. 2010;3(6):624–631.

40. Friberg L, Rosenqvist M, Lip GY. Net clinical benefit of warfarin in patients with atrial fibrillation: a report from the Swedish atrial fibrillation cohort study. *Circulation*. 2012;125(19):2298–2307.

41. Bajorek BV, Ogle SJ, Duguid MJ, Shenfield GM, Krass I. Management of warfarin in atrial fibrillation: views of health professionals, older patienst and their carers. *Med J Aust*. 2007;186(4):175–180.

42. Bo S, Valpreda S, Scaglione L, et al. Implementing hospital guidelines improves warfarin use in non-valvular atrial fibrillation: a before–after study. *BMC Public Health*. 2007;7(1):203.

43. Brophy MT, Snyder KE, Gaehde S, Ives C, Gagnon D, Fiore LD. Anticoagulant use for atrial fibrillation in the elderly. *J Am Geriatr Soc*. 2004;52(7):1151–1156.

44. Srivastava A, Hudson M, Hamoud I, Cavalcante J, Pai C, Kaatz S. Examining warfarin underutilization rates in patients with atrial fibrillation: detailed chart review essential to capture contraindications to warfarin therapy. *Thromb J*. 2008;6:6.

45. Tulner LR, Van Campen JP, Kuper IM, et al. Reasons for undertreatment with oral anticoagulants in frail geriatric outpatients with atrial fibrillation. *Drugs Aging*. 2010;27(1):39–50.

46. Grimshaw JM, Russell IT. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet*. 1993;342(8883):1317–1322.

47. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA*. 1999;282(15):1458–1465.

48. Rewiuk K, Wizner B, Fedyk-Lukasik M, et al. Heart failure and atrial fibrillation – does practice meet the anticoagulation guidelines? *Int J Cardiol*. 2012;157(2):274–275.

49. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). *Chest*. 2008;133(6 Suppl):160S–198S.

50. Connolly SJ, Laupacis A, Gent M, Roberts RS, Cairns JA, Joyner C. Canadian Atrial Fibrillation Anticoagulation (CAFA) study. *J Am Coll Cardiol*. 1991;18(2):349–355.

51. Albers GW, Diener HC, Frison L, et al. Ximelagatran vs warfarin for stroke prevention in patients with nonvalvular atrial fibrillation: a randomized trial. *JAMA*. 2005;293(6):690–698.

52. Stroke Prevention In Atrial Fibrillation Investigators. Adjusted-dose warfarin versus low-intensity, fixed-dose warfarin plus aspirin for high-risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial. *Lancet*. 1996;348(9028):633–638.

53. Appelboam R, Thomas EO. Warfarin and intracranial haemmorhage. *Blood Rev*. 2009;23(1):1–9.

54. Sjoblom L, Hardemark HG, Lindgren A, et al. Management and prognostic features of intracerebral hemmorhage during anticoagulant therapy: a Swedish multicenter study. *Stroke*. 2001;32(11):2567–2574.

55. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. *New Engl J Med*. 2011;365(11):981–992.

56. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *New Engl J Med*. 2011;365(10):883–891.

57. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *New Engl J Med*. 2009;361(12):1139–1151.

58. Battinelli EM. Reversal of new oral anticoagulants. *Circulation*. 2011;124(14):1508–1510.

59. Mussigbrodt A, Hindricks G. Clinical implications from recent trials and new guidelines for stroke prevention in atrial fibrillation. *Eur Cardiol*. 2012;8(3):174–178.
60. Horstkotte D, Piper C. Improvement of oral anticoagulation therapy by INR self-management. *J Heart Valve Dis*. 2004;13(3):335–338.

61. Giuffrida A, Torgerson D. Should we pay the patient? Review of financial incentives to enhance patient compliance. *BMJ*. 1997;315(7110):703–707.

62. Ali A, Bailey C, Abdelhafiz AH. Stroke prophylaxis with warfarin or dabigatran for patients with non-valvular atrial fibrillation-cost analysis. *Age Ageing*. 2012;41(5):681–684.

63. Dunlay SM, Eveleth JM, Shah ND, McNallan SM, Roger VL. Medication adherence among community-dwelling patients with heart failure. *Mayo Clin Proc*. 2011;86(4):273–281.

64. Dolor RJ, Ruybalid RL, Uyeda L, et al. An evaluation of patient self-testing competency of prothrombin time for managing anticoagulation: pre-randomization results of VA Cooperative Study #481 – The Home INR Study (THINRS). *J Thromb Thrombolysis*. 2010;30(3):263–275.

65. Wu JR, Moser DK, Chung ML, Lennie TA. Predictors of medication adherence using a multidimensional adherence model in patients with heart failure. *J Card Fail*. 2008;14(7):603–614.

66. Brown SB, Shannon RP. Improving medication compliance in patients with heart failure. *Am J Cardiol*. 2008;101(2):274–277.

67. van der Wal MH, Jaarsma T. Adherence in heart failure in the elderly: problem and possible solutions. *Int J Cardiol*. 2008;125(2):203–208.

68. De Smedt RH, Denig P, van der Meer K, Haaijer-Ruskamp FM, Jaarsma T. Self-reported adverse drug events and the role of illness perception and medication beliefs in ambulatory heart failure patients: a cross-sectional survey. *Int J Nurs Stud*. 2011;48(12):1540–1550.

69. NEHI. Thinking outside the pillbox: a system-wide approach to improving patient medication adherence for chronic disease. August 12, 2009. Available from: http://www.nehi.net/publications/44/thinking_outside_the_pillbox_a_systemwide_approach_to_improving_patient_medication_adherence_for_chronic_disease. Accessed December 6, 2012.

70. McCabe PJ, Schumacher K, Barnason SA. Living with atrial fibrillation: a qualitative study. *J Cardiovasc Nurs*. 2011;26(4):336-344.

71. Bajorek BV, Krass I, Ogle SJ, Duguid MJ, Shenfield GM. Optimizing the use of antithrombotic therapy for atrial fibrillation in older people: a pharmacist-led multidisciplinary intervention. *J Am Geriatr Soc*. 2005;53(11):1912–1920.

72. Tang EO, Lai CS, Lee KK, Wong RS, Cheng G, Chan TY. Relationship between patients' warfarin knowledge and anticoagulation control. *Ann Pharmacother*. 2003;37(1):34–39.

73. Inglis SC, Cark RA, McAlister FA, et al. Structured telephone support or telemonitoring programmes for patients with chronic heart failure. *Cochrane Database Syst Rev*. 2010;(8):CD007228.

74. Robert-Ebadi H, Le Gal G, Righini M. Use of anticogulants in elderly patients: practical recommendations. *Clin Interv Aging*. 2009;4:165–177.

75. Sansossian S, Ovbiagele B. Prevention and management of stroke in very elderly patients. *Lancet Neurol*. 2009;8(11):1031–1041.

76. Krass I, Ogle SJ, Duguid MJ, Shenfield GM, Bajorek BV. The impact of age on antithrombotic use in elderly patients with non-valvular atrial fibrillation. *Australas J Ageing*. 2002;21(1):36–41.

77. Gehi A, Haas D, Pipkin S, Whooley MA. Depression and medication adherence in outpatients with coronary heart disease: findings from the Heart and Soul Study. *Arch Intern Med*. 2005;165(21):2508–2513.

78. Walker GA, Heidenreich PA, Phibbs CS, et al. Mental illness and warfarin use in atrial fibrillation. *Am J Manag Care*. 2011;17(9):617–624.

79. Vaccarino V, Kasl SV, Abramson J, Krumholz HM. Depressive symptoms and risk of functional decline and death in patients with heart failure. *J Am Coll Cardiol*. 2001;38(1):199–205.

80. Forman DE, Rich MW, Alexander KP, et al. Cardiac care for older adults. Time for a new paradigm. *J Am Coll Cardiol*. 2011;57(18):1801–1810.

81. Flaker GC, Pogue J, Yusuf S, et al. Cognitive function and anticoagulation control in patients with atrial fibrillation. *Circ Cardiovasc Qual Outcomes*. 2010;3(3):277–283.

82. Hauptman PJ. Medication adherence in heart failure. *Heart Fail Rev*. 2008;13(1):99–106.

83. Hylek EM. Oral anticoagulants. Pharmacologic issues for use in the elderly. *Clin Geriatr Med*. 2001;17(1):1–13.

84. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24(1):67–74.

85. Marzona I, O'Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with atrial fibrillation: results of the ONTARGET and TRANSCEND studies. *CMAJ*. 2012;184(6):E329–E336.

86. Wong CX, Brooks AG, Leong DP, Roberts-Thomson KC, Sanders P. The increasing burden of atrial fibrillation compared with heart failure and myocardial infarction: a 15 year study of all hospitalizations in Australia. *Arch Intern Med*. 2012;172(9):739–741.

87. Stewart S. Epidemiology and economic impact of atrial fibrillation. *J Cardiovasc Nurs*. 2004;19(2):94–102.

88. McEntee ML, Cuomo LR, Dennison CR. Patient-, provider-, and system-level barriers to heart failure care. *J Cardiovasc Nurs*. 2009;24(4):290–298.

89. Sackett DL, Rosenberg WM, Muir Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ*. 1996;312(7023):71–72.

CHAPTER 4: THE CAREGIVER ROLE IN THROMBOPROPHYLAXIS MANAGEMENT IN ATRIAL FIBRILLATION: A LITERATURE REVIEW.

4.1. CHAPTER PREFACE

Publication Reference:

Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. The caregiver role in thromboprophylaxis management in atrial fibrillation: a literature review. *European Journal of Cardiovascular Nursing*. 2014; EPub Ahead of Print.

Chapter 3 provided insights into patient-centered approaches to thromboprophylaxis in CHF with AF. This chapter explores the enabling role of the caregiver in addressing adherence to thromboprophylaxis.

This chapter presents an article in its original form, published in the *European Journal of Cardiovascular Nursing* as an e-publication in August 2014. This article is provided in its published form as an appendix.

Background:

Atrial fibrillation is a common arrhythmia and a risk factor for adverse events including stroke. People living with atrial fibrillation are commonly elderly and have multiple comorbidities. The role of a caregiver in supporting the individual to manage a chronic and complex condition has received limited attention.

What we already know:

- Internationally the numbers of individuals living with atrial fibrillation is growing
- Atrial fibrillation increases the risk of stroke
- Adherence with recommendations for thromboprophylaxis is low

Aim of the study:

This review aims to summarize available information on the caregiver role in atrial fibrillation, specifically in promoting adherence to thromboprophylaxis and evidence for strategies to support and enable the caregiver.

A review of electronic databases and search engines were undertaken including Medline, Scopus and CINAHL. The search terms '*atrial fibrillation*' '*anticoagulation*' *'carer'* '*caregiver*' '*family support'* were used. Dates searched from Jan 1990 – Nov 2012.

Summary of the results:

The review found limited original clinical research studies. The majority of the literature identified in the initial search included review papers, and work which recommends the inclusion of the caregiver in the care of patients with atrial fibrillation but limited empirical evidence.

Caregivers have an essential role to play in advocacy; family centered care and shared decision-making. This may influence thromboprophylaxis treatment choices and potentially adherence. Assessment of caregiver needs and support should be central to patient assessment and care planning. There is need for clinical intervention studies which greater target and address the caregiver role.

Implications:

- To date, the role of the caregiver in atrial fibrillation is poorly described
- Emphasis of the consideration of atrial fibrillation as a cardio-geriatric syndrome
- Support for adherence with thromboprophylaxis may be enhanced by caregiver support and involvement in care planning. There is need for systematic development of models for AF management that formalize caregiver participation.

4.2. BACKGROUND

It is estimated 3 million people in the United States (US) are affected by atrial fibrillation (AF).[1] Hospitalization for AF is common and costly.[2] Stroke is a major complication of AF and is associated with a 3 to 5 fold increased risk.[3] AF is likely to be an aetiological factor in approximately 30% of strokes in the elderly.[4] Patients with AF post stroke will have significantly worse outcomes.[5] Patients with AF who experience a stroke are often cared for in the community by caregivers with little healthcare support. There is also a need to explore the role of caregiving in people living with AF in the community. Interventions should be targeted to support caregivers.[6] Chronic conditions including AF create the need for self-care strategies. Numerous examples of inadequate self-management emphasize the importance of looking at innovative models. Commonly, self-care models target the individual and although implicit, the role of the caregiver is less well described.

4.2.1. WHO IS A CAREGIVER?

The nomenclature of care giving can be confusing. As the word caregiver may sometimes be used synonymously with family caregiver, carer, support, or family support. For the purposes of this paper we have defined a caregiver as *"a spouse, adult child, other relative, partner or friend who has a personal relationship with, and provides a wide range of unpaid care for an adult with a chronic condition"*. There are diverse and heterogeneous models of care giving as well as caregiver needs and resources.[7] There are many different cultural nuances to care giving. This paper is approached from an Angelo-Western-Caucasian perspective.

It is recognised that in a Western, primarily Caucasian context, feelings and emotions of responsibility for family member may be associated with feelings of guilt or inadequacy for some caregivers. This may be due to caregiving responsibilities placing restrictions on personal and parental autonomy and independence that run counter to dominant Western ideals.[8]

There are more than 65 million people, (*29% of the U.S. population*) who provide care for a chronically ill, disabled or elderly family member, or friend during any given year and spend an average of 20 hours per week providing care.[9] The typical caregiver is a 49-year-old woman who cares for her widowed 69-year-old mother, who does not live with her; she is married and employed.[9] The economic value of caregiving in the context of today's society must not be underestimated. Whilst the value of services provided by caregivers is '*free*', it is estimated to be $375 USD billion per year. This is more than twice as much ($158 USD billion), when contrasted against what is actually spent on home care and nursing home services.[10] Caregivers may provide care and assistance with a wide range of activities of daily living. These may include bathing, dressing, feeding, toileting, helping with incontinence, assisting with mobility, cooking, house cleaning, handling finances, transport to health professional appointments, and overseeing or assisting with medications.[10] These trends are replicated around the world. [11] Examples of caregiving activities in individuals with AF may include: Opening medication packaging and assisting or confirming correct dosage to be taken; driving patients to the primary care GP or anticoagulation clinic to have venous blood samples taken; assisting with activities of daily living due to tiredness experienced due to AF; monitoring for signs of bleeding; ensuring adherence to any dietary restrictions.

In spite of the importance of caregivers, most multidisciplinary clinical practice guidelines fail to recommend the inclusion of the caregiver throughout the spectrum of care. This may be due to limited data supporting their role or potentially their lack of visibility in the policy context. Enhancing caregiver support to enable better self and family management may lead to favourable patient outcomes.[12] Moreover, many discussions of caregivers highlight that they are commonly unrecognised and underemphasised.

Although management of all chronic illness is complex, the use of thromboprophylaxis in AF increases the risk of adverse events and the complexity of caregiving. The most worrisome from the perspective of the clinician is that of stroke and bleeding risk.[13] Most clinical practice

guidelines recommend thromboprophylaxis for patients with AF with a Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes, prior Stroke or TIA, Vascular disease, Age 65 – 74, Sex category (*CHA_2DS_2-VASc*) score of > 1.[14-19] Thromboprophylaxis may come in the form of traditional Vitamin K Antagonists (VKAs) (*warfarin*) or novel anticoagulants including dabigatran, rivaroxaban and apixaban that have a lower need for need for haematological monitoring. Warfarin may be burdensome due to the requirements of regular INR monitoring to ensure optimal time spent in the therapeutic range.[20] The attraction of novel agents such as direct thrombin inhibitors (eg. dabigatran, rivaroxaban and apixaban) are the simplified dosing regimens and reduction in the need for routine monitoring.[21]

Adverse events can occur because of failing to adhere with management recommendations. Adherence is defined as "*the extent to which a person's behavior taking medication corresponds with agreed recommendations from a clinician*".[22] Non - adherence to oral medications is common and complex, particularly in chronic diseases including AF.[23] It is estimated to cost the US healthcare system in excess of $100 billion per year.[24] Poor adherence may lead to suboptimal patient outcomes including increased hospitalization, morbidity and mortality.[22,23] It is estimated 40 – 60% of patients fail to take their medications as prescribed by their physician.[25] In a US longitudinal cohort study one third of the AF population who were initially prescribed warfarin for stroke prevention had discontinued treatment after 30 months.[26] Similarly, a study by Fang *et al* identified that more than a quarter of patients newly commenced on warfarin for AF were found to have discontinued treatment within the first year.[27] The World Health Organisation recognises that there are five domains that impact medication adherence. These include socio-economic, patient related, treatment related, health system related and condition related factors.[22]

Frailty, functional and cognitive dysfunction are a common occurrence in this population.[28] Within the context of this paper, frailty may be present in both the caregiver and patient. These factors may impact adversely on non-adherence to prescribed therapy. Patients who are frail or

are unable to self-care are less likely to receive anticoagulant therapy.[29] This may be due to clinician apprehension due to the fear of patient falls. Consequently, this may lead to increased morbidity and mortality.[30,31] Functional and cognitive decline are commonly associated with a diagnosis of AF,[28] demanding additional caregiver support, formally and informally. [32] Potentially involving the caregiver may result in more individuals receiving prophylactic treatment and less adverse events.

Many interventions focus on optimizing adherence to therapy. Most interventions include combinations of reminders (including reminder packaging),[25] aide devices, self-monitoring strategies, reinforcement, counseling, telephone support or tele-health.[23] Many of the interventions recommended involvement of caregivers. A caregiver can provide ongoing support, encouragement and reminders on a frequent basis.[23] The assistance of caregivers is often required due to the complex nature of anticoagulant therapy including altered dosing requirements, the need for frequent monitoring, and medication costs.[20,33] Caregivers may also have a role in the physical assistance to administer oral medication to more disabled and frail patients with AF.[33]

4.3. OBJECTIVES

This review aims to:

1) Discuss the role of caregivers and their role in supporting thromboprophylaxis in AF.

2) Identify strategies for developing the caregiver role in AF management, specifically in promoting adherence.

4.4. METHODS

A review of electronic databases and search engines were undertaken including Medline, Scopus and CINAHL. The search terms '*atrial fibrillation*' '*anticoagulation*' *'carer'* '*caregiver*' '*family support'* were used. Dates searched from Jan 1990 – Nov 2012. Literature prior to 1990 was not searched to provide a contemporary perspective of the caregiver role over the last decade. Reference lists of retrieved articles were hand searched. Papers were included that addressed the role and responsibilities of the caregiver in patients with AF. Review papers, correspondence, letters to editors, and abstracts of conference proceedings were excluded. Only primary research papers were included.

4.5. RESULTS

There was a limited description of the role of the caregiver in patients with AF. The volume of primary research undertaken in the area is poor. Refer to Figure 4.1. PRISMA Flow Chart. The majority of the literature reviewed through our search included review papers, and work which recommends the inclusion of the caregiver in the care of patients with AF. However there was limited original clinical research work. The papers included in this review are discussed below and are provided in Table 4.1.

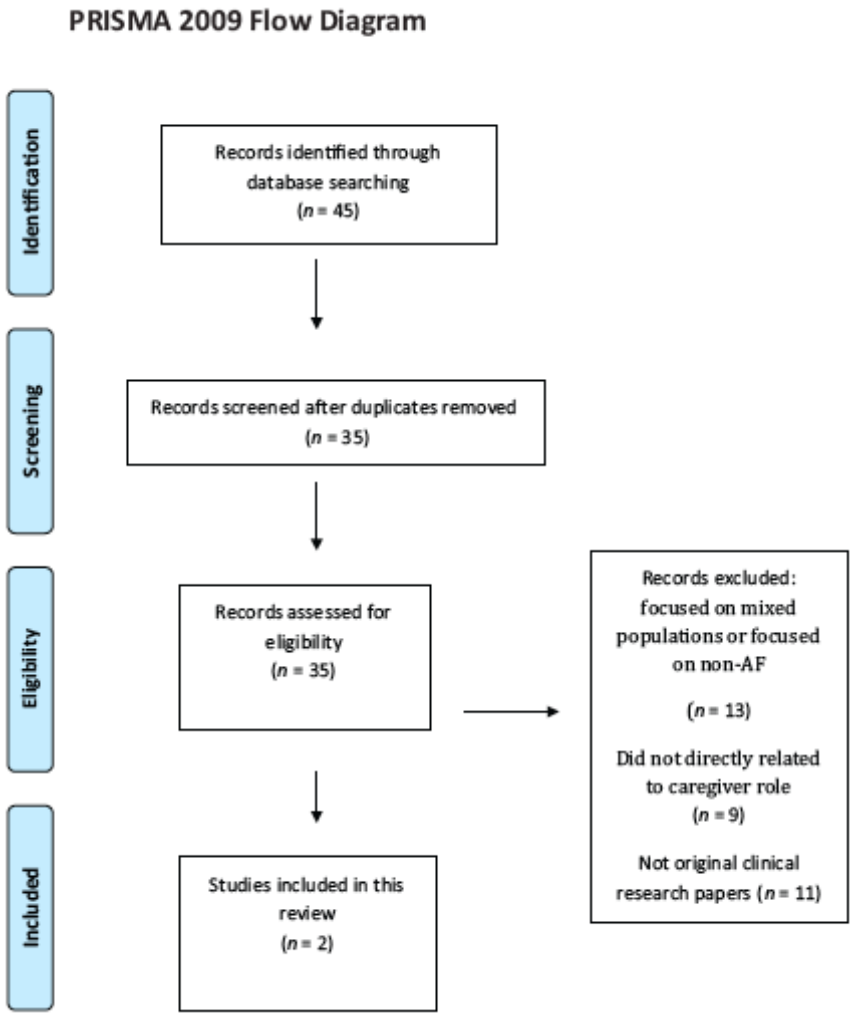

FIGURE 4.1 PRISMA FLOW DIAGRAM

TABLE 4.1 SUMMARY OF STUDIES

AUTHORS	Study design and purpose	Characteristics & Setting	Results	Limitations	Implications
Chen et al 2012 *USA*	***Design*** Cross-sectional study to compare medicare beneficiaries with AF with beneficiaries without AF. ***Purpose*** To describe patients characteristics and caregiver assistance among Medicare beneficiaries with AF and examine factors associated with receiving anticoagulant treatment	2990 patients with AF and 5980 control patients were included in the burden of disease analysis and 1481 patients with AF were included in the anticoagulant predictor analysis. Multistage, stratified sampling design. Allowing for analysis of a nationally representative sample of all Medicare beneficiaries.	Patients with AF had a higher level of comorbidity, worse self-perceived health status, a greater level of disability than their matched counterparts. A greater proportion of patients with AF require caregiver assistance. (62.8% vs 51.5%; $p<0.01$) A greater need for caregiver assistance was observed in patients with AF. Logistic regression found that a higher Charlson Comorbidity Index score, difficulty in obtaining necessary healthcare, older ages, being widowed, a history of psychiatric disorders and being underweight decreased the likelihood of receiving anticoagulant therapy. Subgroups characterised by frailty, inability for self-care were identified as being less likely to receive anticoagulant therapy. The need for caregiver assistance should be considered when making treatment decisions.	Medicare claims data sets are subject to underreporting and miscoding of diagnoses. Several proxies were used to assess caregiver assistance. Study findings are associations and not causal, so they may not be generalisable to institutionalized Medicare beneficiaries or non-Medicare patients.	Patients with AF have a greater need for caregiver assistance ($p<0.01$). Individuals with AF who are not able to self-care are identified as being less likely to receive anticoagulant therapy. The need for caregiver assistance must be considered when making thromboprophylaxis treatment decisions.

AUTHORS	Study design and purpose	Characteristics & Setting	Results	Limitations	Implications
Coleman et al 2012 *USA, Pharmacy*	***Design*** Cross sectional survey of AF patient-caregiver dyads recruited from cardiology clinics at an urban teaching hospital. ***Purpose*** To examine the interrelationship between unpaid caregiver, patient and thromboprophylaxis characteristics and caregiver burden in AF	80 patient caregiver dyads were surveyed	Significantly greater caregiver burden due to 'disrupted schedule' was seen in those spending >4hrs/ week providing care and when caring for frail, sick or disabled patients with higher CHADS2 scores and requiring help with their medications. Financial problems burden scores were significantly associated with caring for frail patients and those requiring more frequent office follow up. Lack of family support scores were inversely associated with having somebody else help provide care and increased as patients $CHADS_2$ score increased. Lower health problem scores were associated with female gender and higher scores with the need to spend > 4 hours/ week providing care. The greatest burden to caregivers of AF patients occurs due to schedule disruption.	Small study population. Small sample size may have resulted in type 2 error in analysis. Caregiver dyads were recruited from only a handful of arrhythmia clinics affiliated with a single urban teaching hospital in the US. All participants had healthcare insurance Caregivers were younger than the patients they cared for, they were still relatively old, few were still working and most were women. Very few patients received alternate treatment strategies to warfarin or aspirin	Individuals with AF and higher CHADS2 scores who require help with their medication may impose greater caregiver burden. The greatest burden to caregivers of AF patients occurs due to schedule disruption.

In a prospective, cross-sectional survey in 80 AF caregiver-dyads (average age was 66 years, mostly married and of female gender) caregiving responsibilities were usually for greater than 1 year when caring for someone with AF and out of pocket payment for healthcare was required by 55%. Most participants described that they were required often to eliminate things from their schedule and experienced less time to visit family and friends. However, 61% strongly agreed that caring was important to them, and 52% strongly disagreed that they resented having to care. Coleman and colleague's study suggest that the greatest burden is placed on caregivers due to the disruption of schedules and followed by financial problems. Of particular highlight is the finding that medications, particularly thromboprophylaxis medication problems appeared to be a notable source of burden. And patients that required need for help in managing their medications have a greater predicator of burden due to disrupted schedules and health problems. 'Financial problems' burden scores were significantly associated with caring for frail patients and those requiring more frequent clinician follow-up. 'Lack of family support' scores were inversely associated with having somebody else to help provide care and increased as patients $CHADS_2$ score increased. Lower 'Health problem' burden scores were associated with female gender and higher scores with the need to spend > 4 h/week providing care.[33]

4.6. DISCUSSION

In light of the paucity of primary research in this area, findings from the broader literature search have been framed and augmented within existing caregiver literature. Special attention has been drawn to how the caregiver role can be best enabled to promote optimal adherence to thromboprophylaxis.

4.6.1. MODELS OF AF MANAGEMENT

C. Everett Koop, MD is famously quoted as saying *"Drugs don't work in patients who don't take them."* Adherence can be defined as the "*active, voluntary, and collaborative involvement of the patient in a mutually acceptable course of behavior to produce a therapeutic result*."[34] Poor adherence to thromboprophylactic therapies is common and complex and not fully understood. This contributes to worsening of disease, increases stroke and haemorrhagic risk and leads to increased health care costs.[35] In the majority of cases, patients with AF who are prescribed thromboprophylaxis may be on therapy for lifetime duration. This duration of treatment adds to the complexity of issues of adherence. There are different models of management for AF to facilitate optimal adherence. These are affected by personal factor including socio-demographic influences, psychosocial, cognitive and functional abilities. Although models emphasise the socio-cultural context of the individual the role of the caregiver receives scant attention.

Methods of facilitating adherence to anticoagulant therapy are outlined in a conceptual model proposed by Brown and colleagues (2012).[36] These include:

1. Knowledge about the condition and continuous reinforcement by clinicians through regular visits and interaction.
2. Short-term and long-term motivation (e.g., avoidance of negative health consequences);
3. Development of a personalized system, habit formation, and system adaptation (e.g., developing a routine or external reminders i.e. Text messaging, smart-phone apps or alarms for medication reminders)
4. Self-efficacy loop (i.e., reinforcement of the personalized system and its adaptability as patients become more consistent, confident, and adherent)

In each of the key steps identified above, the caregiver can play a critical role in providing both physical and psychosocial support.

Nurse-led clinics have been successful in the management of other chronic conditions including as chronic heart failure, asthma and diabetes. Such models of care for patients with AF may be worthwhile to explore further in practice. In a recent RCT conducted by Hendriks *et al*, that included 712 patients with AF assigned to nurse-led care vs. usual care. Nurse-led care intervention consisted of guidelines based, software supported integrated chronic care supervised by a cardiologist. Nurse-led care of patients with AF proved superior to usual care, with decreased rates of cardiovascular hospitalisation and cardiovascular mortality.[37]

A new, emergent care model is that of interdisciplinary, nurse coordinated AF expert programs. This model aims to reduce symptom burden and prevent severe complications, including stroke. This model appears a pragmatic way to optimise access for patients with clinicians given time restraints imposed with physicians. Whereby, patients are educated and empowered, trained and counselled on self-management and this would contribute to improved outcomes in mortality and hospitalisation. These models hold hope as an innovative method to improve self-management, education and adherence to treatment regimes. Importantly these approaches enable the caregiver and involve them in the education and decision -making processes.[38]

4.6.2. CAREGIVER EDUCATION

There are many factors that influence a patient's time in therapeutic range. These may include diet, alcohol consumption, medication and health service cost and availability.[39] A patient's knowledge of their condition and treatment plan are often determinants of their overall quality of anticoagulation control.[40] Patients with low health literacy or cognitive impairment may be more likely to require caregiver assistance. This may be an impacting factor in their understanding of medication importance. Therefore, caregiver education should be a core

element of routine anticoagulation management. It is essential that the patient's primary caregiver receive adequate anticoagulant counselling that is individually tailored to meet their needs.[41]

Clinicians, patients and their caregivers are increasingly demanding customised resources to support anticoagulant use and management.[42] This may include education translated in languages other than English for a culturally diverse population. Promoting adherence requires educational approaches involving patients and caregivers in the management of their therapy (e.g. self-monitoring).[43] Successful home monitoring of prothrombin time (PT) with a self-testing device requires adequate levels of cognition, health literacy and manual dexterity. Whilst cognitive impairment and functional decline are common in AF,[28] training a caregiver can modestly increase the proportion of patients who are able to perform home monitoring.[44] The ability of patients to undertake home monitoring can improve a patients time in the therapeutic range (TTR) and may lead to improved outcomes and decrease the prevalence of stroke and other adverse events.[45]

A caregiver may also be trained in how to undertake a simple manual radial pulse check, to ascertain if a patient is in a regular or irregular rhythm. This education may be particularly useful for elderly patients with recurrent episodic paroxysmal AF and those whom are greatly affected by burdensome symptoms. This may be helpful to assist in identify potential triggers and coping mechanisms, and help form the basis of treatment plans.

4.6.3. MEDICATION MANAGEMENT

A study of patients attending the anticoagulation clinic identified that nearly 20% of those participating identified another person as responsible for their medication.[46] Given that AF often coexists with multiple comorbidities[47] and therefore poly-pharmacy is likely,[48] clinicians must be responsive of this additional complexity. Complex dosing regimens should be reduced where

possible. In the VARIA (*Veterans AffaiRs Study to Improve Anticoagulation*) study, patients receiving 16 or more medications predicted a 4.3% lower TTR than for patients receiving 0 - 7 medications.[49] Therefore reducing the number of medications prescribed where possible is highly justified. However, judgement as to whether there are many (i.e. appropriate poly-pharmacy) or too many (i.e. inappropriate poly-pharmacy) medications is complex.[50] The hospital pharmacist plays a key role in the assessment for medication aides upon discharge. The issue of altered cognition in this population adds a layer of complexity to dosing regimens. Caregiver assistance may be of help in the community setting to assist with dosing regimens and understanding medication packing for those individuals with poor health literacy.

4.6.4. ADVOCACY AND SHARED DECISION-MAKING

The decision to anticoagulate a patient with AF is multifaceted. Stroke and bleeding risk must be considered.[51] Views between clinicians and patients when weighing up outcomes of thromboprophylaxis in AF vary considerably.[52] Therefore patient preferences must be central to decisions to anticoagulate. Treatment must be patient-centered and individualised.[53] Clinicians who fail to include the patient and their caregivers in decisions about commencing thromboprophylaxis risk disengaging with those whose care they are trying to improve.[52] Patients and caregivers should have an active role in treatment decisions, as this may prove helpful in achieving favourable outcomes of therapy.[54] Previous studies have highlighted that the absence of a caregiver may bias against initial prescription of anticoagulation.[55] The need for caregiver assistance should be considered when making treatment decisions.[29] Patients may be perplexed by complicated stroke and bleeding risk information such as risk-benefit ratios. Whilst clinicians may be aware of patient limitations they should not use this to influence clinician desired treatment choices.[56] Caregivers play a vital role in advocacy and shared decision-making. Shared decision-making with frail older adults where cognitive impairment can influence competency may be challenging. Such consultations may involve lengthy detailed discussions that take time.[57]

4.6.5. SUPPORT FROM HEALTH CARE

Arrhythmia nurse specialists or consultants act as a designated clinical contact to provide specialised care. They may support patients who are newly diagnosed with AF, and their caregivers, through the provision of education.[58] This may include; timely provision of health information, counselling and advice on medications, and reassurance. Nurse specialists may also coordinate AF support groups. Support groups are identified as value adding to caregiver support. As they can provide platforms for patients and caregivers to meet, engage and exchange health information and stories.[58] This may encourage supportive community networks and reduce caregiver burden. Support for coping and adjusting with the emotional aspects of burden in AF are generally lacking.[59] And there is growing demand for newer educational programs to address the emotional burden of AF to be developed.[59]

4.6.6. CAREGIVER BURDEN

Whilst thromboprophylaxis remains chronically underutilized,[60] the advent of new agents, enhanced risk prediction modelling and an epidemic of AF; it could be assumed that more patients are receiving oral anticoagulation than ever before. Such factors likely result in a greater reliance on caregivers.

Patients with AF have a greater need for caregiver assistance.[29] However this assistance may come at a cost, in both forms of physical or emotional stress. An early definition by Townsend in the 1950's describes a phenomenon of '*strain of illness*'. "*This strain can be a change of employment as a result of caring for a family member, or excessive physical or mental demands imposed on the entire family structure*". Turner and Catania (1997) provide a more up to date broader definition of caregiver burden as a "*caregiver's subjective experience of problems or strains that were linked to the caregiver's role*". Caregivers who report emotional or mental strain associated with caregiving are more likely to die than non-caregivers.[61] Amongst elderly spousal caregivers, experiencing psychological or emotional strain is an independent risk factor for mortality.[61]

There is significantly greater caregiver burden due to '*disrupted schedule'* in those spending >4hrs/ week providing care and when caring for frail, sick or disabled patients with higher $CHADS_2$ scores and requiring help with their medications.[33] The greatest burden to caregivers of AF patients occurs due to schedule disruption.[33] Patients living in rural and remote regions may have to endure lengthy travel to a healthcare professional for INR checking. Point of care INR testing may be a strategy which can be implemented by caregivers to reduce unnecessary expensive medical travel.[62] Additionally, point of care testing may lead to increased time in the therapeutic range (TTR) and improved outcomes if successfully integrated into a caregivers routine.[62] The impact of caregiver burden may lead to less adequate patient support, physical and emotional stress, caregiver burnout, and suboptimal patient outcomes. It is therefore vital

for health professionals to recognise and support caregivers in their role. There is need for studies that examine interventions that reduce caregiver burden in AF. Higher burden scores were significantly associated with caring for frail patients who require frequent office follow up.[33] Therefore, clinical interventions that target the frail AF population should be developed further.

4.7. LIMITATIONS

There is a scarce amount of original research in the area of the role of the caregiver in AF. This review is limited by only including primary research studies available via the identified databases. Studies were only included if published in English language. In spite of these limitations, there is a robust literature that identifies issues germane to caregiving. This review casts the spotlight on some specific issues in AF research that enables the development of effective caregiver support.

4.8. UNDERREPRESENTATION IN RESEARCH

The role of the caregiver and the relationship to health outcomes in AF is underrepresented in clinical research.[63] Data suggest that living alone and poor social support is associated with adverse outcomes. This emphasising the need for looking at elements of caregiver support.[64,65]

AF is associated with functional decline.[28] Frail patients are more unlikely to be prescribed anticoagulation than non-frail patients.[29,66] Similarly; patients with poor self-care are less likely to receive anticoagulation.[29] The need for caregiver assistance in the frail and patients with poor self-care must be carefully considered when making decisions about thromboprophylaxis. Whilst useful in clinical practice, the $CHADS_2$ and CHA_2DS_2-VASc models of risk assessment are limited. Such models do not consider frailty, ability to self-care, or the need for caregiver assistance.[39] The need for caregiver assistance must be carefully assessed when making

complex treatment decisions. The lack of a caregiver may be a factor that influences clinician's behavior when prescribing thromboprophylaxis. Treatment choices must be individualised and best balanced to consider the abilities of the caregiver. Involving the caregiver at the outset in education is essential.

4.9. Implications for Clinical Practice and Research

Health professionals must recognise the pivotal role of caregivers across all care settings. Support strategies for caregivers must be implemented and routinely reviewed to avoid burnout. Many barriers exist for caregivers who seek support. However, caregivers may not always be aware of the various support services on offer. They may not regard the services offered as relevant to meet their needs or the needs of their spouse. Or they may not think that the services are of sufficient quality. Health professionals must gain better understanding of the vital role of the caregiver in AF. The caregiver has an essential role to play in advocacy; family-centered care and shared decision-making around thromboprophylaxis treatment choices. Urgent research is required that examines the role of the caregiver in AF and patient outcomes in greater detail. This will inform recommendations in multidisciplinary clinical practice guidelines in the future which must move to value the role of the caregiver.

AF is a primarily cardio-geriatric condition affecting an elderly population with comorbidities and health disparities.[67] AF frequently co-exists with other chronic conditions including hypertension, chronic heart failure and diabetes.[3,68] It is also associated with cognitive dysfunction, reduced functional abilities[28] and frailty.[66] This population are more likely to need caregiver assistance.[29] Medication regimens are routinely complex, where poly-pharmacy is problematic.[48] Managing these multiple medications can be particularly difficult for those who experience functional and cognitive decline as a consequence of AF.

Caregiving is a complex experience. It is important to assess the individual's needs, social circumstances, networks and community support.[11] Recent research conducted on caregiving in the heart failure population, identified disparities for caregivers in access of support services for caregivers of non-malignant conditions, compared to that of those dying from other conditions such as cancer. The disparities and unmet needs in caregiver support for those with non-malignant conditions, including AF should be examined further.[11]

4.10. CONCLUSION

There is a limited amount of original clinical research that examines the role of the caregiver in individuals with AF. This review highlights that whilst the caregiver role seems to be important, how this role is best utilised has not been best studied and evidence is lacking. Furthermore, patients with AF have a greater need for caregiver assistance and that this need must be considered when making complex decisions on thromboprophylaxis. Patients without caregiver support are less likely to receive anticoagulation. Assessment of caregiver support should be central to patient assessment and care planning. Support from a caregiver may help to improve adherence to treatment regimes. There is ongoing need to include the caregiver in treatment decisions in a paradigm shift towards shared decision-making and promotion of adherence.

4.11. REFERENCES

1. Naccarelli G, Varker H, Lin J, Schulman K. Increasing prevalence of atrial fibrillation and flutter in the United States. *American Journal of Cardiology.* 2009;104:1534-1539.

2. Wong CX, Brooks AG, Leong DP, Roberts-Thomson KC, Sanders P. The increasing burden of atrial fibrillation compared with heart failure and myocardial infarction: A 15 year study of all hospitalisations in Australia. *Archives of Internal Medicine.* 2012;172(9):739-740.

3. Ball J, Carrington M, McMurray JJV, Stewart S. Atrial fibrillation: Profile and burden of an evolving epidemic in the 21st century. *International Journal of Cardiology.* 2013;IN PRESS(XX):XX.

4. Kannel WB, Wolf PA, McGee DL, Dawber TR, McNamara P, Castelli WP. Systolic Blood Pressure, Arterial Rigidity, and Risk of Stroke: The Framingham Study. *JAMA.* 1981;245(12):1225-1229.

5. Gattellari M, Goumas C, Aitken R, Worthington JM. Outcomes for patients with Ischameic Stroke and Atrial Fibrillation: The PRIMS Study (A Program of Research Informing Stroke Management). *Cerebrovascular Diseases.* 2011;32(370-382).

6. Khan M, Ahmed B, Ahmed M, et al. Functional, cognitive and psychological outcomes, and recurrent vascular events in Pakistani stroke survivors: A cross sectional study. *BMC Research Notes.* 2012;5.

7. Kang X, Li Z, Nolan M. Informal Caregovers' Experiences of Caring for Patients With Chronic Heart Failure. *Journal of Cardiovascular Nursing.* 2011;26(5):386-394.

8. Funk L, Chappell N, Liu G. Associations between filial responsibility and caregiver well-being: are there differences by cultural group? *Research on Aging.* 2013;35(1):78-95.

9. The National Alliance for Caregiving in collaboration with AARP. Caregiving in the US. http://www.caregiving.org/data/Caregiving_in_the_US_2009_full_report.pdf2009:1-79.

10. Evercare by United Healthcare. *The Evercare Survey of The Economic Downturn and its Impact on Family Caregiving: Report of Findings.* http://www.caregiving.org/data/EVC_Caregivers_Economy_Report%20FINAL_4-28-09.pdf2009.

11. Davidson PM, Abernethy AP, Newton PJ, Clark K, Currow DC. The caregiving perspective in heart failure: a population based study. *BMC Health Services Research.* 2013;13(342).

12. Grey M, Knafl K, McCorkle R. A framework for the study of self- and family management of chronic conditions. *Nursing Outlook.* 2006;54(5):278-286.

13. Lip GYH. Implications of the CHA2DS2-VASc and HAS-BLED scores for thromboprophylaxis in atrial fibrillation. *The American Journal of Medicine.* 2011;124:111-114.

14. Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation. *Circulation.* 2006;114(7):e257-e354.

15. European Society of Cardiology. Guidelines for the management of atrial fibrillation. *European Heart Journal.* 2010;31:2369-2429.

16. National Institute for Clinical Excellence. Atrial Fibrillation. The management of atrial fibrillation. *National Institute for Clinical Excellence.* 2006.

17. Singer D, Albers G, Dalen J, Go A, et al. Antithrombotic Therapy in Atrial Fibrillation: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest.* 2004;126(3):429S.

18. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Updating the 2006 Guideline): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;123(1):104-123.

19. Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. *European Heart Journal.* 2012;33:2719-2747.

20. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and Management of the Vitamin K Antagonists. *Chest.* 2008;133(6 suppl):160S-198S.

21. Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. Atrial fibrillation: Stroke prevention in focus. *Australian critical care : official journal of the Confederation of Australian Critical Care Nurses.* 2013.

22. World Health Organisation. *Adherence to Long Term Therapies: Evidence for Action.* Geneva, Switzerland: World Health Organisation;2003.

23. Haynes R, Ackloo E, Sahota N, McDonald H, Yao X. Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews.* 2008(2).

24. O'Connor PJ. Improving Medication Adherence: Challenges for Physicians, Payers and Policy Makers. *Archives of Internal Medicine.* 2006;166(17):1802-1804.

25. Mahtani K, Heneghan C, Glasziou P, Perera R. Reminder packaging for improving adherence to self-administered long-term medications. *Cochrane Database of Systematic Reviews.* 2011(9).

26. Reynolds MR, Shah J, Essebag V, et al. Patterns and Predictors of Warfarin Use in Patients With New-Onset Atrial Fibrillation from the FRACTAL Registry. *The American Journal of Cardiology.* 2006;97(4):538-543.

27. Fang MC, Go AS, Chang Y, et al. Warfarin Discontinuation After Starting Warfarin for Atrial Fibrillation. *Circulation: Cardiovascular Quality & Outcomes.* 2010;3(6):624-631.

28. Marzona I, O'Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with atrial fibrillation: results of the ONTARGET and TRANSCEND studies. *Canadian Medical Association Journal.* 2012.

29. Chen S-Y, Vanderpoel J, Mody S, et al. Caregiver assistance among medicare beneficiaries with atrial fibrillation and factors associated with anticoagulant treatment. *American Journal of Geriatric Pharmacotherapy.* 2012;10(5):273-283.

30. Appelboam R, Thomas EO. Warfarin and intracranial haemmorhage. *Blood Reviews* 2009;23:1-9.

31. Sjoblom L, Hardemark HG, Lindgren A, et al. Management and prognostic features of intracerebral hemmorhage during anticoagulant therapy: a Swedish multicentre study. *Stroke.* 2001;32:2567-2574.

32. Lackie CL, Garbarino KA, Pruetz JA. Warfarin therapy for atrial fibrillation in the elderly. *Annals of Pharmacotherapy.* 2002;36(2):200-204.

33. Coleman CI, Coleman SM, Vanderpoel J, et al. Factors associated with 'caregiver burden' for atrial fibrillation patients. *International Journal of Clinical Practice.* 2012;66(10):984-990.

34. Ho P, Bryson C, Rumsfeld J. Medication Adherence. *Circulation.* 2009;119(23):3028-3035.

35. Osterberg L, Blaschke T. Adherence to Medication. *New England Journal of Medicine.* 2005;353(5):487-497.

36. Brown T, Siu K, Walker D, Pladevall-vila M, Sander S, Mordin M. Development of a conceptual model of adherence to oral anticoagulants to reduce risk of stroke in patients with atrial fibrillation. *J Manag Care Pharm.* 2012;18(5):351-362.

37. Hendriks JML, deWit R, Crijns HJGM, et al. Nurse-led care vs usual care for patients with atrial fibrillation. *European Heart Journal.* 2012;33:2692-2699.

38. Berti D, Hendriks JML, Brandes A, et al. A proposal for interdisciplinary, nurse-coordinated atrial fibrillation expert programmes as a way to structure daily practice. *European Heart Journal.* 2013;34:2725-2730.

39. Ferguson C, Inglis S, Newton P, Middleton S, Macdonald P, Davidson P. Atrial fibrillation and thromboprophylaxis in heart failure: the need for patient-centrered approaches to address adherence. *Vascular Health & Risk Management.* 2013;9:1-9.

40. Tang E, Lai C, Lee K, Wong R, Cheng G, Chan T. Relationship between patient's warfarin knowledge and anticoagulation control *The Annals of Pharmacotherapy* 2003;37(34-39).

41. Bockwoldt D. Antithrombosis Management in Community-Dwelling Elderly: Improving Safety. *Geriatric Nursing.* 2010;31(1):28-36.

42. Bajorek BV, Ogle SJ, Duguid MJ, Shenfield GM, Krass I. Management of warfarin in atrial fibrillation: Views of health professionals, older patients and their carers. *Medical Journal of Australia.* 2007;186(4):175-180.

43. Bereznicki LR, Peterson GM, Jackson SL, Jeffrey EC. The risks of warfarin use in the elderly. *Expert Opinion on Drug Safety.* 2006;5(3):417-431.

44. Dolor RJ, Ruybalid RL, Uyeda L, et al. An evaluation of patient self-testing competency of prothrombin time for managing anticoagulation: pre-randomization results of VA Cooperative Study #481-The Home INR Study (THINRS). *Journal of Thrombosis and Thrombolysis.* 2010:1-13.

45. Horstkotte D, Piper C. Improvement of oral anticoagulation therapy by INR self-management. *Journal of Heart Valve Disease.* 2004;13(3):335-338.

46. Hylek E. Oral anticoagulants: Pharmacological issues for use in the elderly. *Clinics in Geriatric Medicine.* 2001;17(1):1-13.

47. Lip GYH, Tse H. Management of atrial fibrillation. *Lancet.* 2007;370:604-618.

48. Murray MD, Morrow DG, Weiner M, et al. A conceptual framework to study medication adherence in older adults. *The American Journal of Geriatric Pharmacotherapy.* 2004;2(1):36-43.

49. Rose AJ, Hylek EM, Ozonoff A, Ash AS, Reisman JI, Berlowitz DR. Patient characteristics associated with oral anticoagulation control: results of the Veterans AffaiRs Study to Improve Anticoagulation (VARIA). *Journal of Thrombosis and Haemostasis.* 2010;8(10):2182-2191.

50. Patterson S, Hughes C, Kerse N, Cardwell C, Bradley M. Interventions to improve the appropriate use of polypharmacy for older people (Review). *Cochrane Database of Systematic Reviews.* 2012(5):1-81.

51. Lip GYH. The balance between stroke prevention and bleeding risk in atrial fibrillation: A delicate balance revisited. *Stroke.* 2008;39:1406-1409.

52. Devereaux PJ, Fahey T, Anderson DR, et al. Differences between perspectives of physicians and patients on anticoagulation in patients with atrial fibrillation: observational studyCommentary: Varied preferences reflect the reality of clinical practice. *BMJ.* 2001;323(7323):1218.

53. Forman DE, Rich MW, Alexander KP, et al. Cardiac care for older adults: Time for a new paradigm. *Journal of the American College of Cardiology.* 2011;57(1801-10).

54. Abdelhafiz AH. A review of anticoagulation with warfarin in patients with nonvalvular atrial fibrillation. *Clinical Therapeutics.* 2001;23(10):1628-1636.

55. Johnston JA, Cluxton Jr RJ, Heaton PC, Guo JJ, Moomaw CJ, Eckman MH. Predictors of warfarin use among Ohio Medicaid patients with new-onset nonvalvular atrial fibrillation. *Archives of Internal Medicine.* 2003;163(14):1705-1710.

56. Dudley N. Importance of risk communication and decision making in cardiovascular conditions in older patients: A discussion paper. *Quality in Health Care.* 2001;10(SUPPL. 1):i19-i22.

57. Milte CM, Ratcliffe J, Davies O, Whitehead C, Masters S, Crotty M. Family meetings for older adults in intermediate care settings: the impact of patient cognitive impairment and other characteristics on shared decision making. *Health Expectations.* 2013:n/a-n/a.

58. Ismail H, Lewin RJ. The role of a new arrhythmia specialist nurse in providing support to patients and caregivers. *European Journal of Cardiovascular Nursing.* 2013;12(2):177-183.

59. McCabe PJ, Schumacher K, Barnason SA. Living with atrial fibrillation: A qualitative study. *Journal of Cardiovascular Nursing* 2011;26(4):336-344.

60. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GYH. Underuse of Oral Anticoagulants in Atrial Fibrillation: A Systematic Review. *The American Journal of Medicine.* 2010;123:638-645.

61. Schulz R, Beach SR. Caregiving as a risk factor for mortality: The caregiver health effects study. *JAMA.* 1999;282(23).

62. James M. An analysis of the use of a point-of-care system for international normalized ratio testing in remote areas of Canada: A literature review. *Point of Care.* 2008;7(1):34-37.

63. Berg AM. Dabigatran compared with warfarin for stroke prevention in atrial fibrillation. *Annals of Internal Medicine.* 2011;154(8):570.

64. Perissinotto CM, Cenzer IS, Covinsky KE. Loneliness in Older Persons. *Archives of Internal Medicine.* 2012;172(14):1078-1083.

65. Udell JA, Steg PG, Scirica BM, et al. Living Alone and Cardiovascular Risk in Outpatients at Risk of or With Atherothrombosis. *Archives of Internal Medicine.* 2012;172(14):1086-1095.

66. Perera V, Bajorek BV, Matthews S, Hilmer SN. The impact of frailty on the utilisation of antithrombotic therapy in older patients with atrial fibrillation. *Age and Ageing.* 2009;38:156-162.

67. Murphy NF, Simpson CR, Jhund PS, et al. A national survey of the prevalence, incidence, primary care burden and treatment of atrial fibrillation in Scotland. *Heart.* 2007;93(5):606-612.

68. Smit MD, Moes ML, Maass AH, et al. The importance of whether atrial fibrillation or heart failure develops first. *European Journal of Heart Failure.* 2012.

CHAPTER 5: BARRIERS AND ENABLERS TO ANTICOAGULATION IN HEART FAILURE WITH ATRIAL FIBRILLATION: PATIENT, PROVIDER & HEALTH SYSTEM PERSPECTIVES.

5.1. CHAPTER PREFACE

Publication Reference:

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Chapters two, three and four explored the previous literature on AF. Chapters five, six and seven provide new insights and are based on primary research findings.

This chapter complements Chapter three which offered solution focused approaches to thromboprophylaxis in order to address issues of adherence. This chapter presents an article in its original form, submitted to the journal *Drugs & Aging*, currently undergoing peer review.

Background:

Chronic heart failure (CHF) and atrial fibrillation (AF) commonly coexist and are associated with increased stroke risk and mortality. Oral anticoagulation significantly reduces stroke risk and improves outcomes. Yet, in approximately 30% of cases thromboprophylaxis is not commenced for a variety of reasons.

Aim of the study:

The purpose of this study was to elucidate the barriers and enablers to thromboprophylaxis in individuals with CHF with concomitant AF from the perspective of patients, providers and health systems.

Data from face to face individual interviews with patients and information retrieved from healthcare file note review documented the clinician perspective. This study is a synthesis of the two data sources, obtained during patient clinical assessments as part of the AFASTER Study.

Summary of the results:

Patient choice and preference were important factors in thromboprophylaxis decisions, including treatment burden, unfavourable or intolerable side effects and patient refusal. Financial barriers included cost of travel, medication cost and reimbursement. Psychological factors included psychiatric illness, cognitive impairment and depression. Social barriers included homelessness and the absence of a caregiver or lack of caregiver assistance. Clinician reticence included fear of falls, frailty, age, fear of bleeding and the challenges of multi-morbidity. Facilitators to successful prescription and adherence were caregiver support, reminders and routine, self-testing and the use of technology.

Many complex barriers remain to patients receiving thromboprophylaxis. Shared decision-making allows clinicians to consider patients values, attitudes and beliefs towards thromboprophylaxis.

Implications:

- Thromboprophylaxis remains underused in clinical practice for patients with CHF and concomitant AF.
- Perceived barriers to thromboprophylaxis should be thoroughly scrutinised by clinicians to ascertain if prescription is possible.
- Clinicians must adopt person-centered models of care. Shared decision-making allows clinicians to consider patients values, attitudes and beliefs towards thromboprophylaxis. Including these factors alongside risk versus benefit ratios may assist in improving issues of adherence.
- The caregiver in thromboprophylaxis management is under-recognised in practice.
- Clinicians need to better understand the role of the caregiver and routine in assisting to improve adherence to prescribed therapies.

5.2. BACKGROUND

Chronic heart failure (CHF) and atrial fibrillation (AF) commonly coexist and are associated with high mortality and risk of stroke.[1] CHF and AF primarily affect older adults.[2,3] Consequently, stroke risk increases with age.[4] Thromboprophylaxis reduces stroke risk; yet, in approximately 30% of cases treatment is not initiated for a range of reasons.[5] Decisions to initiate thromboprophylaxis balance a range of factors, including stroke and bleeding risk, previous comorbidities and age. Prior to commencement of thromboprophylaxis, a detailed assessment should occur. This must include careful assessment of comorbidity, the potential for treatment adherence, frailty, and cognitive and functional ability, and social supports including caregiver support.[6,7] In the elderly, rates of frailty, functional and cognitive dysfunction are more pronounced. Despite international guidelines advocating the use of validated stroke and bleeding risk stratification tools (*such as CHA_2DS_2VASC and HAS-BLED schemata*), and clear consensus treatment algorithms; clinical factors particularly advancing age and frailty continue to be deterrents to optimal anticoagulant use.[8,9] Adherence to thromboprophylaxis at the patient level is complex and this may be due to treatment regimens, dosing schedules and a number of sociocultural and economic factors.[10]

Shared decision-making is a process whereby clinicians, patients and their caregivers mutually, actively participate in making healthcare treatment decisions. This involves careful, but balanced discussions regarding risks and benefits of treatment options, and considering the individual patient's values, beliefs, preferences and own circumstances.[11] Patients and caregivers must be central to thromboprophylaxis treatment decision-making.[7,12] Creating mutually acceptable, shared treatment choices, has the potential to positively impact on adherence to prescribed treatment regimes.

5.3. AIMS & OBJECTIVES

This paper aimed to elucidate the barriers and enablers to thromboprophylaxis in individuals with CHF with concomitant AF from the perspective of patients, providers and health systems. This was achieved through an integrated synthesis of interviews and field notes collected during a 6-month cohort study, presented within chapter 7 of this thesis.

5.4. METHOD

5.4.1. DATA SOURCES, DESIGN AND SETTING

Two primary data sources were included: 1) Patient interviews during bedside clinical assessments; 2) Healthcare file note review provided a written clinician perspective. This study is a synthesis of the two data sources, obtained during patient clinical assessments as part of the *Atrial Fibrillation And Stroke Thromboprophylaxis in hEart failure* (AFASTER) Study. This study was conducted at a single site, tertiary metropolitan referral hospital in Sydney, Australia.

5.4.2. PARTICIPANTS

Screening was conducted on a daily basis by a nurse researcher. Prospective consecutive participants with CHF and concomitant AF of any type and aetiology, consistent with international guidelines,[13,14] admitted to a cardiology ward were enrolled in the over-arching cohort study between April – October 2013. Exclusion criteria were < 18 years of age or AF due to reversible causes, such as thyrotoxicosis. Socio-demographic data and clinical characteristics were assessed at index hospitalisation. A sample of 137 patients with CHF and concomitant AF were included in the cohort study. Data were generated from researcher field notes. These were obtained from both healthcare records and quotes transcribed during assessments with participants. Data were analysed and framed within the WHO's Multidimensional model of medication adherence.[15] The findings were supported and augmented with existing scholarly literature.

5.4.3. ETHICAL CONSIDERATIONS

The *Atrial Fibrillation And Stroke Thromboprophylaxis in hEart failure* (AFASTER) study was approved by the hospital and university human ethics committees. Data included in this sub-study are an analysis of field notes collected during patient clinical assessments as part of the AFASTER cohort study. Consent was waived for baseline data collection as part of the over-arching cohort study to reduce selection bias. An opt-out approach to consent to adopted. Participants were free to withdraw at any stage of the study. Interviews were conducted in the clinical area. Protection of data confidentiality was ensured through the de-identification and secure storage of participant records.

5.4.4. INTERVIEW SCHEDULE

A standardised format was followed during the clinical assessments. A therapeutic relationship was established with each participant. Routinely asked open-ended questions included:

1. What helps you to remember to take your warfarin?
2. Tell me about your warfarin, how do you get your International Normalised Ratio (INR) checked?
3. Do you ever forget to take your medication? Tell me more about this.
4. Do you ever get any bleeding with warfarin?

5.5. DATA ANALYSIS

Responses to open-ended questions were documented during the interview and immediately following assessments in a standardised format using the four questions above. Additional data were generated from researcher field notes and healthcare records that explained clarified and elucidated responses and also juxtaposed clinician and patient views. Data were analysed using qualitative thematic analysis. Emergent themes were framed within the WHO's Multidimensional model of medication adherence. Themes were synthesised with existing literature. Narrative inquiry was used to greater understand individuals' reasoning processes. Narrative inquiry uses stories, conversations, interviews, family stories, and life experiences, as the units of analysis to research and understand the way people create meaning in their lives as narratives.[16] This method allowed for the characterisation of factors where improving patient involvement may lead to better outcomes.

5.6. RESULTS

5.6.1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

A total of 137 participants were enrolled in the cohort study. Mean age was 72 years (SD 16), range 19 – 94 years, mostly male (65%), and 28% lived alone. Participants were primarily NYHA class II – III (62%), mean LVEF was 43% (SD 19.), and most participants were identified as having permanent AF. Mean Charlson Comorbidity Index Score = 3.9 (SD 2.1), mean CHA_2DS_2VASc Score = 4.3 (SD 1.9), Mean HASBLED Score = 2.9 (SD 1.6). Mean number of medications on discharge = 10 (SD 3.9).

Frailty assessments were obtained on 92 participants using the SHARE Frailty Index, 63% (n=58) were assessed as frail. Thromboprophylaxis information was obtained upon electronic prescription summary:

58% (n=77) were prescribed warfarin

41% (n=55) were prescribed an antiplatelet

5% (n=5) were prescribed a novel anticoagulant

TABLE 5.1 KEY BARRIERS FROM THE PERSPECTIVE OF THE PATIENT, PROVIDER & HEALTH SYSTEM

Results: Key barriers to thromboprophylaxis
• Burden of routine monitoring is unfavourable or intolerable • Cannot afford medication or travel to clinic or appointments • Homelessness • Psychiatric illness • Patient refusal • Fear of falls • Frailty • Fear of bleeding • Clinician apprehension • Age • Cognitive impairment • Multi-morbidity • Lack of caregiver assistance • Depression • End-of-life considerations

Results were summarised below within the five dimensions to the World Health Organisation's multidimensional adherence model. These included socioeconomic, health care system, condition, treatment and patient related factors.[15]

5.6.2. TREATMENT-RELATED FACTORS

Familiarity of burden

During the participant clinical assessments, the burden of warfarin was immediately recognisable. One patient exclaimed ... *"It's a nuisance!"* – referring to warfarin therapy. This combined with the often lifetime duration of therapy increases the complexity of issues of adherence and compliance. Conversely, a 90-year old gentleman explained: *"Aww I've been taking it* [warfarin] *for over 20 years now, so I suppose I'm used to it"* (0069). This helps to understand, that with time patients may become more familiar with their therapy, requirements for routine testing and dose adjustment as treatment endures.

Carelessness with adherence to treatment requirements

Some patients admitted non-adherence to treatment requirements, such as having regular INR testing when indicated: *"I get my bloods checked every 2 – 3 weeks, I know I should go more though, you know"* (0069) and another… *"I've got to admit I'm a bit slack on the INR testing"* (0056). Further, a 74-year old male patient explained about how he was careless at times when managing his medications at home: *"Sometimes I take 1 – 2 weeks to refill my scripts, just for the non-essential ones, you know"* (0058). Yet, in contrast, some patients found self-monitoring, including point of care testing helpful. *"I go to my GP weekly for my finger prick test"* (0045). Patient self-testing was also found to be useful with younger patients. *"I take it* [INR] *twice a week at home. My GP recommended I purchase"* – Referring to INR self-checking and device purchase (0119) - 20 year old female patient. Studies have shown patients and caregiver can successfully be trained in INR self-testing in approx. 2 – 4 weeks,[17] highlighting that all patients should be given the opportunity to learn how to self-test, and if competent should be given the opportunity to continue with home self-testing.[17] Patient self-management has been found to

lead to more stable anticoagulant therapy and subsequently lower rates of adverse stroke and bleeding events.[18]

5.6.3. SOCIO-ECONOMIC FACTORS

Financial burden

Financial factors, such as hardship may impact patient adherence to thromboprophylaxis. These include funding frequent travel to clinics, for check-ups and routine blood tests.[10] A 79-year-old female patient explained how she was able to obtain support from a government scheme: *"It's expensive to travel to all the appointments, but my GP got me these cab-charge things, you get half of your fare paid, which is handy"* (0020). Cost-related medication non-adherence (CRN) is a common problem, particularly for the elderly within multi-morbidity, often on complex medication regimes. In our cohort, the mean number of prescribed medications was 10.

5.6.4. CONDITION-RELATED FACTORS

Mental health considerations

Adherence within the context of chronic heart failure in the setting of psychiatric disorder is complex. Current initiatives and guidelines do not consider this. A physician documenting in a patient's medical record with a history of schizophrenia writes: *"Refuses to take regular medications, only takes frusemide"* (0107). When this patient was asked about how he manages his medications at home and medication adherence, he replied, *"They are trying to poison me, you know!"* (0107). The clinical assessment was ceased following this statement and the participant not deemed suitable for inclusion in the cohort study. This patient was later readmitted to hospital and found to be in decompensated heart failure secondary to poor medication compliance. Issues of medication non-adherence in CHF & AF and mental illness

are neither well-understood nor managed in clinical practice. This is similar to research by Walker *et al* (2011) who found that patients with mental health conditions and AF were less likely to have adequate management for their AF than those without.[19] Individually tailored environmental supports can improve medication adherence and outcomes in patients with mental health conditions.[20] Further research is urgently needed to direct interventions to improve care for those with AF and mental health conditions.

Depression and adherence

A nursing note entry in a patient's health record stated: *"patient saying doesn't want medications, wants to sleep, and wants to die".* A subsequent medical entry further detailed... *"Depressed mood – wants to go home. Refusing medications, Plan: Palliative care review"* (0141)

In the setting of coronary heart disease, depression is associated with medication non-adherence.[21] However, systematic review evidence demonstrates that the relationship between depression and medication adherence in CHF is inconsistent.[22] The above participant was not prescribed anticoagulation upon discharge. The moral and ethical considerations regarding the continuation of thromboprophylaxis during end-of-life are difficult. Treatment with warfarin may be deemed futile and minimising the number of medications prescribed and achieving comfort may be the most appropriate care goals. This patient later was transferred to hospice care and passed away with the support of the palliative care service. Understanding and balancing a patient's needs and wants is important and this is an essential component in making treatment choices and shared decision-making around thromboprophylaxis, and toward achieving person-centered care.

5.6.5. HEALTH-SYSTEM RELATED FACTORS

Frailty and fears of falls

Functional decline is a common consequence of both CHF and AF.[23] A study by Bajorek *et al* (2002) identified that warfarin was being withheld in AF patients > 80 years for reasons other than recognised contraindications and is potentially underused in this target population.[24] In our study, a medical officer details his rationale for non-prescription due to frailty and age. *"Although scoring 3 on $CHADS_2$ (CHF, Hypertension & Age) given her age, frailty and previous GI bleed it was felt that in her case risks would outweigh benefits of anticoagulation, thus she was commenced on clopidogrel alone (vague history of GI bleed on aspirin)."* 94-year-old female patient with supportive family, seeking respite care on discharge from hospital (0125).

Olesen et al (2011) emphasises that with advanced ageing, the risk of stroke increases and oral anticoagulation should not be avoided in elderly patient because of concerns regarding bleeding risk and age alone.[25-27] The authors highlight that the decision to anticoagulate should always be based on careful evaluation of the balance between stroke risk vs. bleeding risk. During a review of medications, documented on a discharge summary: *"Warfarin ceased this admission due to high falls risk and malignancy. Commenced on aspirin."* (0124) An 84-year-old female patient.

Sellers *et al* (2011) suggest that an elderly patient taking warfarin would have to experience approximately 300 falls per year for the risk of bleeding complications from falling to outweigh the benefits for prevention of embolic stroke. This finding emphasises that clinician education is needed with regard to the actual risk that falls pose to patients receiving thromboprophylaxis.[28] Similar research conducted by Man-Son-Hing et al (1999) determined that patients taking warfarin must fall approximately 295 times in a year for warfarin not to be optimal therapy.

These authors suggested that a patient's propensity to fall should not be an important factor in decision making on thromboprophylaxis.[29] Yet, the myth of falls as a factor to withhold thromboprophylaxis, and that the risk of bleeding in this scenario would outweigh the benefits, remains in clinical practice today, as demonstrated from the quote provided above.

In a large real-world cohort study (Olesen *et al*, 2011) investigating the use of aspirin and oral anticoagulation in patients with AF, Olesen and co-authors reported that aspirin was not protective at any level of stroke risk, and was not safe or effective for stroke prevention in AF. [25] To this point, the now focused update of the ESC Guidelines for the management of AF (Camm *et al*, Euro Heart Rhythm Association, 2012) advocate that *"The evidence for effective stroke prevention with aspirin in AF is weak, with a potential for harm"* and "*given the availability of NOACs, the use of antiplatelets for stroke prevention in AF should be limited to the few patients who refuse any form of oral anticoagulation*". A study conducted by Perera *et al* (2010) identified that frail older people with AF are significantly less likely to receive warfarin than non-frail. Elderly frail people with AF appear to be more vulnerable to adverse clinical outcomes with and without thromboprophylaxis.[9]

Fears of bleeding

Bleeding remains the most feared adverse event amongst clinicians when making decisions about thromboprophylaxis choice in AF.[30] The biggest fear is that of massive catastrophic haemorrhage, particularly intracranial or gastro-intestinal, with associated increased morbidity and mortality. Documented in a letter by cardiologist regarding a male patient: *"He is not on warfarin because of GI bleeding which is related to the cancer. He is not keen to be re-trialled with it"*. Further – Cardiologist, Jan 2013 *"I am not keen to have him on warfarin or dabigatran because of significant bleeding from warfarin in the past and the dangers associated with dabigatran, which has made us a lot less interested in using it over the past 12 months."*

5.6.6. PATIENT-RELATED FACTORS

Cognitive Dysfunction

Cognitive dysfunction is a common consequence of AF and CHF.[23,31,32] This may be an effect of micro thrombi, hypo-perfusion or other pre-existing health condition such as dementia. A MMSE score <23 is independently associated with suboptimal INR control and likely poor time in therapeutic range (TTR).[33] This needs to be considered when making judicious treatment decisions about thromboprophylaxis in this primarily elderly population. Cognitive dysfunction is a complex challenge for those whom clinicians seek to treat with thromboprophylaxis and often the cooperation and support of caregivers is vital to making decisions in this circumstance. The Montreal Cognitive Assessment (MOCA) is a valuable tool to identify patients with AF who may need additional support to maintain optimal TTR and effective anticoagulation control.[34]

During our medical file reviews, a clinician documented in the notes of this 88-year-old lady who lived alone: *"Refuses to use medication aide. Has a history of mild cognitive impairment."* The patient explained further when assessed... *"I like to know what each one is for. I put the next day's one out"*.... Stating... *"I never forget!... now what's my routine..."* (0117). This highlights the complexity of the situation. Familiarity and routine are important factors in medication taking. Evidence supports that living alone is a risk factor for increased morbidity and mortality.[35] Medication aides are helpful, however may not be suitable for everyone.

Current guidelines neglect to address the complexity of multi-morbidity. AF is unlikely to be a singular health complaint in a geriatric population. Patients with AF are likely to be elderly with multiple comorbidities. Given that AF risk increases with age, guidelines must move to address the issue that AF often exists with other conditions. There are limited interventions that provide support for patients with AF and cognitive dysfunction to adequately manage their

anticoagulation. Novel oral anticoagulants may offer promise for this population, as use of these drugs would minimise the need for routine monitoring and dose adjustment.

Visual Impairment

When this patient was asked about barriers to chronic heart failure self-management, specifically monitoring a daily weight; in response to the question of "*Do you weigh yourself every day?"*, she replied *"I have macular degeneration and I can't see the numbers!"* (0120). Similarly, this was thought to be an issue when managing her medications. Older people are more likely to experience age-related changes such as impaired vision and manual dexterity issues when opening (*often difficult*) childproof medication packaging.[36]

Social support

Homelessness

Clinicians frequently documented their rationale for the non-prescription of thromboprophylaxis in the setting of AF and CHF. A physician of a 65-year-old homeless man detailed a consultation with a patient in his medical record: "*Warfarin and Clexane* [Enoxaparin] *have been ceased following consultation with patient X re: likelihood of medication compliance. Patient happy not to continue with anticoagulant therapy."* (0054). Homelessness creates a challenge for the healthcare system and how we provide primary care services to the vulnerable. Homeless people are not often able to rest or recover, nor able to find a safe place to store and manage their vital medications. Continuity of care is problematic. Many of our current systems fail to meet the needs of the homeless with AF and care is well below standard.[37] Homelessness should not be a barrier to thromboprophylaxis in 2014. This emphasizes the need to develop innovative management strategies that are individually tailored to meet the needs of patients.

Caregiver role

The role of the caregiver is under recognised by healthcare professionals in clinical practice.[7] Caregivers play a vital role in supporting patients with AF, particularly those who may have functional decline or cognitive dysfunction as a consequence of their AF. During the assessments an 83-year-old man explained how he relies on his sister for support when managing his medications at home and how this is important for him: *"My sister looks after all that, if it was up to me I'd have to put a big sign up to remember"* (0112). Caregivers play an important role in thromboprophylaxis management. Examples of caregiver assistance range from verbal reminders transport to refill prescriptions and attend anticoagulation clinics, to physical assistance to read medication bottles and take tablets. Further to this, the importance of caregiver respite was highlighted. *"If my sister goes away, I get the respite. I get Meals on Wheels then"* (0112). Davidson *et al* (2013) identified that there is significant burden placed on caregivers of people with non-malignant conditions, caring for individuals in the community over extended periods.[38] Health professionals must recognise this burden, and develop family and person centered interventions to address and reduce burden.

Importance of routine and reminders

Many patients highlighted the theme of developing and maintaining routine and reminder systems. An 87-year-old female patient highlighted the importance of routine in self-care management: "It's habit. Every morning I just check my blood pressure" (0109). Caregiver assistance in medication management and routine was explained in more detail: "*Once a week, Sunday morning – my husband helps me refill my dosett box" "XXX helps me remember" "Me and XXX do it on a Sunday morning, he helps me sort the tablets out the boxes into the thing" "XXX helps me remember"* (0092). *"First I put the plants in vases, then the tablets and make the porridge and then the swim*" – highlighting the importance of routine in assisting with medication adherence. 72-years-old lady; still manages to swim 5 times per week in the morning (0108).

Technology to assist with reminder and adherence to medication regimes was found to be helpful by this 74-years-old female patient. *"The kids have set an alarm on that thing twice a day for me"* – refers to her smartphone (0113). *"You got to have a system, or else you'd be doubling up on lots*" (0118) – highlighting the importance of developing a 'system' and a routine in medication taking. Systematic review data suggest that interventions that include convenient care, information, reminders, self-monitoring, reinforcement, counselling, family or psychological interventions, telephone follow up or supportive care, or a combination of the aforementioned may be effective for long term care, such as in AF . However, these interventions have been shown to produce at best modest improvements in adherence or treatment outcomes.[39]

5.7. DISCUSSION

The results of this study are similar to research conducted by Eapen et al (2014), whereby one third of eligible patients with CHF and AF were not prescribed warfarin therapy at discharge from a heart failure hospitalisation.[5] A systematic review conducted by Ogilvie et al (2010) report oral anticoagulation treatment levels below 60% (range 19 – 81%) and demonstrates the underuse of OAC therapy for patients with an elevated stroke risk.[40]

A recent systematic review highlights that nurse managed protocols are effective in the outpatient management of a range of chronic conditions including diabetes, hypertension and hyperlidipaemia. A nurse-led intervention was associated with improvement in biomarkers including a decrease in 0.4% of HbA1c in diabetes, a reduction in SBP of 3.68mmHg and DBP of 1.56mmHg in hypertension management, and a decrease of total cholesterol by 0.24 mmol/L and LDL cholesterol by 0.31 mmol/L.[41]

Further, nurse-led models of care in AF have also shown promise. A recent RCT in Europe examined nurse-led care intervention of protocol-based, software supported integrated chronic care, supervised by a cardiologist. This innovative model of care was superior to usual care, with decreased rate of hospitalization and mortality.[42] These findings further support a team approach that adopts nurse-managed protocols can have positive effects on the management of individuals with chronic diseases including diabetes, hypertension, hyperlipidemia and atrial fibrillation. Developing nurse-led programs appears to be an innovative method of optimizing access for patients with clinicians. Nurse-led chronic care models have the opportunity to improve self-management, and fully engage the individual and their caregiver in the shared-decision making process.[7]

5.8. PATIENT PREFERENCE, CHOICE AND SHARED DECISION-MAKING

Results from a study conducted by Dantas et al (2004) identified that patients have limited input into the decision to commence thromboprophylaxis, and that patients lack understanding of the risks and benefits associated with treatment.[43] Patients prefer treatment discussions to include individual risk-based information, in contrast to generic population risk-based information.[44] Empowering patients to make informed decisions based on risks and benefits stands to improve patient knowledge about treatment.[11] Previous research has highlighted both the condition and treatment knowledge deficit that exists for patients receiving anticoagulation.[45] Knowledge insufficiency is often a determinant itself of poor time in the therapeutic range. Clinicians need to thoroughly explain the risks and benefits of each treatment. An individual risk profile should be presented to the patient, and tailored and presented in a way to the patient, whereby the information is meaningful and understood. Pictorial faces and images may be helpful to describe risk to those with limited health literacy.[46] This may improve patients and caregivers knowledge and empower them to make informed decisions about available treatment choices. Taking time to understand patient values and preferences towards treatments is essential and should not be overlooked. This may help to increase adherence to treatment regimes.[12]

5.9. LIMITATIONS

This study has some limitations. Firstly, the majority of the quotes selected for inclusion in this paper originated from informal bedside interviews, whilst conducting clinical assessments as part of a larger cohort study. Whilst the interviews were not audiotaped, or transcribed verbatim, this is a pragmatic method of data collection in healthcare research.[47] The use of field notes documented during or immediately post interview has previously been reported as having greater importance and utility, than the sole use of audiotaping and verbatim transcription.[47] Though the researcher attempted to create an open environment and ask standardised questions, there may have been bias introduced in how the questions were delivered. However, the quotes

obtained were transcribed during the assessment and field notes about the assessment were gathered and taken immediately post assessment. The researcher reflected on these data and augmented the findings with supporting existing literature. This study reflects a contemporary narrative of the barriers and enablers to thromboprophylaxis for patients with CHF and AF.

5.10. CONCLUSION

CHF and AF are burdensome conditions that habitually coexist. In this study, warfarin was the most frequently used type of thromboprophylaxis and this remains a problematic drug for many clinicians, patients and caregivers. Almost one third of participants were not prescribed thromboprophylaxis on discharge from hospital. The results of this study suggest that there remain many barriers to patients receiving thromboprophylaxis. Concerns remain amongst clinicians with regards to falls and bleeding events. The barriers highlighted in this sub-study were frailty, age, cognitive dysfunction, homelessness, mental illness, vision impairment, and depression. Facilitators to successful prescription and adherence were caregiver support, reminders and routine, self-testing and the use of technology.

5.11. REFERENCES

1. Lau YC, Lane DA, Lip GYH. Atrial Fibrillation and Heart Failure: A Bad Combination. *The American journal of cardiology.* 2014.

2. Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham Study. *J Am Coll Cardiol.* 1993;22(4 Suppl A):6a-13a.

3. Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). *The American Journal of Cardiology.* 1994;74(3):236-241.

4. Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. *Am J Cardiol.* 1998;82(8a):2n-9n.

5. Eapen ZJ, MI X, Qualls LG, et al. Adherence and persistence in the use of warfarin after hospital discharge among patients with heart failure and atrial fibrillation. *Journal of Cardiac Failure.* 2014;20(1):23-30.

6. Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. Atrial fibrillation and thromboprophylaxis in heart failure: the need for patient-centered approaches to address adherence. *Vascular health and risk management.* 2013;9:3-11.

7. Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. The caregiver role in thromboprophylaxis management in atrial fibrillation: a literature review. *European Journal of Cardiovascular Nursing.* 2014;INPRESS.

8. Brophy MT, Snyder KE, Gaehde S, Ives C, Gagnon D, Fiore LD. Anticoagulant Use for Atrial Fibrillation in the Elderly. *Journal of the American Geriatrics Society.* 2004;52(7):1151-1156.

9. Perera V, Bajorek BV, Matthews S, Hilmer SN. The impact of frailty on the utilisation of antithrombotic therapy in older patients with atrial fibrillation. *Age and Ageing.* 2009;38:156-162.

10. Ferguson C, Inglis S, Newton P, Middleton S, Macdonald P, Davidson P. Atrial fibrillation and thromboprophylaxis in heart failure: the need for patient-centrered approaches to address adherence. *Vascular Health & Risk Management.* 2013;9:3-11.

11. Hoffmann TC, Legare F, Simmons MB, et al. Shared decision making: what do clinicians need to know and why should they bother. *Medical Journal of Australia.* 2014;201(1):35-39.

12. Lip GYH, Lane DA. Patient's values and preferences for stroke prevention in atrial fibrillation: balancing stroke and bleeding risk with oral anticoagulation. *Thrombosis and Haemostasis.* 2014;IN PRESS:1-3.

13. Wann L, Curtis A, January C, et al. 2011 ACCF/ AHA/ HRS focused update on the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;123:104-123.

14. Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. *European Heart Journal.* 2012;33:2719-2747.

15. World Health Organisation. *Adherence to Long Term Therapies: Evidence for Action.* Geneva, Switzerland: World Health Organisation;2003.

16. D J Cladinin, Connelly FM. *Narrative inquiry; experience and story in qualitative research.* San Francisco CA: Jossey-Bass; 2000.

17. Dolor RJ, Ruybalid RL, Uyeda L, et al. An evaluation of patient self-testing competency of prothrombin time for managing anticoagulation: pre-randomization results of VA Cooperative Study #481--The Home INR Study (THINRS). *Journal of Thrombosis and Thrombolysis.* 2010;30(3):263-275.

18. Horstkotte D, Piper C. Improvement of oral anticoagulation therapy by INR self-management. *Journal of Heart Valve Disease.* 2004;13(3):335-338.

19. Walker GA, Heidenreich PA, Phibbs CS, et al. Mental illness and warfarin use in atrial fibrillation. *The American Journal of Managed Care.* 2011;17(9):617-624.

20. Velligan DI, Diamond PM, Mintz J, et al. The Use of Individually Tailored Environmental Supports to Improve Medication Adherence and Outcomes in Schizophrenia. *Schizophrenia Bulletin.* 2008;34(3):483-493.

21. Gehi A, Haas D, Pipkin S, Whooley M. Depression and Medication Adherence in Outpatients With Coronary Heart Disease: Findings From the Heart and Soul Study. *Archives of Internal Medicine.* 2005;165(21):2508-2513.

22. Oosterom-Calo R, van Ballegooijen A, Terwee C, et al. Determinants of adherence to heart failure medication: a systematic literature review. *Heart Failure Reviews.* 2012;18(4):409-427.

23. Marzona I, O'Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with atrial fibrillation: results of the ONTARGET and TRANSCEND studies. *Canadian Medical Association Journal.* 2012.

24. Bajorek BV, Krass I, Ogle SJ, Duguid MJ, Shenfield GM. The impact of age on antithrombotic use in elderly patients with non-valvular atrial fibrillation. *Australasian Journal on Ageing.* 2002;21(1):36-41.

25. Olesen JB, Lip GYH, Hansen PR, et al. Bleeding risk in real world patients with atrial fibrillation: Comparison of two established bleeding prediction schemes. *J Thromb Haemost.* 2011;9:1460-1467.

26. Camm AJ, Kirchhof P, Lip G, et al. Guidelines for the management of atrial fibrillation: the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC). *European Heart Journal.* 2010;31(19):2369-2429.

27. Marinigh R, Lip GYH, Fiotti N, Giansante C, Lane DA. Age as a risk factor for stroke in atrial fibrillation patients. *Journal of American College of Cardiology.* 2010;56(11):827-837.

28. Sellers MB, Newby KL. Atrial fibrillation, anticoagulation, falls risk, and outcomes in elderly patients. *Am Heart J.* 2011;161:241-246.

29. Man-Son-Hing M, Nichol G, Lau A, Laupacis A. Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk of falls. *Arch Intern Med.* 1999;159(7):677-685.

30. Pugh D, Pugh J, Mead GE. Attitudes of physicians regarding anticoagulation for atrial fibrillation: a systematic review. *Age and Ageing.* 2011.

31. Cameron J, Worrall-Carter L, Page K, Riegel B, Lo SK, Stewart S. Does cognitive impairment predict poor self-care in patients with heart failure? *European Journal of Heart Failure.* 2010;12(5):508-515.

32. Pressler SJ. Cognitive functioning and chronic heart failure: a review of the literature (2002-July 2007). *The Journal of cardiovascular nursing.* 2008;23(3):239-249.

33. van Deelen BAJ, van den Bemt PMLA, Egberts TCG, van't Hoff A, Maas HAAM. Cognitive Impairment as Determinant for Sub-Optimal Control of Oral Anticoagulation Treatment in Elderly Patients with Atrial Fibrillation. *Drugs Aging.* 2005;22(4):353-360.

34. Flaker GC, Pogue J, Yusuf S, et al. Cognitive Function and Anticoagulation Control in Patients With Atrial Fibrillation. *Circulation: Cardiovascular Quality and Outcomes.* 2010;3(3):277-283.

35. Case RB, Moss AJ, Case N, McDermott M, Eberly S. Living alone after myocardial infarction: Impact on prognosis. *JAMA.* 1992;267(4):515-519.

36. Gazmararian JA, Kripalani S, Miller MJ, Echt KV, Ren J, Rask K. Factors Associated with Medication Refill Adherence in Cardiovascular-related Diseases: A Focus on Health Literacy. *Journal of General Internal Medicine.* 2006;21(12):1215-1221.

37. McCary JM, J OCJ. Health, Housing and the Heart: Cardiovascular Disparities in Homeless People. *Circulation.* 2005;111:2555-2556.

38. Davidson P, Abernethy A, Newton P, Clark K, Currow D. The caregiving perspective in heart failure: a population based study. *BMC Health Services Research.* 2013;13(1):342.

39. Haynes R, Ackloo E, Sahota N, McDonald H, Yao X. Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews.* 2008(2).

40. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GYH. Underuse of Oral Anticoagulants in Atrial Fibrillation: A Systematic Review. *The American Journal of Medicine.* 2010;123:638-645.

41. Shaw RJ, McDuffie JR, Hendrix CC, et al. Effects of Nurse-Managed Protocols in the Outpatient Management of Adults With Chronic Conditions. *Annals of Internal Medicine.* 2014;161(2):113-121.

42. Hendriks JML, deWit R, Crijns HJGM, et al. Nurse-led care vs usual care for patients with atrial fibrillation. *European Heart Journal.* 2012;33:2692-2699.

43. Dantas G, Thompson B, Manson J, Tracy CS, Upshur R. Patients' perspectives on taking warfarin: qualitative study in family practice. *BMC Family Practice.* 2004;5(1):15.

44. Edwards A, Elwyn G, Mulley A. Explaining risks: turning numerical data into meaningful pictures. *BMJ.* 2002;324(7341):827-830.

45. Tang E, Lai C, Lee K, Wong R, Cheng G, Chan T. Relationship between patient's warfarin knowledge and anticoagulation control. *The Annals of Pharmacotherapy.* 2003;37(34-39).

46. Goodyear-Smith F, Arroll B, Chan L, Jackson R, Wells S, Kenealy T. Patients Prefer Pictures to Numbers to Express Cardiovascular Benefit From Treatment. *The Annals of Family Medicine.* 2008;6(3):213-217.

47. Halcomb EJ, Davidson PM. Is verbatim transcription of interview data always necessary? *Applied nursing research : ANR.* 2006;19(1):38-42.

CHAPTER 6: EDUCATION AND PRACTICE GAPS ON ATRIAL FIBRILLATION AND ANTICOAGULATION: A SURVEY OF CARDIOVASCULAR NURSES

6.1. CHAPTER PREFACE

Publication Reference:

Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. Education and practice gaps on atrial fibrillation and anticoagulation: A survey of cardiovascular nurses. *BMC Medical Education.* Submitted; Under review.

Chapter 5 discussed the barriers and enablers to thromboprophylaxis from the perspective of the patient, provider and the health system. This chapter reports findings from a survey of cardiovascular nurses on current education and practice on AF and anticoagulation. This chapter presents an article in its original form, submitted to the journal *BMC: Medical Education*, currently undergoing peer review.

Background

Patients' knowledge of their atrial fibrillation (AF) and anticoagulation therapy are determinants of the efficacy of thromboprophylaxis. Nurses are best-placed to provide counselling and education to patients on all aspects of anticoagulation, including self-management. It is important that nurses are well informed to provide optimal education to patients. Current practice and knowledge of cardiovascular nurses on AF and anticoagulation in the Australian and New Zealand (ANZ) context is not well reported.

Aim of the study:

This study aimed to; 1) Explore the nurse's role in clinical decision making in anticoagulation in the setting of AF; 2) Describe perceived barriers and enablers to anticoagulation in AF; 3) Investigate practice patterns in the management of anticoagulation in the ANZ setting; 4) Assess cardiovascular nurses' knowledge of anticoagulation.

A paper-based survey on current practices and knowledge of AF and anticoagulation was distributed during the Australasian Cardiovascular Nursing College (ACNC) Annual Scientific Meeting, February 2014. This survey was also emailed to nursing members of the Cardiac Society of Australia and New Zealand (CSANZ) and Cardiovascular Trials Nurses throughout New South Wales, Australia.

Brief summary of the results:

There were 42/73 (58%) respondents to the paper-based survey. A further 13 surveys were completed online via nurse members of the CSANZ, and via an investigator developed NSW cardiovascular trials nurse email distribution list. A total of 55 surveys were completed and included in analyses. Prior education levels on AF, stroke risk, anticoagulation and health behaviour modification were mixed. The CHA_2DS_2VASc and HAS-BLED risk stratification tools were reported to be underused by this group of clinicians. Reported key barriers to anticoagulation included; fears of patients falling, fears of poor adherence to medication taking and routine monitoring. Patient self-monitoring and self-management were reported as underutilised. ANZ cardiovascular nurses reported their key role to be counselling and advising patients on therapy regimens. Anticoagulant-drug interaction knowledge was generally poor. This study identified poor knowledge and practice in the areas of AF and anticoagulation. There is scope for improvement for cardiovascular nurses in ANZ in relation to AF and anticoagulation knowledge and practice.

Implications:

- ANZ cardiovascular nurses need to improve their knowledge on oral anticoagulant therapy.
- Lack of clinician knowledge may lead to inaccurate patient advice and impact adherence to therapy.
- Including a comprehensive education program pre-discharge may help to improve the quality and safety of anticoagulation
- Due to the duration of therapy for this chronic condition, there is need for education refreshment and re-assessment of patients and clinicians knowledge, across all care settings.
- There is need to explore the scope for professional organisations to credential nurses on AF and anticoagulation.

6.2. INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac rhythm irregularity and increases stroke risk three to five-fold.[1] The population prevalence is estimated at 2.3 - 3.4%. The lifetime risk of AF is approximately 1 in 4.[1] This incidence increases with age and rises to affect 11% of the population over 80 years.[2] This primarily cardiogeriatric condition is characterised by chaotic electrical activity in the upper chambers of the heart. Stroke and thromboembolism are major complications of AF. Evidence-based interventions to reduce stroke risk in AF include cardioversion, catheter ablation, insertion of a left atrial appendage (LAA) device or anticoagulation.[3] Oral anticoagulation is the most common way to reduce stroke risk in individuals with AF. Whilst the recent advent of new oral anticoagulants (NOACs) such as the thrombin inhibitor dabigatran, and factor Xa inhibitors rivaroxaban and apixaban have held the promise of simplified dosing without the need for frequent blood testing, concerns persist of bleeding risk and the lack of any reversal agent for these agents.[3] To date, warfarin remains the most commonly used oral anticoagulant, and its use is inherently burdensome. This burden is often related to the need for routine monitoring, adaptation of lifestyle habits and more often than not; complex dosing requirements.[4] The quality of overall anticoagulation quality can be assessed by an individual's time in therapeutic range. An individual with AF should aim to maintain their INR between 2 and 3.[5,6] However, many individuals may find this challenging to achieve due to a variety of factors. Unstable INRs are likely to be a consequence of medication, food or lifestyle interactions.[7] Quality anticoagulation is reliant on patients and caregivers' knowledge of their chronic condition and anticoagulation therapy.[8] The often lifetime duration of treatment increases the complex issues of adherence, and emphasises the need for education refreshment throughout all care settings. Previous studies have highlighted that clinicians including physicians, pharmacists, dieticians and nurses fail to meet adequate knowledge levels to provide accurate and up-to-date information to patients.[9,10] A recent European study drew attention to the need for improvement in cardiovascular nurses' knowledge and practice on oral anticoagulant therapy.[9] With an increasing prevalence of AF, there is greater need for

innovative strategies to improve patient outcomes. Strategies may include patient self-testing and self-management. The success of these strategies are dependent upon appropriate patient selection.[11] Patients must have good manual dexterity and cognitive abilities.[12] Further, they must be adept in managing the device; interpreting, understanding and taking action based on results. Self-testing and self-management should not be discounted by clinicians, as a method to improve knowledge, self-efficacy, overall quality of anticoagulation, and patient outcomes.[11] Nurses are best-placed to provide patient education and promote self-management on an ongoing basis.

6.3. STUDY AIM

The aim of this study was to:

1) Explore the nurse's role in clinical decision making in anticoagulation in the setting of AF.
2) Describe perceived barriers and enablers to anticoagulation in AF.
3) Investigate practice patterns in the management of anticoagulation.
4) Assess cardiovascular nurses' knowledge of anticoagulation.

6.4. METHODS

6.4.1. DESIGN, SETTING AND SAMPLE

Data were collected by survey methods. The survey was conducted at the 8th Annual Scientific Meeting of the Australasian Cardiovascular Nursing College, Gold Coast, Australia on 22nd Feb 2014. All delegates attending on this date were invited to participate in the study. Additional responses were sought via an email distribution list of the Nurses Council of the Cardiac Society of Australia and New Zealand, and a state-wide cardiovascular research nurse email distribution list. Additionally, nurses working in a single site CCU of a metropolitan teaching hospital were invited to participate. (Refer to Figure 6.1 for sampling frame response).

6.4.2. MEASUREMENTS AND ITEM GENERATION

A self-report questionnaire, recently used during a European study of cardiovascular nurses was used to assess variables related to warfarin-drug, warfarin-food interactions and knowledge on novel anticoagulants and self-management.[9] Permission to reproduce these survey items was approved by the corresponding author. The original questionnaire was reported as demonstrating good face validity. Additional investigator developed questions were included; these were developed following consultation with expert cardiovascular nurses and an extensive review of the literature. Some questions were adapted from other surveys that addressed barriers to anticoagulation or elicited the cardiovascular nurse's role in decision-making around anticoagulation therapy.[13] The questionnaire was distributed in English.

6.4.3. *DATA COLLECTION*

All delegates were provided with a paper-based survey on their chair during the session and invited by the convenor to participate. Attendees were asked to place the completed questionnaires in a designated collection box following the session. Subsequent to the conference, the same survey was electronically distributed to nursing members of the Cardiac Society of Australia and New Zealand and via a state-wide cardiovascular research nurse email distribution list. Additionally, nurses working in the hospital CCU were invited to participate. Online survey methods have previously been used to gain understanding of practice patterns in the ANZ setting.[14] Therefore, the research team believed this would yield worthy response and enhance findings from the paper-based survey. Investigators included a statement in the online survey, stating that this survey had been conducted at the ACNC conference, and only to complete the survey once.

6.4.4. *DATA MANAGEMENT AND DATA ANALYSIS*

The online survey was conducted using the web-based SurveyMonkey™ platform (*www.surveymonkey.com*) and remained open until 12/05/2014. The survey ascertained the basic demographic and education characteristics of nurses related to highest qualification and length of time working in cardiovascular nursing. Descriptive analyses were used to describe the sample and the responses to study variables.

6.4.5. *ETHICAL CONSIDERATIONS*

This study was approved by the hospital and university human ethics committees. The executive committee of the Australasian Cardiovascular Nursing College approved survey distribution during the conference event. All conference attendees were informed of the aims of the study. Informed consent was implied by the completion of the survey. No identifying information was collected from the participants to assure confidentiality.

6.5. RESULTS

6.5.1. SAMPLE CHARACTERISTICS, DEMOGRAPHIC INFORMATION AND EXPERIENCE

ACNC	41
CSANZ CNC	2
HF Coordinator Email List	9
Cardiology Ward	3
Total responses	55

FIGURE 6.1 FINAL SAMPLING FRAME RESPONSE

Legend: *ACNC; Australasian Cardiovascular Nursing College, CSANZ CNC; Cardiac Society of Australia and New Zealand Cardiovascular Nursing Council; HF; Heart Failure.*

Most respondents were female (86%), the majority of respondents (50/55; 91%) came from the three most populated states in Australia (New South Wales, Victoria and Queensland). The remaining respondents were from New Zealand (5/55; 9%). The majority worked in a metropolitan area (71%), and held a Bachelor degree qualification or above (93%). 30% identified their current role as registered nurse (RN). The seniority of the clinicians was also reflected by the number in expert positions, (19/55; 36%) identified as Clinical Nurse Consultants or Nurse Practitioners. Three respondents were not clinicians and were employed in the higher education & research sectors. Most (77%) had over 10 years of clinical experience, and 62% had worked in cardiovascular nursing specialty practice for more than 10 years. Baseline demographic information is summarised in Table 6.1.

TABLE 6.1 CHARACTERISTICS OF CARDIOVASCULAR NURSES

Demographic variable	n (%)
Female *(n=55)*	47 (86)
Highest level of education *(n=55)*	
• Nursing training	5 (9)
• Bachelor degree	15 (27)
• Graduate certificate	11 (20)
• Master's degree	**16 (29)**
• PhD	5 (9)
• Other	3 (6)
Work location *(n=55)*	
• Metro	**39 (70)**
• Regional or rural	16 (29)
Country of workplace *(n=55)*	
• New South Wales	**24 (44)**
• Australian Capital Territory	0
• Victoria	4 (7)
• Western Australia	0
• Northern Territory	0
• Queensland	22 (40)
• Tasmania	0
• South Australia	0
• New Zealand	5 (9)
Area of specialty practice *(n=55)*	
• Chronic Heart Failure	**21 (38)**
• Acute Coronary Syndrome	8 (15)
• Coronary Care Unit	20 (36)
• Cardiac Rehabilitation	8 (15)
• Cardiac Step Down	5 (9)
• Cath Lab	5 (9)
• Research	3 (6)
• Education	3 (6)
• General Medicine	3 (6)
• Other	1 (2)
Current position *(n=55)*	
• Registered Nurse	**18 (33)**
• Clinical Nurse Specialist	12 (22)
• Clinical Nurse Educator	3 (6)
• Clinical Nurse Consultant	10 (18)
• Nurse Practitioner	9 (18)
• Other	3 (6)
Years working in clinical practice *(n=52)*	
• Less than 3	2 (4)
• 4-5	7 (8)
• 6-10	6 (12)
• More than 10	**40 (77)**

Years working in cardiovascular nursing *(n=55)* • Less than 3 • 4-5 • 6-10 • More than 10	 6 (11) 2 (4) 13 (24) **34 (62)**
Years working in current department *(n=55)* • Less than 3 • 4-5 • 6-10 • More than 10	 13 (24) 13 (24) 14 (26) **15 (27)**
Proportion of patients seen aged 65+ *(n=54)* • Less than 25% • 26-50% • 51-75% • 76% or more	 0 (0) 4 (7) **31 (57)** 19 (35)

Participation in formal educational programs was reported to be 41-61% across four associated topics. 48% had attended a previous education program about AF, 41% about stroke risk, 57% about anticoagulation and 61% about health behaviour modification. Previous education participation is summarised in Table 6.2.

TABLE 6.2 PREVIOUS PARTICIPATION IN EDUCATIONAL PROGRAMS

Education program	Yes (%)
Atrial fibrillation	26 (48)
Stroke risk	20 (41)
Anticoagulation	29 (57)
Health behaviour modification	31 (61)

6.5.2. *ADVERSE OUTCOMES*

50% of respondents had cared for a patient with AF who had experienced an intracranial haemorrhage when receiving anticoagulation. And 74% of respondents had cared for a patient with AF who had experienced a stroke whilst not receiving anticoagulation. Results are summarised in Table 6.3.

TABLE 6.3 CLINICAL FACTORS

Variable (Clinical Factor)	n (%)
Estimated prevalence of AF in CHF • Less than 25% • 25-50% • 51-75% • 76% or more	 3 (6) **29 (54)** 19 (35) 3 (6)
Have cared for a patient with AF who has experienced an ICH whilst receiving anticoagulation	27 (50)%
Have cared for a patient with AF who has experienced a stroke whilst not receiving anticoagulation	39 (74%)
Actively involved in MDT discussions when making treatment decisions on anticoagulation management with patients with AF	25 (46%)

6.5.3. *NURSES ROLE IN DECISION MAKING AND ANTICOAGULATION*

Results of the nurses' role in decision making are summarised in Table 6.4. More than half of respondents (*54%, n=29*) said they were not involved in multidisciplinary team (MDT) discussions when making treatment decisions on anticoagulation management with patients with AF. Nearly half of respondents agreed (*44%, n=24*) or strongly agreed (*7%, n=4)* that the risk of stroke versus the risk of bleeding was clearly articulated to patients at commencement of anticoagulation for stroke prevention in AF. Most disagreed (*41%, n=22)* or strongly disagreed (*13%, n=7)* that they were unsure to advocate for thromboprophylaxis or not, when involved in team decisions. Most disagreed *(50%, n=27)* or strongly disagreed (*6%, n=3)* that it was difficult to decide where the benefits of thromboprophylaxis outweighed the risks of haemorrhage. Over half disagreed *(57%, n=30)* that they did not feel they knew enough about the risks and benefits of different anticoagulants.

Most respondents *(57%, n=31)* agreed that they took time to understand their patients views on the risks and benefits of anticoagulation, and that they *(52%, n=28)* felt that generally, their patients were well informed about their risks and benefits of anticoagulation at the time of commencement. Just under half *(n=26, 48%)* agreed that their patients received comprehensive education about anticoagulation prior to discharge after hospitalisation. Stroke and bleeding risk stratification tools were reported to be underutilised by this group of clinicians. Specifically, only 25% *(n=13)* agreed that they used a $CHADS_2$ or CHA_2DS_2-VASc tools, whilst only 18% *(n=9)* agreed they used the HAS-BLED tool, despite the fact that both are recommended in international guidelines for anticoagulation in AF.[5] Over half *(n=28, 52%)* agreed, or strongly agreed that they made use of a shared decision-making model of care to explain the risks and benefits of anticoagulation for stroke prevention in AF.

TABLE 6.4 CLINICAL DECISION MAKING IN ANTICOAGULATION

Statement	SD *n(%)*	D *n(%)*	N *n(%)*	A *n(%)*	SA *n(%)*	Rating Count
The risk of stroke versus the risk of bleeding is clearly articulated to patients when commencing anticoagulation for stroke prevention in AF	3(6)	9(17)	14(26)	**24(44)**	4(7)	54
I am unsure whether to advocate for thromboprophylaxis or not when involved in team decisions	7(13)	**22(41)**	14(26)	10(19)	1(2)	54
It's difficult to decide where the benefits of thromboprophylaxis outweigh the risks of hemorrhage	3(7)	**27(50)**	10(19)	14(26)	0(0)	54
I feel I do not know enough about the risk and benefits of different anticoagulants	5(9)	**30(57)**	4(8)	12(23)	2(4)	53
I take time to understand my patients views on the risks and benefits of anticoagulation	0(0)	7(13)	10(19)	**31(58)**	6(11)	54
Generally, my patients are well informed about the risks and benefits of anticoagulation at time of commencement	3(6)	8(15)	11(20)	**28(52)**	4(7)	54
My patients receive comprehensive education about anticoagulation prior to discharge	2(4)	5(9)	10(19)	**26(48)**	11(20)	54
I use the CHADS2 or CHA2DS2-VASc scores with patients to help risk stratify stroke risk in clinical practice	6(12)	12(23)	**15(29)**	13(25)	6(12)	52
I use the HAS-BLED score with patients to help risk stratify bleeding risk in clinical practice	11(22)	13(26)	**16(31)**	9(18)	2(4)	51
I use shared decision making with patients to explain the risks and benefits of anticoagulation for stroke prevention in AF	5(9)	7(13)	14(26)	**23(43)**	5(9)	54

6.5.4. *BARRIERS TO ANTICOAGULATION*

Barriers to anticoagulation are summarised in Table 6.5. Barriers to anticoagulation included fears of the patient falling *(75%, n=39)*, fears of poor adherence to: routine monitoring *(75%, n=39) and* medication taking *(71%, n=36).* Other barriers included lack of social support (e.g. patient living alone, or a lack of a caregiver), *(41%, n=21)*, and fears of poor literacy *(26%, n=13).* Factors facilitating optimal management of thromboprophylaxis were identified, these are summarised in Table 6.6 and 6.7

TABLE 6.5 BARRIERS TO ANTICOAGULATION

Variable (*Barrier*)	**n = Y (%)**	**Rate count**
Fear of the patient falling	39(70)	52
Lack of social support (e.g. patient living alone or lack of caregiver)	21(41)	51
Fear of poor adherence to medication taking	36(71)	51
Fear of poor compliance to routine monitoring (e.g. INR checking)	39(75)	52
Fears of poor literacy	13(26)	50

TABLE6.6 FACTORS FACILITATING OPTIMAL MANAGEMENT OF THROMBOPROPHYLAXIS

• Case Management • Good GP/ GP support • Ease of access to INR checking • Education • Counselling assessment • Discharge planning • Follow up • Family support & involvement • A HAS-BLED and CHADS2 Score • Open discussion and understanding of thromboprophylaxis • Good understanding of risks and benefits • Pharmacy education • Regular adherence and INR monitoring	• Multi-disciplinary care • Good communication (including listening, interpreters, written info) • Warfarin booklets (written information) • Self-management & community support • Careful assessment, reassessment of factors if change • Monitoring of adherence • Ensuring type of lifestyle and therapy is matched with patients capacity to self-manage • Nurse-led anticoagulation clinics

TABLE 6.7 NURSES GENERAL COMMENTS ABOUT THROMBOPROPHYLAXIS.

General comments about thromboprophylaxis use in patients with AF
"new agent dabigatran easier to manage patients"
"If medical officers have had a patient with a bleed, I find it makes them more cautious with subsequent patients"
"Some INR levels are very hard to control despite well-educated and compliant patient. Need new ideas i.e. Watchman LAA devices"
"It's variable and physician choice"
"Until an antidote is developed for the newer anticoagulants we don't use them. In some rare cases we do but often last choice"
"Dr's do all the decision making. Uses $CHADS_2$/ CHA_2DS_2VASc"
"Quick uptake of NOAC agents but often without evidence (e.g. prosthetic valves & AF)"

6.5.5. PRACTICE PATTERNS

Results of practice patterns are summarised in Table 6.8. Warfarin remains the most widespread anticoagulant used in daily practice for this cohort of clinicians (100%, n=51). Less extensive use of the novel agents was reported. Only 16% *(n=8)* of respondents stated that most patients would be given a choice of anticoagulant, 82% *(n=41),* stated that 'some' patients may be offered new anticoagulants. 59% *(n=29)* of respondents stated that patients may modify therapy based on difficulties maintaining INR within therapeutic range (i.e. 2-3). Patient self-testing and self-management were not offered by 60%, *(n=30)* of respondents and 28%, *(n=14)* had never heard of such services. One respondent highlighted a possible rationale for this could be the limited remuneration and funds for the use of point-of-care machines. It was also noted by another that pharmacists had a key role in counselling and education prior to discharge following a hospitalisation. A number of respondents highlighted that the role of decision-making around anticoagulation is usually lead by the physician, cardiologist or GP and often the nurses and patients input were minimal.

TABLE 6.8 CARDIOVASCULAR NURSES PRACTICE PATTERNS

Question	n (%)
Oral anticoagulants in use in daily practice	
• Warfarin (Coumadin)	**51(100)**
• Dabigatran (Pradaxa)	33(65)
• Rivaroxaban (Xareltro)	33(65)
• Apixaban (Eiliquis)	11(22)
Will patients be offered a choice of drug?	
• No, all patients will be put on warfarin first	1(2)
• Some patients may be offered new anticoagulation	**41(82)**
• Most patients will be given a choice	8(16)
Will patients on warfarin be able to change to one of the new drugs?	
• No, they will need to stay on warfarin	1(1)
• May change if difficulties keeping INR in therapeutic range	**29(59)**
• Any patient can change to one of the new drugs	19(39)
Do you offer patients INR self-testing or self-management?	
• Both self-testing and self-management of INR	6(12)
• Only self-testing of INR	0(0)
• Neither self-testing nor self-management	**30(60)**
• Never heard about self-testing of self-management of INR	14(28)
The role of nurses regarding anticoagulants in your country	
• Do not have a specific role	11(21)
• Counsel patients regarding adherence to drug regimen	**34(65)**
• Advice patients on dosing warfarin based on INR results	8(15)
• Teach about drugs, how to take them and side effects	33(64)

INR: international normalized ratio

6.5.6. *CARDIOVASCULAR NURSES' KNOWLEDGE ON WARFARIN INTERACTIONS*

The majority of respondents *(n= 34, 69%)* answered correctly that aspirin enhanced the effect of oral warfarin anticoagulation therapy. It is of concern that 48% *(n=23)* of respondents answered incorrectly to interactions related to ibuprofen and 48% *(n=23)* did not know of interactions with topical salicylates. Whilst ibuprofen has no effect on oral anticoagulant therapy, it may impact on overall haemostasis and may increase the risk of gastrointestinal bleeding when used in combination with oral anticoagulants.[15] Only 23% *(n=11)* of respondents answered correctly that topical salicylates enhance oral warfarin anticoagulant therapy. Whilst results of how cardiac agents including propanolol, cholestyramine and atenolol trend towards the correct answers (propanolol enhancing, cholestyramine inhibiting and atenolol having no effect), the rate of respondents who did not know the interactions of these cardiac agents on warfarin therapy was 44-67%. Only 9-22% answered the questions on warfarin interactions with gastrointestinal agents correctly. More than two-thirds answered "don't know" to the question on sucralfate-warfarin interaction. The majority of respondents did not know how any of the vitamin supplements listed affected warfarin therapy (range 42-58% across the 5 supplements). The questions on the interaction between antibiotics and warfarin were poorly completed; the majority of respondents answered "don't know". Results on warfarin interactions are summarised in Table 6.9.

TABLE 6.9 CARDIOVASCULAR NURSES KNOWLEDGE ON WARFARIN DRUG INTERACTIONS.

Question	n (%) Enhance	n (%) Inhibit	n (%) No effect	n (%) Don't know	Rating Count
How to these anti-inflammatory agents affect oral warfarin anticoagulant therapy?					
• Aspirin	**34(69)**	2(4)	9(18)	4(8)	49
• Ibuprofen	23(48)	8(17)	**9(18)**	8(17)	48
• Topical salicylates	**11(23)**	3(6)	11(23)	23(48)	48
How do these cardiac agents affect oral warfarin anticoagulant therapy?					
	7(15)	2(4)	15(32)	23(49)	47
• Propanolol	0(0)	**10(21)**	6(13)	32(67)	48
• Cholestyramine	5(11)	1(2)	**20(44)**	20(44)	46
• Atenolol					
How do these gastrointestinal agents affect warfarin anticoagulant therapy?					
• Antiacids	0(0)	23(49)	**7(15)**	17(36)	47
• Cimetidine	**4(9)**	11(24)	4(9)	27(59)	46
• Metamucol	1(2)	10(22)	**5(11)**	30(65)	46
• Sucralfate	0(0)	**10(22)**	5(11)	30(67)	45
How do these vitamin supplement(s) affect oral anticoagulant therapy?					
• Multivitamin	2(4)	9(20)	**15(33)**	19(42)	45
• Multivitamin and minerals	2(4)	9(20)	**15(33)**	19(42)	45
• Antioxidant formula	7(16)	3(7)	**9(21)**	25(57)	44
• 1200 IU vitamin E	**18(39)**	5(11)	3(7)	20(44)	46
• 1000mg vitamin C	**4(9)**	3(7)	12(27)	26(58)	45
Most antibiotics affect warfarin therapy by the process of:					
• Potentiation		**7(23)**	0(0)	24(78)	31
• Inhibition		5(17)	**0(0)**	25(84)	30
• Both		6(19)	**1(4)**	25(78)	32
• Neither (other process)		1(4)	**2(8)**	23(89)	26

6.5.7. *CARDIOVASCULAR NURSES' KNOWLEDGE ON WARFARIN RELATED ADVICE*

There were eight questions that assessed cardiovascular nurse's knowledge on warfarin advice. Responses are summarised in Table 6.10. Most questions were answered correctly with the exception of advice around warfarin use and pregnancy. 70% *(n=34)* of respondents knew that patients who are taking warfarin can consume spinach, however that they need to eat the same amount regularly every week. Over half *(55%, n=26)* correctly answered that consuming three glasses of wine will cause an increased in INR. Yet, 21% *(n=10)* of respondents did not know the answer to this question. 88% *(n=44)* of cardiovascular nurses knew that the best time of day to take warfarin was the evening, and 90% *(n=45)* were aware that patients with a stable INR should have it checked every four weeks. Only 58% *(n=29)* of nurses would have given correct advice to patients on the action to take if a patient remembered missing a last dose. Over three quarters *(76%, n=38)* of respondents correctly answered that once warfarin is ceased, it takes five days to be cleared from the patient's body. Most *(84%, n=43)* nurses correctly identified that the length of time a patient is expected to be taking warfarin is patient centric, and dependant on individual needs. Only 12% *(n=6)* of respondents correctly answered that women who are pregnant can safely take warfarin during the second and third trimester. Less than half, 48% *(n=24)* of respondents incorrectly answered this question, wrongly identifying that pregnant women should not take warfarin, which is concerning around the correct information provision to this patient population.

TABLE 6.10 CARDIOVASCULAR NURSES KNOWLEDGE ON HOW TO ADVISE PATIENTS ON WARFARIN

Question	n (%)
While on warfarin the patient:	
• Should not eat spinach	9(18)
• Can eat spinach once a month	1(2)
• Can eat as much spinach as he likes whenever he likes	2(4)
• Can eat spinach but needs to eat the same amount every week	**34(69)**
• *Don't know*	3(6)
• *Skipped question*	6
While out with friends for dinner, your patient has just finished his third glass of wine. This amount of alcohol consumed in a single evening will:	
• Cause a decrease in INR	7(15)
• Cause an increase in INR	**26(55)**
• Does not affect warfarin in any way	3(6)
• Make the patient sick when taking warfarin medication	1(2)
• *Don't know*	10(21)
• *Skipped question*	8
The best time of day to take warfarin is:	
• At lunchtime	0(0)
• In the evening	**44(88)**
• In the morning before breakfast	2(4)
• Any time of the day when you remember	3(6)
• *Don't know*	1(2)
• *Skipped question*	5
Once the patient has reached a stable warfarin dose, a PT/ INR blood test:	
• Should be checked once a year	0(0)
• Should be checked once every 3 months	5(10)
• Should be checked at least once every 4 weeks	**45(90)**
• Does not need to be checked once on a stable warfarin does	0(0)
• *Don't know*	0(0)
• *Skipped question*	5

Continued overleaf

A patient just remembered that he forgot to take his warfarin medication dose last night. He/She should:	
• Skip in the dose of warfarin he/she missed	**29(58)**
• Take the missed warfarin dose right now	8(16)
• Wait and take two doses right now	0(0)
• Take one-half of the missed dose of warfarin right now	8(16)
• *Don't know*	5(10)
• *Skipped question*	5
Once the patient's warfarin is stopped, how long does it take to get the medication out of his/ her system?	
• 5 hours	1(2)
• 5 days	**38(76)**
• 5 weeks	2(4)
• 5 months	0(0)
• *Don't know*	9(18)
• *Skipped question*	5
After starting warfarin, how long (in months/years) would you expect the patient to be taking warfarin?	
• 1 year	0(0)
• 1 month	0(0)
• It depends on each person's needs	**43(84)**
• If you start warfarin you will have to be on the medication for the rest of your life	9(18)
• *Don't know*	0(0)
• *Skipped question*	4
Women who are pregnant:	
• Should not take warfarin	24(48)
• Can safely take warfarin during the second and third trimester	**6(12)**
• Can take warfarin but only need to take it every others day	0(0)
• Would not need to take warfarin, since being pregnant prevents them from getting blood clots	0(0)
• *Don't know*	20(40)
• *Skipped question*	5

Correct answers are shown in bold

6.6. DISCUSSION

This study demonstrates that cardiovascular nurses in Australia and New Zealand have insufficient knowledge on oral anticoagulant therapy, warfarin-diet, and warfarin-medication interactions. Our findings are consistent with international research. The less extensive reported use of novel agents may be due to their gradual introduction to the Pharmaceutical Benefit Scheme (PBS). The PBS is the national pharmaceutical rebate scheme providing medicines at a government subsidised price. It is of concern that such a small percentage stated that most patients would be given a choice of anticoagulant. There remains considerable scope for improvement in this area of shared decision-making.

The lack of knowledge of warfarin-medication interactions is alarming. It is of concern at the lack of knowledge on warfarin related advice, particularly pertaining to pregnancy and how alcohol affects INR. Our findings represent a typically older and more experienced cardiovascular nursing population, working in specialised positions with advanced qualifications. And as such, are likely to be more knowledgeable on anticoagulation than other nurses. Given the overall poor results, it is feared that knowledge is likely to be even poorer in the broader nursing population.

6.6.1. PRACTICE PATTERNS

The cardiovascular nurses surveyed stated that warfarin remains the most widespread oral anticoagulant for stroke prevention in AF, whilst NOACs are reported to have lesser usage. It is concerning that only 16% of respondents stated that most patients would be given a choice. It appears that there is scope for improvement in the practice of shared decision-making and patient-centered care. It is important that nurses maintain an active role in the decision-making processes and act as an advocate for patients and caregivers. This may be particularly problematic when patients are presented with complex risk calculators and benefit statistics of various treatments. Patient self-testing and self-management strategies have been not yet been

embraced as innovative practices that support able patients. Barriers to patient self-management and self-testing include frailty, poor manual dexterity and cognitive dysfunction[12]; however these practices should not be discounted by clinicians. Additionally, a poor rebate for self-testing devices may also impede uptake in Australia and New Zealand. The nurse's role in education and counselling on anticoagulation was highlighted. Some respondents expressed that they often delegate this to the pharmacist for education. This practice appears commonplace, and is worrisome. A respondent expressed "most times, little education is given". This has immense implication for the quality of thromboprophylaxis.

6.6.2. KNOWLEDGE

Cardiovascular nurses must ensure that they are up-to-date with current evidence-based information on AF and anticoagulation therapy to inform the education and care they provide to patients. Incorrect and inaccurate knowledge on drug-drug, drug-food interactions and monitoring requirements was prevalent among the respondents to our survey. This may lead to inappropriate patient counselling and education. This would adversely impact patient outcomes. It is therefore vital that cardiovascular nurses are knowledgeable and keep abreast with new information related to AF and anticoagulation practices. Support for self-testing and self-management practices must be preferred over teaching alone. Nurses are best-placed to provide ongoing counselling throughout the spectrum of care; from hospitalisation to discharge and within primary care settings. However, the quality of this counselling is dependent on a strong contemporary knowledge base. Cardiovascular nurses must refrain from simple task delegation of anticoagulation education to pharmacists or other clinicians, it is important to adopt a combined and comprehensive approach. This may assist in optimising therapy, improving issues of adherence and ultimately patient outcomes. Clinicians must engage further with this topic to ensure safe care. Results from this study highlight the need for cardiovascular nurses to maintain a contemporary knowledge base. The Australian Health Practitioner Regulation Agency (AHPRA) mandates that all registered nurses must participate in at least 20 hours of

continuing nursing professional development per year that is relevant to the context of practice.[16] Education modules specific to AF and anticoagulation, including stroke and bleeding risk and lifestyle modification may be of assistance in maintaining minimum standards for continuing professional development for cardiovascular nurses.

6.7. LIMITATIONS

This study has some limitations. Firstly, whilst the response rate of 58% to the paper-based survey distributed during the conference is encouraging, the generalizability of these findings is difficult. These findings represent a typically older and more experienced cardiovascular nursing population, working in specialised positions with higher qualifications. Therefore this may not be representative of the general Australian and New Zealand cardiovascular nursing population whom provide bedside patient education on anticoagulation. Secondly, the majority of respondents (80%) were attending a cardiovascular nursing conference, for many of the workforce this remains a privilege to secure funding and time to attend such professional development events. The seniority of respondents may reflect the demographic that normally attends conferences, hold a professional society membership or has access to a workplace email account. Again, this limits the generalizability of findings.

6.8. CONCLUSION AND IMPLICATIONS

The results of our study demonstrate that of the cardiovascular nurses surveyed in Australia and New Zealand most had inadequate knowledge on oral anticoagulant therapy. There is need for improvement, to ensure quality of care for patients with AF receiving anticoagulation. Cardiovascular nurses need to be able to provide accurate, robust and timely advice to patients to topics including lifestyle, medication and food interactions to anticoagulation. A lack of knowledge on these topics may contribute to inappropriate counselling and education. Further, the communication of inaccurate information may implicitly reinforce myths and misconceptions around anticoagulation. The education of patients on anticoagulation is not a role of a single health professional. A team approach must be taken and nurses have a key role in providing answers to questions and sound clinical advice across all care settings. Future research should address modes of delivery of AF and anticoagulation education for clinicians, individuals and their caregivers.

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6.9. REFERENCES

1. Ball J, Carrington M, McMurray JJV, Stewart S. Atrial fibrillation: Profile and burden of an evolving epidemic in the 21st century. *International Journal of Cardiology.* 2013;167(5):1807-1824.

2. Shea JB, Sears SF. A Patient's Guide to Living With Atrial Fibrillation. *Circulation.* 2008;117(20):e340-e343.

3. Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. Atrial fibrillation: Stroke prevention in focus. *Australian Critical Care.* 2013.

4. Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. Atrial fibrillation and thromboprophylaxis in heart failure: The need for patient-centered approaches to address adherence. *Vascular Health and Risk Management.* 2013;9(1):3-11.

5. Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. *European Heart Journal.* 2012;33:2719-2747.

6. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/ AHA/ HRS Focused Update on the Management of Patients with Atrial Fibrillation: A report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;1234:104-123.

7. Couris R, Tataronis G, McCloskey W, et al. Dietary vitamin K variability affects International Normalized Ratio (INR) coagulation indices. *International journal for vitamin and nutrition research. Internationale Zeitschrift fur Vitamin- und Ernahrungsforschung. Journal international de vitaminologie et de nutrition.* 2006;76(2):65-74.

8. Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. The caregiver role in thromboprophylaxis management in atrial fibrillation: a literature review. *European Journal of Cardiovascular Nursing.* 2014;INPRESS.

9. Oterhals K, Deaton C, De Geest S, et al. European cardiac nurses' current practice and knowledge on anticoagulation therapy. *European Journal of Cardiovascular Nursing.* 2014;13(3):261-269.

10. Couris RR, Tataronis GR, Dallal GE, Blumberg JB, Dwyer JT. Assessment of healthcare professionals' knowledge about warfarin-vitamin K drug-nutrient interactions. *Journal of the American College of Nutrition.* 2000;19(4):439-445.

11. Heneghan C, Alonso-Coello P, Garcia-Alamino JM, Perera R, Meats E, Glasziou P. Self-monitoring of oral anticoagulation: a systematic review and meta-analysis. *Lancet.* 2006;367(9508):404-411.

12. Dolor RJ, Ruybalid RL, Uyeda L, et al. An evaluation of patient self-testing competency of prothrombin time for managing anticoagulation: pre-randomization results of VA Cooperative Study #481--The Home INR Study (THINRS). *Journal of Thrombosis and Thrombolysis.* 2010;30(3):263-275.

13. Gattellari M, Worthington J, Zwar N, Middleton S. Barriers to the use of anticoagulation for nonvalvular atrial fibrillation. *Stroke.* 2008;39:227-230.

14. Newton P, Davidson P, Sanderson C, on behalf of the Improving Palliative Care through Clinical Trials group. An online survey of Australian physicians reported practice with the off-label use of nebulised frusemide. *BMC Palliative Care.* 2012;11(1):6.

15. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and Management of the Vitamin K Antagonists. *Chest.* 2008;133(6 suppl):160S-198S.

16. Australian Health Practitioner Regulation Agency (AHPRA). Nursing and Midwifery Continuing Professional Development Registration Standard. 2010. Accessed 4th August 2014, 2014.

CHAPTER 7: MULTIMORBIDITY, FRAILTY AND SELF-CARE: IMPORTANT CONSIDERATIONS IN ANTICOAGULATION.

7.1. CHAPTER PREFACE

Publication Reference:

Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. Multimorbidity, frailty and self-care: Important considerations in anticoagulation: Outcomes of the AFASTER Study. *Journal of Cardiac Failure.* Submitted: Under review.

Chapter 6 reports findings from a survey of cardiovascular nurses on current education and practice on AF and anticoagulation. This chapter presents results from the AFASTER cohort study. This study is a cohort of individuals with HF and concomitant AF, and examines clinical characteristics, practice patterns and clinical outcomes. This chapter presents an article in its original form, submitted to the *Journal of Cardiac Failure*, currently undergoing peer review.

Background:

Chronic heart failure (CHF) and atrial fibrillation (AF) are complex cardiogeriatric syndromes, mediated by physical, psychological and social factors. Thromboprophylaxis is an important part of avoiding adverse events, particularly stroke.

Aim of the study:

This study sought to: describe the clinical characteristics of a cohort of individuals hospitalised with CHF and concomitant AF; document the rate and type of thromboprophylaxis; examine practice patterns of therapy prescription; and determine the predictors of adverse events.

Design: Prospective cohort study.

Methods: Prospective consecutive participants with CHF and concomitant AF of any type and aetiology admitted to a cardiology ward were enrolled during April – October 2013. Socio-demographic and clinical characteristics including medical history, frailty, medication adherence, self-care behaviour and thromboprophylaxis prescription were assessed at index hospitalisation. Participants were followed-up by telephone at 12 months to collect the following outcome data: all –cause rehospitalisation and mortality, stroke or transient ischaemic attack, and bleeding.

Brief summary of the results:

All-cause rehospitalisation was frequent (68%) and 12-month all-cause mortality was high (29%). Prescription of anticoagulation at discharge was statistically significantly associated with lower mortality at 12 months [23% vs. 40%, p=0.037, HR 0.51, 95% CI 0.27-0.96], but was not associated with lower rates of rehospitalisation among individuals with chronic heart failure and concomitant atrial fibrillation. 66% of participants were prescribed an anticoagulant at discharge from hospital. Self-reported self-care behaviour and 'not for CPR' were associated with not receiving anticoagulation at discharge. Whilst statistical significance was not achieved, those who were assessed as frail or having greater comorbidity, were less likely to receive anticoagulation at discharge.

This study highlights multimorbidity, frailty and self-care to be important considerations in thromboprophylaxis. Shared-decision making with patients and caregivers offers promise to potentially improve treatment knowledge, adherence and outcomes in this group of individuals with complex care needs.

Implications:

- Although the CHA_2DS_2VASc and HAS-BLED models are useful tools in clinical practice to stratify stroke and bleeding risk, they do not consider other important factors in thromboprophylaxis decision making and should not be used in isolation.
- Whilst preventing stroke is important in this high risk cohort of individuals, rates of rehospitalisation and mortality are very high and are often related to chronic heart failure symptom management.
- Results suggests that clinicians are prepared to prescribe an anti-platelet in some patients as thromboprophylaxis in circumstances where they are not prepared to use oral anticoagulation, this warrant further research.
- Future research should explore clinicians fear and patient choice in thromboprophylaxis.
- Optimising AF management needs to be considered in the context of multimorbidity, frailty, self-care ability, cognitive functioning, and caregiver support.
- There is need to target clinical interventions that improve self-care behavior and self-management of AF in the setting of CHF.

7.2. INTRODUCTION

Chronic heart failure (CHF) is a common and multifaceted syndrome with complex self-care needs.[1] Previous studies have highlighted that atrial fibrillation (AF) is a concomitant condition in up to 50% of CHF cases,[2] and as a consequence are at a high risk of stroke. The use of thromboprophylaxis, including anticoagulation significantly reduces stroke risk.[3] In spite of evidence based recommendations, rates of thromboprophylaxis remain poor.[4] There is need to better understand factors influencing thromboprophylaxis decision making within existing risk prediction models.

7.3. PURPOSE

The aim of this study was to:

1) Describe the clinical characteristics of a cohort of individuals hospitalised with CHF and concomitant AF.

2) Describe the frequency and type of thromboprophylaxis.

3) Examine practice patterns of therapy prescription.

4) Compare the overall quality of AF and CHF care in this cohort, when benchmarked against recommendations of international guidelines.

5) Determine the predictors of adverse events (including all-cause rehospitalisation and all-cause mortality, stroke/ TIA, and bleeding events).

7.4. METHODS

7.4.1. DESIGN AND SETTING

The AFASTER (***A**trial **F**ibrillation **A**nd **S**troke **T**hromboprophylaxis in h**E**art failu**R**e*) cohort study was an observational single site, 6-month cohort study, of adults' ≥ 18 years, conducted during April – October 2013, enrolling prospective consecutive participants with CHF and concomitant AF of any type and aetiology admitted to a cardiology ward at an academic medical center. Exclusion criteria were age <18 years, AF due to reversible causes, or enrolment in another clinical trial. Socio-demographic and clinical characteristics including medical history, frailty and thromboprophylaxis prescription were assessed at index hospitalization.

7.4.2. MEASUREMENTS

Baseline demographic and clinical data were obtained using a standardised case report form. Biochemical, haematological, echocardiographic and medication data were obtained upon discharge from hospital. The Charlson Comorbidity Index (CCI) was used to quantify comorbidity. This index is a simple and valid method to classify comorbid disease.[5] Social and living situation as well as social support information was collected.

Stroke and bleeding risk

The CHA_2DS_2VASc[6] and HAS-BLED[7,8] stroke and bleeding risk stratification tools were used to stratify stroke and bleeding risk. Both schemata are well validated and simple to use in clinical practice, they are both recommended for use throughout international guidelines for the management of AF.[9-11]

In a retrospective study of patients with a history of AF and an implanted pacemaker the CHA_2DS_2-VASc score had a high sensitivity to predict stroke with good sensivity, predictive ability however low specificty (7 – 24%).[12] The $CHADS_2$ tool is more widely used in clinical practice, however $CHADS_2$ data can be derived from a CHA_2DS_2-VASc score and assesses for a greater number of well established independent risk factors for stroke. In a recent post hoc analysis of the AMADEUS study population, in a comparison of the performance of the $HEMORR_2HAGES$, ATRIA and HAS-BLED bleeding risk prediction scores in patients with AF undergoing treatment with anticoagulation, the HAS-BLED was identified to have superior predictive performance for overall bleeding and intracranial haemmorhage (c-index: 0.75).[13]

Current international guidelines advocate stroke risk stratification using the CHA_2DS_2VASc score and prescription of a vitamin K antagonist (VKA) or novel oral anticoagulant (NOAC) if $CHA_2DS_2VASc > 1$. Further, assessment of bleeding risk should occur using the HAS-BLED score, and considerations should be made towards patient's individual values and preferences. Antiplatelet therapy should only be considered for thromboprophylaxis in AF for low risk patients (i.e. $CHA_2DS_2VASc <1$) or those deemed unsuitable for treatment with a VKA or NOAC.[9]

Medication adherence

Patient self-reporting is a useful method of assessing medication adherence. Self-reporting offers reliable predictors of a vary of cardiovascular health outcomes such as blood pressure control, and hospitalization for CHF.[14] There are a number of tools available to measure self-reported adherence, the 4-point Morisky Scale (MMAS) provides good predictive ability and can be easily integrated into a patient assessment.[15] The MMAS has reported sensitivity and specificity of 81% and 44% respectively, Cronbach's alpha reliability is 0.61, which is below the accepted value of 0.7. However this tool has been implemented in a large number of studies within clinical research, and has the advantage of being able to easily integrate into a quick clinical assessment.[16]

Self-care behaviour

The European Heart Failure Self Care Behaviour Scale (EHFScBS)[17] was used to measure self-care behaviour. This questionnaire is widely used in heart failure research and has been validated using pooled data from 6 European countries. Cronbach's alpha was 0.81. This is a 5 point scale ranges from 1 (I completely agree) to 5 (I completely disagree), with a global score ranging from 12 (better self-care behaviour) to 60 (worse self-care behaviour). This scale is specifically designed for evaluating the outcome of CHF management with focus on self-care behaviour in the chronic heart failure population. A lower score indicates better self-care behaviour and a higher score indicates inferior self-care behaviour.[18]

Frailty

The SHARE Frailty Index is a simple frailty screening instrument.[19] This instrument has been validated for use in the primary care setting, with a community dwelling population and has demonstrated good predictive validity. This instrument is available with free and easy to access web-based calculators. There are 5 key variables of the SHARE-FI including; fatigue, loss of appetite, handgrip strength, functional difficulties and physical activity. The SHARE-FI was selected for use in the study due to its brevity and simplicity to conduct during an assessment by a research nurse. Many other frailty instruments include a variable for weight; this is replaced with a variable for 'loss of appetite' in the SHARE-FI. This was an important consideration in chronic heart failure management where weight fluctuations may influence measurement. This instrument was delivered using a standardised method, which was important in the measurement of handgrip strength using the dynamometer. Frailty was assessed as close to discharge from hospital as clinically possible, to maintain consistency in measurement. Two research nurses were trained to deliver the frailty screen to achieve consistent measurement.

7.4.3. DATA MANAGEMENT, STATISTICAL ANALYSES

Data were managed and analysed using IBM SPSS Statistics version 21 (IBM Corp., Armonk, NY, USA). Baseline characteristics of the study cohort were described using frequencies and percentages for categorical variables; and means and SD, medians and IQR for continuous variables. Event-free survival time was calculated using Kaplan-Meier survival analysis, for a composite endpoint of all-cause hospitalization and mortality. Cox regression was used to calculate hazard ratios.

7.4.4. ETHICAL CONSIDERATIONS

This study was approved by the hospital and university Human Research Ethics Committee, Approval LNR/12/SVH/62 and 2013000181. Consent was waived for baseline data collection and a 12 routine month follow up phone call. Participants were provided with written information on the study and were free to withdraw at any stage.

7.5. RESULTS

7.5.1. SAMPLE BASELINE CHARACTERISTICS AND DEMOGRAPHIC INFORMATION

A total of 1,860 patients were screened between April – October 2013 at a single site. Of these, 365 had a diagnosis of CHF, consistent with international guidelines. 156/365 (43%) were eligible for inclusion, as they had concomitant AF of any type. Six died during hospital admission, 11 were not included for other reasons (declined or enrolled in other clinical trial), and two withdrew from the study. Of the final cohort of 137 participants; four were not included in the comparative analysis due to missing medication data at discharge *(Refer to Figure 7.1; participant screening and recruitment).*

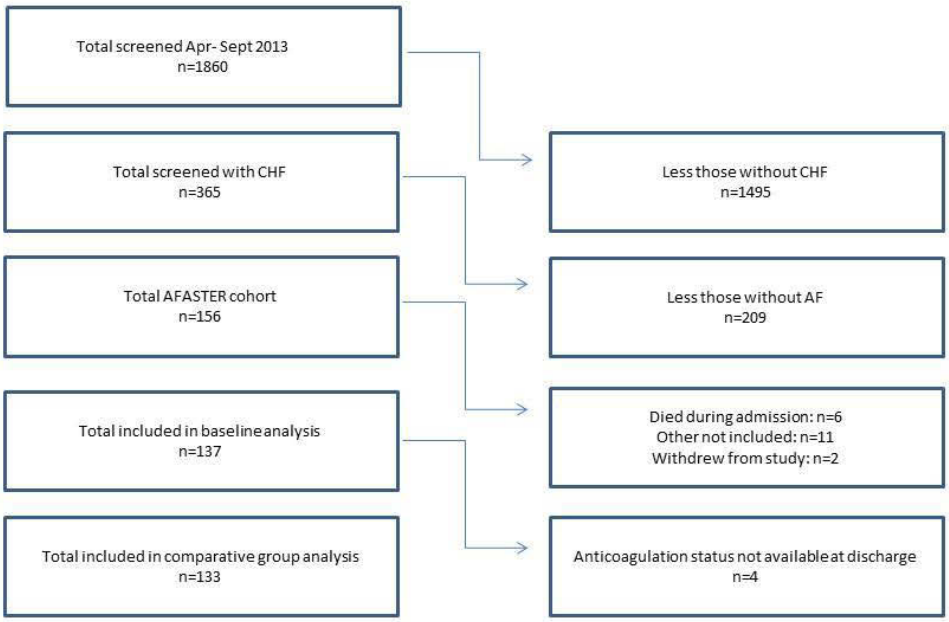

FIGURE 7.1 PARTICIPANT RECRUITMENT AND SCREENING

The baseline analysis included 137 hospitalised patients consecutively enrolled between April – October 2013 on discharge. Mean age was 72 years (SD 16), mostly male (65%), primarily NYHA class II-III (62%), LVEF <45% = 59%. Mean CHA_2DS_2VASc Score = 4.25 (SD 1.85); mean HASBLED Score = 2.85 (SD 1.55); mean Charlson Comorbidity Score = 3.86 (SD 2.05); mean number of medications on discharge = 11 (SD 4). 28% lived alone. Baseline characteristics are outlined in Table 7.1.

70% of participants (96/137) had a CHA_2DS_2VASc score ≥ 4 points. Mean 4.25 (SD 1.85). *(Refer to Figure 7.2; Distribution of CHA_2DS_2VASc scores)*. 68 % of participants (56/137) had a HAS-BLED score ≥ 3. (This equates to greater than 3.74 bleeds per 100 patient-years. Mean 2.85 (SD 1.55). *(Refer to Figure 7.3 Distribution of HAS-BLED scores).* Although differences were not significant, participants who were not prescribed anticoagulation at discharge were at greater risk of stroke *(4.71 vs. 4.13 p=0.571)* and bleeding *(3.42 vs. 2.66 p=0.569)* as indicated on the CHA_2DS_2VASc and HASBLED schemata, and had greater comorbidity *(p=0.085)* when compared to those prescribed anticoagulation. Only 66% of participants were prescribed an anticoagulant *(58% warfarin, 4% NOAC and 2% subcutaneous anticoagulation)*.

Worse self-reported heart failure self-care behaviour *(p=0.010)* and having a resuscitation status as 'not for CPR' *(p=0.038)* were associated with not receiving anticoagulation at discharge. Whilst statistical significance was not achieved, being frail and having higher comorbidity were associated with not receiving anticoagulation at discharge. The majority of patients were classified as frail = 63% (n=58). When the categories of non-frail and pre-frail were combined, frailty was associated with suboptimal prescription of anticoagulation in individuals with CHF and concomitant AF *(78% vs. 58% p= 0.081).*

TABLE 7.1 BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS.

Characteristic	Total Sample (n = 137)	Non-Anticoagulated (n =45)	Anticoagulated (n =88)	P value
Age, mean (SD), y Range	72 (16) (19-94)	77 (13)	70 (16)	0.169
Male, n (%)	87 (65)	27 (60)	60 (68)	0.348
Unplanned admission, n. (%)	117 (88)	44 (98)	73 (83)	**0.013**
Heart failure related admission, n (%)	90 (68)	30 (67)	60 (68)	0.860
Length of stay, median days	7	7	8	0.600
Ethnicity, Caucasian, No. (%) (n=127)	114 (90)	36 (86)	78 (92)	0.290
Lives alone, No. (%) (n=119)	33 (28)	14 (34)	19 (24)	0.257
English Language Spoken at Home, No. (%) (n=126)	94 (75)	28 (68)	66 (79)	0.148
Myocardial Infarction (n=131)	33 (25)	16 (36)	17 (20)	**0.036**
Hypertension (n=133)	85 (64)	29 (65)	56 (64)	0.927
Hypercholesterolemia (n=131)	68 (52)	24 (55)	44 (51)	0.667
Diabetes (n=133)	46 (37)	18 (40)	28 (32)	0.348
Stroke or transient ischaemic attack (n=133)	29 (22)	9 (20)	20 (23)	0.719
Coronary Artery Disease (n=129)	56 (43)	22 (52)	34 (40)	0.209
Renal Disease (n=131)	50 (38)	18 (41)	32 (37)	0.646
Asthma or Lung Disease (n=131)	52 (40)	20 (46)	32 (39)	0.338
LV ejection fraction < 45%* (n=110)	65 (59)	24 (60)	41 (59)	0.883
Sodium mean, (SD)	138 (3.83)	138 (3.41)	138 (3.97)	0.365
INR mean, (SD) (n=100)	1.9 (0.65)	1.5 (0.7)	2.0 (0.6)	0.890
eGRF mean, (SD)	50 (19)	46 (18)	52 (19)	0.264
Creatinine mean, (SD) (n=135)	130 (67)	143 (93)	124 (49)	0.086
Haemoglobin mean, (SD)	118 (21)	119 (19)	118 (21)	0.666
ACE Inhibitor or ARB (n=133)	52 (39)	12 (27)	40 (46)	**0.036**
Warfarin (n=133)	77 (58)	0 (0)	77 (88)	**<0.01**
Novel anticoagulant (n=133)	5 (4)	0 (0)	5 (6)	0.103
Any antiplatelet (n=133)	55 (41)	31 (70)	24 (27)	**<0.01**
Digoxin (n=133)	43 (32)	10 (22)	33 (38)	0.075
Diuretic (n=133)	106 (80)	34 (76)	72 (82)	0.396
B-Blocker (n=133)	75 (56)	22 (49)	53 (60)	0.212
Antiarrhythmic (n=133)	33 (25)	10 (22)	23 (26)	0.621
Calcium Channel Blocker (n=133)	16 (12)	3 (7)	13 (15)	0.174
CHA_2DS_2VASc Score, mean, (SD)	4.25 (1.85)	4.71 (1.74)	4.13 (1.83)	0.571
HASBLED Score, mean, (SD)	2.85 (1.55)	3.42 (1.53)	2.66 (1.45)	0.569
Charlson Comorbidity Score, mean (SD)	3.86 (2.05)	4.58 (2.38)	3.52 (1.74)	0.085
NYHA Class II – III (%) (n=99)	61 (62)	17 (65)	44 (60)	0.645
Frailty status, (% frail category) (n=92)	58 (63)	18 (78)	40 (58)	0.081
CPR status, (% not for CPR) (n=121)	15 (12)	9 (22)	6 (8)	**0.038**
Self-Care Behaviour (EHFSCBSc) Median (IQR) (n=42, 11 vs. 32)	31 (16)	41(17)	28 (16)	**0.010**
Medication Adherence (Morisky Self Report) (n=83) (% 1 or more responses to non-adherence)	36 (43)	8 (42)	28 (44)	0.899

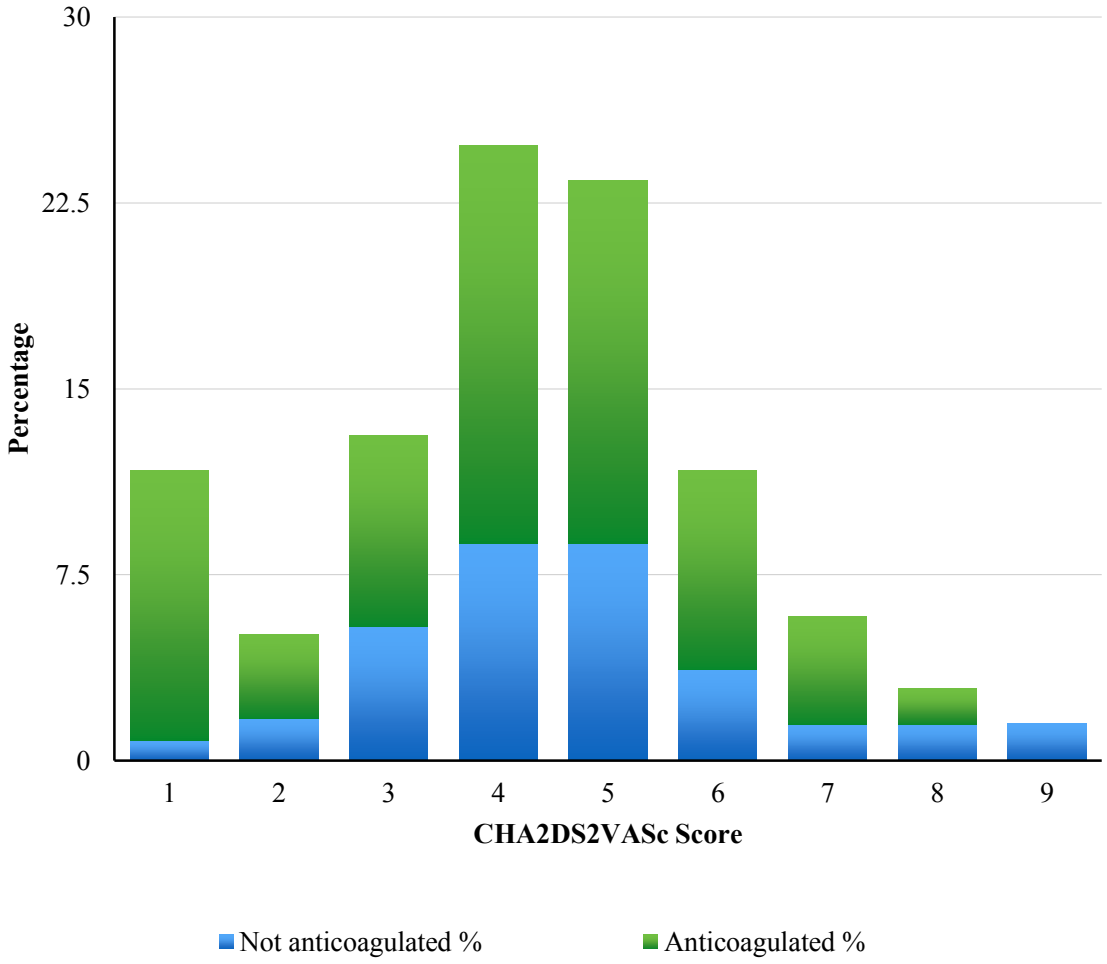

FIGURE 7.2 STROKE RISK DISTRIBUTION PER ANTICOAGULATION STATUS AT DISCHARGE.

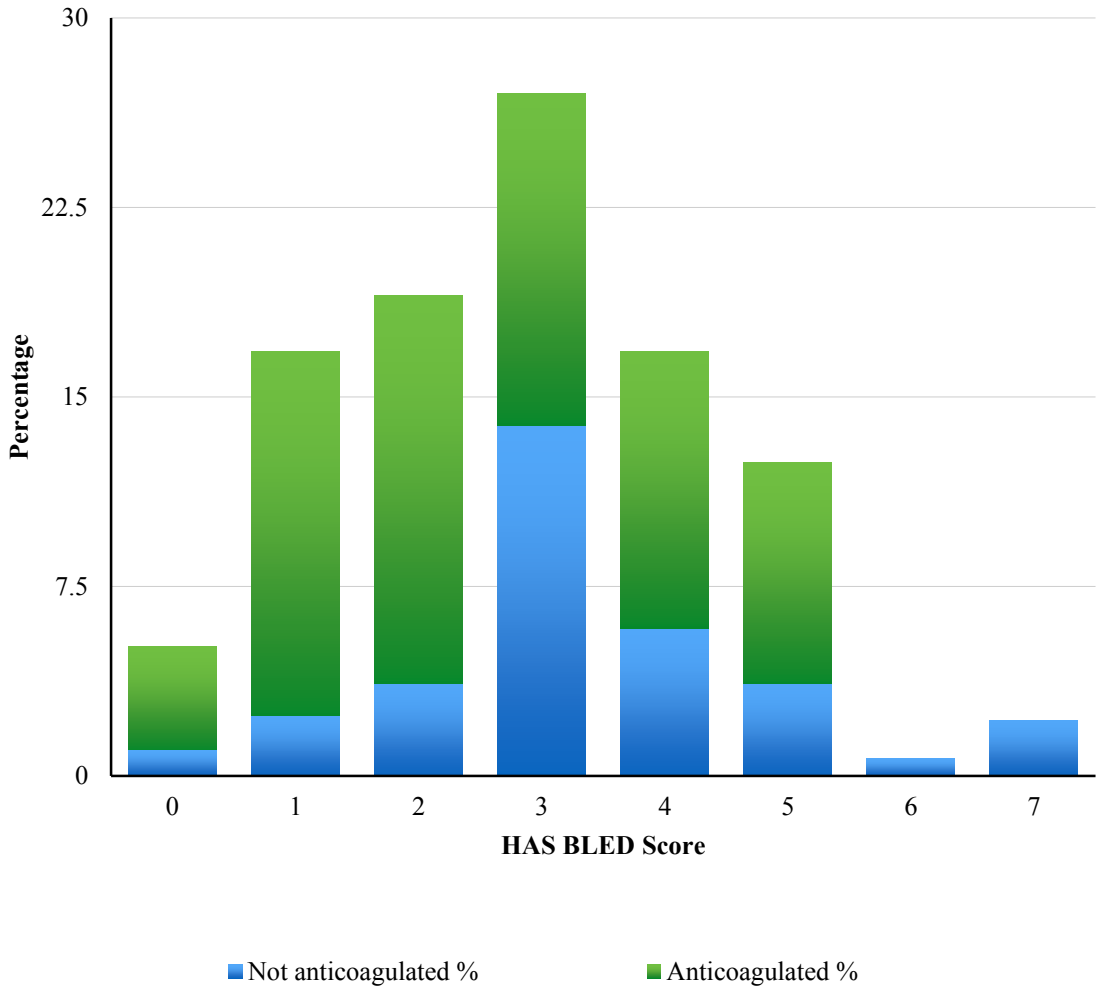

FIGURE 7.3 BLEEDING RISK DISTRIBUTION PER ANTICOAGULATION STATUS AT DISCHARGE.

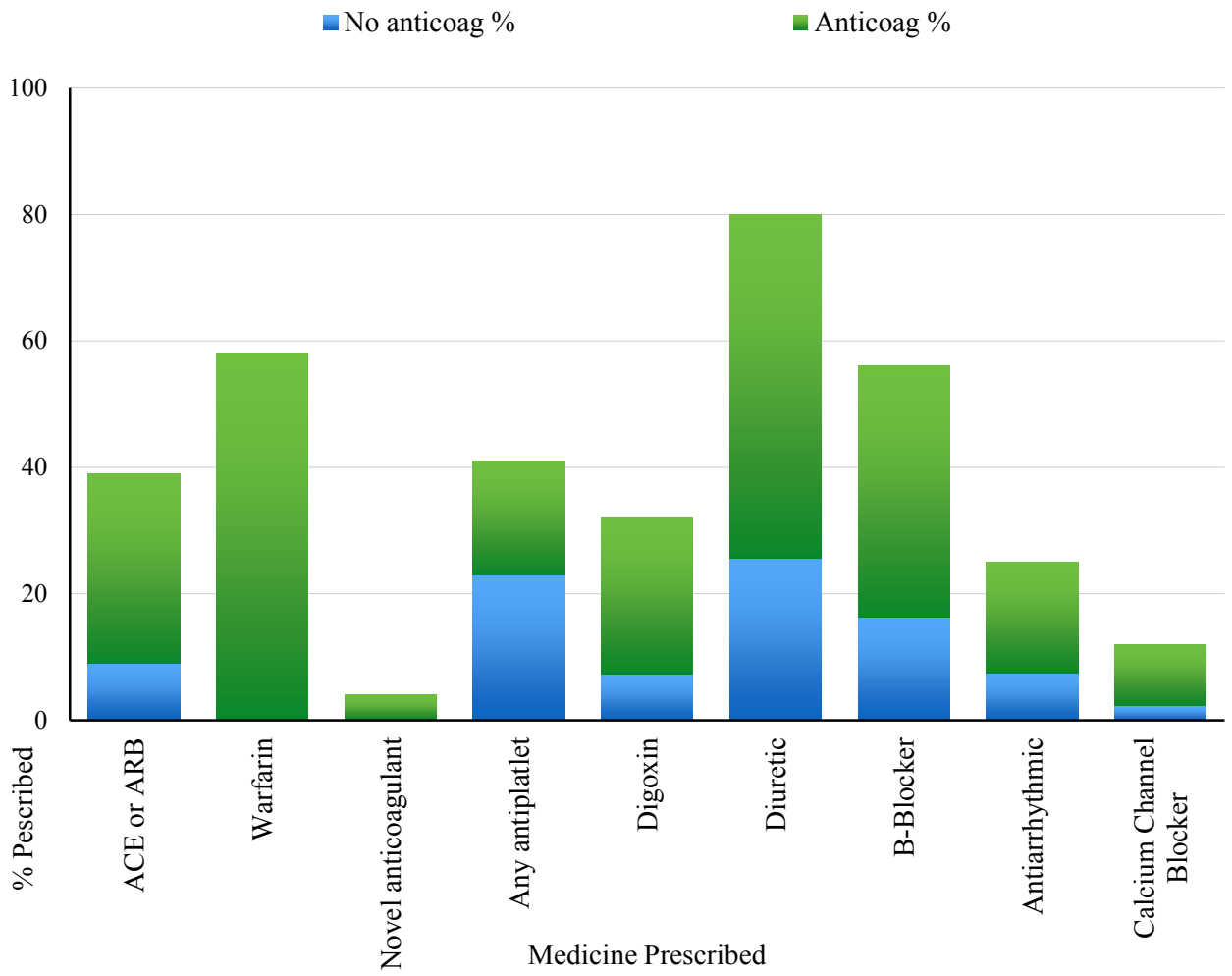

FIGURE 7.4 DISCHARGE PHARMACOTHERAPY CATEGORISED BY DISCHARGE BY COAGULATION STATUS AT DISCHARGE.

7.5.2. 12 MONTH OUTCOMES

All-cause rehospitalisation was frequent (68%) and 12-month all-cause mortality was high (29%). Prescription of anticoagulation at discharge was significantly associated with lower mortality at 12 months, but was not associated with lower rates of rehospitalisation among individuals with CHF and concomitant AF. Patients prescribed anticoagulation at discharge had lower unadjusted rates of all-cause mortality (23% versus 40%; p = 0.037) at 12 months. All-cause mortality was almost half at 12-months in patients receiving anticoagulation when compared to those not receiving anticoagulation at baseline. [p=0.037, HR 0.506, 95% CI 0.267-0.956]

TABLE 7.2 UNADJUSTED EVENTS AT 12 MONTHS POST-HOSPITALIZATION.

Event Type	Total sample n=x (%)	Non-anticoagulated n=x (%)	Anticoagulated n=x (%)	P value	Hazard Ratio
All-cause mortality (n=133)	38 (29)	18 (40)	20 (23)	**0.037**	0.506 [95% CI 0.267-0.956]
All-cause rehospitalisation (n=133)	90 (68)	31 (69)	59 (67)	0.830	1.360 [95% CI 0.867-2.133]
TIA (n=133)	2 (2)	0 (0)	2 (2)	0.308	
Stroke (n=133)	4 (3)	3 (7)	1 (1)	0.077	
Composite for all-cause TIA and Stroke	6 (5)	3 (7)	3 (3)	0.392	0.423 [95% CI 0.068-2.630]
Bleeding (n=133)	25 (19)	6 (13)	19 (22)	0.249	
Composite for all-cause rehospitalisation and mortality (n=133)	98 (80)	34 (76)	64 (73)	0.726	0.961 [95% CI 0.634-1.458]

TABLE 7.3 MEAN EVENT FREE TIME COMPOSITE ENDPOINT OF ALL-CAUSE HOSPITALIZATION AND MORTALITY

Anticoagulant prescribed on discharge	Mean Estimate	Mean Std Error	Mean 95% CI
NO	152	22	109-195
YES	155	16	124-186
Overall	154	13	129-179

(Log Rank Sig 0.852)

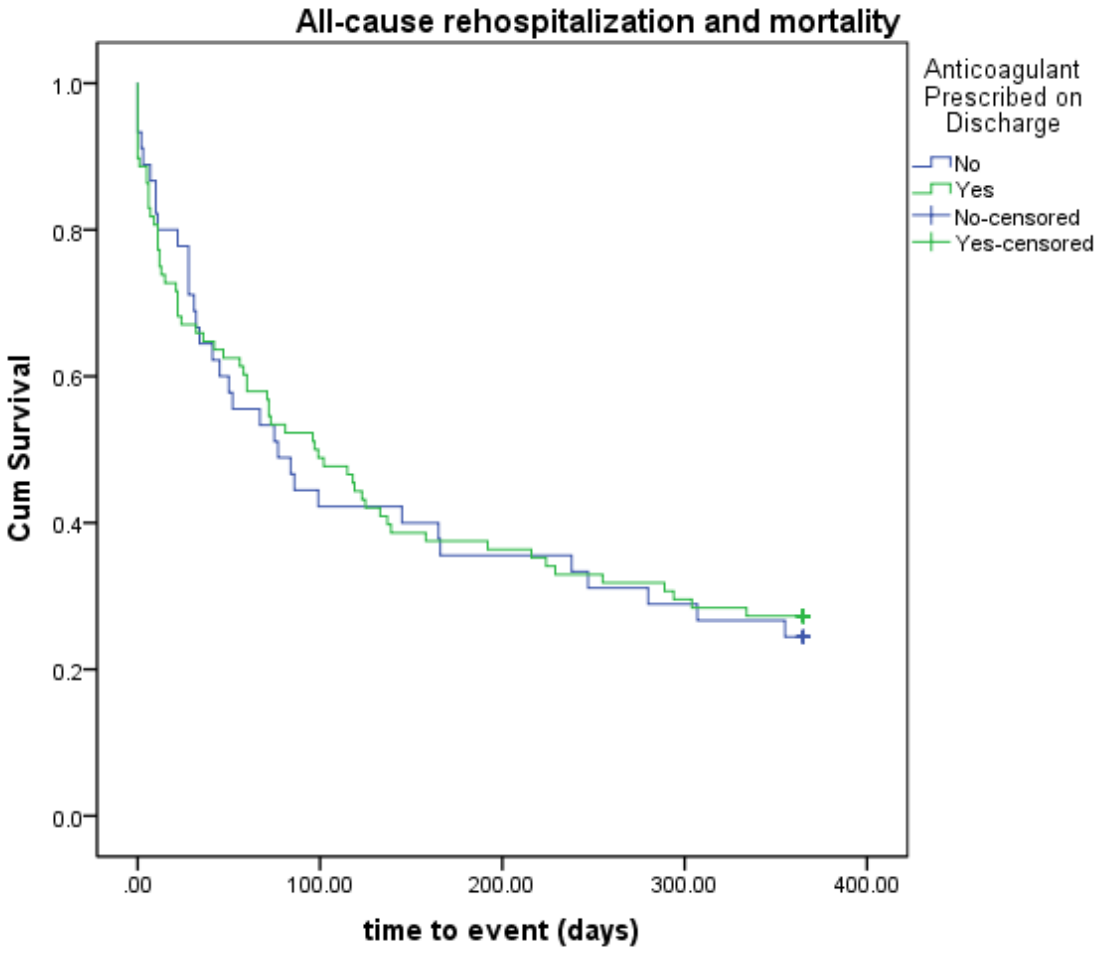

FIGURE 7.5 KAPLAN-MEIER SURVIVAL ANALYSIS FOR COMPOSITE ENDPOINT OF ALL-CAUSE HOSPITALISATION AND MORTALITY.

(Log Rank Sig 0.852)

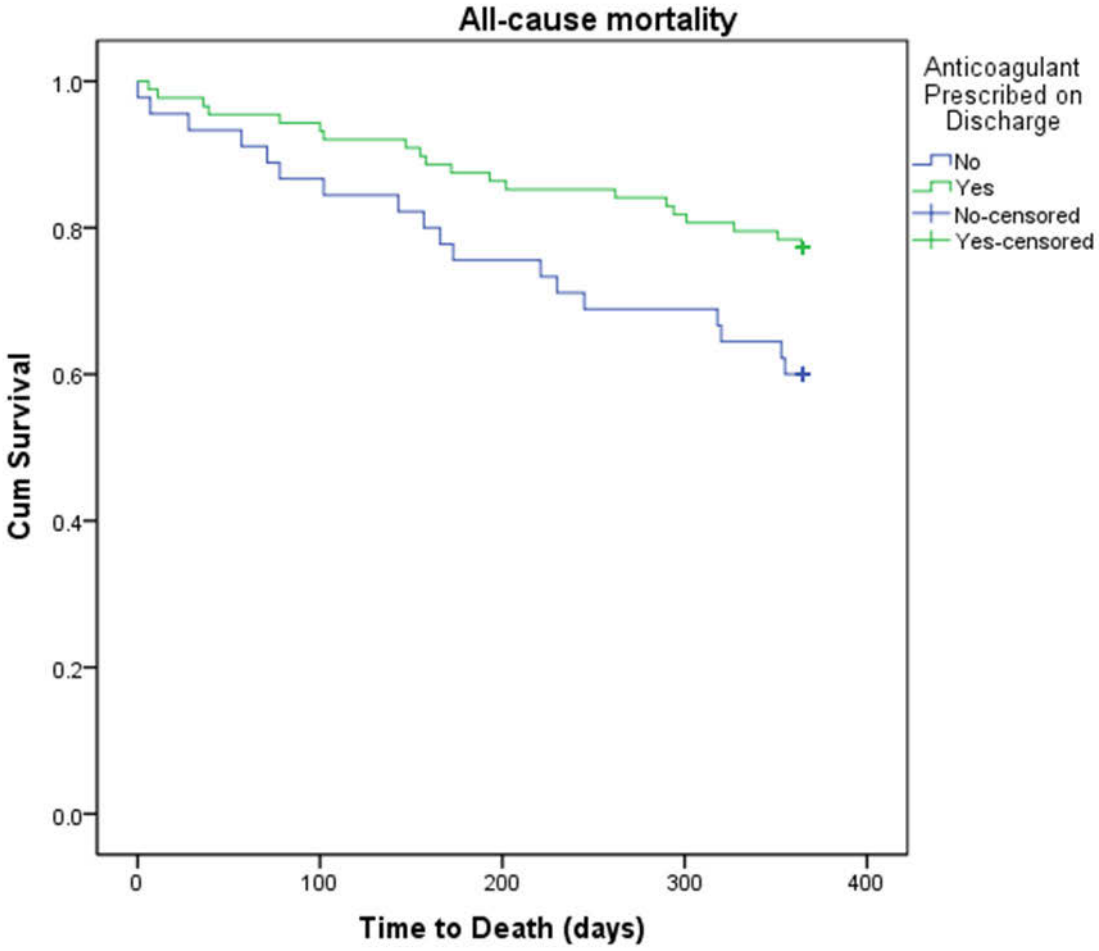

FIGURE 7.6 KAPLAN-MEIER SURVIVAL ANALYSIS FOR COMPOSITE ENDPOINT OF ALL-CAUSE MORTALITY.

(Log Rank Sig 0.032)

7.6. DISCUSSION

The proportion of 43% of AF incidence in CHF, within our overarching screening sample is consistent with other studies.[20] This study demonstrates that thromboprophylaxis in underused in this frail, elderly high-risk cohort. Our findings are similar to that reported in existing studies and systematic review data.[4] There is scope for improvement of thromboprophylaxis for stroke prevention.

Most patients in the non-anticoagulated group were prescribed anti-platelet at discharge (70% compared with 23% in the anticoagulated group *(p = <0.01).* This could be explained by coexistent CAD (52%) or separate carotid disease (20% previous stroke or TIA). This suggests that clinicians are prepared to prescribe an anti-platelet in some patients as thromboprophylaxis in circumstances where they are not prepared to use oral anticoagulation.

Within the AFASTER cohort, 56% were prescribed β-blockers at time of discharge from hospital. A recent study by Kotecha et al (2014) found that the use of β-blockers led to a significant reduction in all-cause mortality in patients with sinus rhythm (HR 0.73, 0.67-0.80; p<0.001), but not in patients with AF (HR 0.97, 0.83-1.14; p=0.73), with a significant p value for interaction of baseline rhythm (p=0.002). The study authors recommend that β-blockers should not be used preferentially over other rate-control medications and not regarded as standard therapy to improve prognosis in patients with concomitant heart failure and atrial fibrillation.[21]

7.6.1. IMPORTANCE OF CONSIDERING MULTIMORBIDITY

CHF and AF occur with complex interplay. They seldom exist independent of other comorbidities and cardiovascular risk factors.[22,23] Multimorbidity including AF, adds further to the complexity of care management for individuals with CHF. Clinical practice guidelines (CPGs) play a vital role in the translation of evidence into practice and the improvement of care quality for individuals with chronic conditions. However, in those with multimorbidity, applications of key care recommendations may lead to polypharmacy and consequently overwhelming treatment burden.[24] This may negatively impact adherence to treatment regimes, including thromboprophylaxis.

There is robust evidence that the use of thromboprophylaxis (including warfarin, dabigatran, rivaroxaban, and apixaban) significantly reduces stroke risk in CHF with AF. In contrast, there is insufficient evidence to support anticoagulation use in CHF alone.[25] Systematic review evidence reveals that thromboprophylaxis in AF continues to be underused in clinical practice.[4] International data from the Global Anticoagulant Registry in the FIELD (GARFIELD) registry draws attention to the concern that thromboprophylaxis is not being best used in accordance with stroke risk scores and guidelines. These data, including 10,641 participants also highlights the overuse of thromboprophylaxis in low risk individuals and underuse in those at high stroke risk.[23] The decision to treat high risk individuals with thromboprophylaxis is a complex choice for patients, caregivers and health care providers.[26] Previous research has highlighted the frequent mismatch between patient and clinician values in the context of decision making.[27] For example, physicians are likely to advocate against thromboprophylaxis when patients would choose it, and in contrast, patients are likely to be prescribed treatment they would not choose.[27] Treatment decisions around thromboprophylaxis ought to be patient-centered. They must be considered in the context of the best evidence to date; within the scope of the clinician expertise; and one that is central to the individual patient's situation, knowledge, attitudes, values and beliefs.[26]

Luong *et al* (2014) emphasise the importance of recognising, that whilst stroke continues to be the most worrisome consequence of AF, it is not the primary cause of death in individuals with AF.[28] The increased utilisation of anticoagulation in the last three decades has seen a decline of the incidence of stroke in individuals with AF.[29] However, there has been no reduction in mortality regardless of effective thromboprophylaxis. This highlights that stroke is not the best predictor for mortality in individuals with AF. Furthermore, these individuals are more likely to die due to chronic heart failure than of stroke.[28,30]

7.6.2. GUIDELINE BASED THERAPY IN THE CONTEXT OF MULTIMORBIDITY

There is need to address comorbidity in the provision of patient-centered care. Guidance incongruence and recommendation divergence may exist for complex individuals, when recommendations are based on a singular comorbidity. Guideline blending is needed for similar chronic conditions.[24] There is scope for the amalgamation of CHF and AF practice guidance and future models of chronic care service delivery. Further, there is need to tailor clinical practice guidelines to account for clinical judgement, acknowledging the role of the individual throughout person-centered models of care.[31]

7.6.3. HIGH RISK OF REHOSPITALISATION AND DEATH

The prevalence of CHF and AF are predicted to increase with the incidence of AF expected to double in the next 20 years.[32] The prevalence of AF increases with the severity of CHF, as defined by the NYHA functional class.[33] Rehospitalisation is common and costly for both chronic conditions. Over 50% of patients with CHF are readmitted to hospital within 6 months and approximately 40% of patients with AF, within 12 months.[34,35] Pre-existing AF has been previously established as an independent predictor of 30-day readmissions for individuals with CHF in an analysis of 3,758 individuals using data from the AFA Get-With-The-Guidelines registry, enrolled from 2007-2010.[36] These data suggest that patients with CHF and AF had a 1.39 times increased odds of readmission than those with CHF but without AF. From this cohort 21% (780/3,758) individuals were hospitalised within 30 days.[36] Further, individuals who experience a CHF related hospitalization have more than double the likelihood of not being alive within 2 years.[37] CHF related hospitalization is a recognised indicator of syndrome progression and is associated with poor outcomes.[37]

Despite recent advances in healthcare technology and pharmacotherapies, CHF continues to place a large burden to the healthcare budget.[38] The annual cost of heart failure was recently estimated at 2% of the total US healthcare budget, amounting to $39.2 billion USD in 2010. Almost 60% of these costs related to hospital care.[38] There has been renewed attention and debate on innovative methods to prevent potentially avoidable HF related hospitalizations.

7.6.4. LIVING ALONE AND FRAILTY AS RISK FACTORS FOR INCREASED HOSPITALIZATION AND MORTALITY

Previous studies have demonstrated that living alone and loneliness are predictors of increased mortality. Data from The global Reduction of Atherothrombosis for Continued Health (REACH) Registry that followed up 44,573 participants, aged ≥ 45 years from 44 countries at 4 years. 19% (n= 8,594) of this cohort lived alone. Living alone was associated with higher 4-year mortality.[39]

Associations between frailty and adverse outcomes (including rehospitalisation and mortality); have been previously established. Worse outcomes are evidenced with increasing frailty severity.[40] Fried (2001) using data from the Cardiovascular Health Study (CHS), including 5,317 participants with a 7-year length of follow up identified worse outcomes for severe frail individuals when compared with intermediate frail individuals including hospitalization [Hazard Ratio (HR) 1.27, 95% CI 1.11-1.46 vs. HR 1.11, 95% CI 1.03-1.19] and mortality [HR 1.63, 95% CI 1.27-2.08 vs. HR 1.32, 95% CI 1.13-1.55].[41] Similarly, previous research by Perera and colleagues (2009) has demonstrated that frail elderly inpatients with AF are less likely to receive warfarin than non-frail ($p< 0.001$), and appear more susceptible to adverse outcomes, regardless of treatment with or without thromboprophylaxis.[42]

7.7. LIMITATIONS

This study has some limitations. Firstly, the SHARE Frailty Index is not validated for use in the inpatient setting.[19] This measure was quick and simple to conduct in the acute inpatient setting. Initially developed for the community setting, this has not been validated for the chronic heart failure population in an inpatient setting. Secondly, participants with cognitive dysfunction and speaking languages other than English were excluded from measures including assessment of frailty, heart failure self-care behavior and medication adherence self-report. Thirdly, outcome assessment of stroke/ TIA and bleeding events were often self-reported. Stroke was confirmed by via electronic methods, where a CT brain report was available. Fourthly, living alone status was obtained via medical record review. Whilst statistical significance was not achieved to compare differences in multimorbidity and frailty, values trend in direction towards significance. Therefore, a larger, more comprehensive snapshot that provides prospective observational data is recommended. The majority of our cohort were English speaking and of Caucasian ethnic background, thus limiting the utility and generalizability of this research. In spite of these limitations, this study has several strengths. This study offered a detailed insight using multiple, routinely collectable clinical variables. Further, selection bias was reduced through the recruitment of prospective consecutive participants and waiver of consent for enrollment at baseline.

7.8. CONCLUSION AND IMPLICATIONS

The results of our study demonstrate that in this frail, elderly and high-risk cohort, thromboprophylaxis was underused. All-cause rehospitalisation was frequent and 12-month all-cause mortality was high. Prescription of anticoagulation at discharge was significantly associated with improved mortality at 12 months, but was not associated with improved rates of rehospitalisation among individuals with CHF and concomitant AF. This study highlights that frailty, multimorbidity, and self-care abilities to be important considerations in thromboprophylaxis decision making. Patients and caregivers must be central to thromboprophylaxis treatment choices. Whilst the CHA_2DS_2VASc and HAS-BLED schemata are useful in practice to risk stratify stroke and bleeding. It is problematic simply to use these tools in isolation to guide treatment decisions. Whilst helpful, they lack ability to provide a comprehensive assessment that includes key considerations including multimorbidity, frailty and self-care ability.

7.9. REFERENCES

1. Krum H, Jelinek MV, Stewart S, Sindone A, Atherton JJ. 2011 Update to National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand. Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006. *Medical Journal of Australia.* 2011;194(8):405-409.

2. Stewart S, Carrington MJ, Marwick T, et al. The WHICH? trial: rationale and design of a pragmatic randomized, multicentre comparison of home- vs. clinic-based management of chronic heart failure patients. *European Journal of Heart Failure.* August 1, 2011 2011;13(8):909-916.

3. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive SummaryA Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Journal of the American College of Cardiology.* 2014.

4. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GYH. Underuse of Oral Anticoagulants in Atrial Fibrillation: A Systematic Review. *The American Journal of Medicine.* 2010;123:638-645.

5. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Diseases.* 1987;40(5):373-383.

6. Lip GYH. Implications of the CHA2DS2-VASc and HAS-BLED scores for thromboprophylaxis in atrial fibrillation. *The American Journal of Medicine.* 2011;124:111-114.

7. Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage: Results from the National Registry of Atrial Fibrillation (NRAF). *American Heart Journal.* 2006;151(3):713-719.

8. Lip GYH, Frison L, Halperin JL, Lane DA. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation. *Journal of American College of Cardiology.* 2011;57(2):173-180.

9. Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. *European Heart Journal.* 2012;33:2719-2747.

10. Wann L, Curtis A, January C, et al. 2011 ACCF/ AHA/ HRS focused update on the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;123:104-123.

11. National Institute for Health Care Excellence. *Atrial fibrillation: the management of atrial fibrillation.* UK: NICE; June, 2014 2014.

12. Boriani G, Botto GL, Padeletti L, et al. Improving Stroke Risk Stratification Using the CHADS2 and CHA2DS2VASc Risk Scores in Patients With Paroxysmal Atrial Fibrillation by Continuous Arrhythmia Burden Monitoring. *Stroke.* 2011;42:1768-1770.

13. Apostolakis S, Lane DA, Guo Y, Buller H, Lip GYH. Performance of the HEMORR2HAGES, ATRIA, and HAS-BLED bleeding risk-prediction scores in patients with atrial fibrillation undergoing anticoagulation. *Journal of American College of Cardiology.* 2012;60(9):000-000.

14. Gehi A, Haas D, Pipkin S, Whooley M. Depression and Medication Adherence in Outpatients With Coronary Heart Disease: Findings From the Heart and Soul Study. *Archives of Internal Medicine.* 2005;165(21):2508-2513.

15. Morisky DE, Green LW, Levine DM. Concurrent and Predictive Validity of a Self-Reported Measure of Medication Adherence. *Medical Care.* 1986;24(1):67-74.

16. Tan X, Patel I, Chang J. Review of the four item Morisky Medication Adherence Scale (MMAS-4) and eight item Morisky Medication Scale (MMAS-8). *Innovations in Pharmacy.* 2014;5(3):1-8.

17. Jaarsma T, Strömberg A, Mårtensson J, Dracup K. Development and testing of the European Heart Failure Self-Care Behaviour Scale. *European Journal of Heart Failure.* June 1, 2003 2003;5(3):363-370.

18. Cameron J, Worrall-Carter L, Driscoll A, Stewart S. Measuring Self-care in Chronic Heart Failure: A Review of the Psychometric Properties of Clinical Instruments. *Journal of Cardiovascular Nursing.* 2009;24(6):E10-E22 10.1097/JCN.1090b1013e3181b5660f.

19. Romero-Ortuno R, Walsh CD, Lawlor BA, Kenny RA. A frailty instrument for primary care: findings from the survey of health, ageing and retirement in Europe (SHARE). *BMC Geriatrics.* 2010;10(57):1-12.

20. Stewart S, Carrington MJ, Marwick TH, et al. Impact of home versus clinic-based management of chronic heart failure: the WHICH? (Which Heart Failure Intervention Is Most Cost-Effective & Consumer Friendly in Reducing Hospital Care) multicenter, randomized trial. *J Am Coll Cardiol.* Oct 2 2012;60(14):1239-1248.

21. Kotecha D, Holmes J, Krum H, et al. Efficacy of B-blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis. *The Lancet.* 2014.

22. Saczynski JS, Go AS, Magid DJ, et al. Patterns of Comorbidity in Older Adults with Heart Failure: The Cardiovascular Research Network PRESERVE Study. *Journal of the American Geriatrics Society.* 2013;61(1):26-33.

23. Kakkar AK, Mueller I, Bassand JP, et al. Risk profiles and antithrombotic treatment of patients newly diagnosed with atrial fibrillation at risk of stroke: perspectives from the international, observational, prospective GARFIELD registry. *PloS one.* 2013;8(5):e63479.

24. Hughes LD, McMurdo MET, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. *Age and Ageing.* January 1, 2013 2013;42(1):62-69.

25. Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation. *Circulation.* August 15, 2006 2006;114(7):e257-e354.

26. Ferguson C, Inglis S, Newton P, Middleton S, Macdonald P, Davidson P. Atrial fibrillation and thromboprophylaxis in heart failure: the need for patient-centrered approaches to address adherence. *Vascular Health & Risk Management.* 2013;9:3-11.

27. Alonso-Coello P, Montori VM, Díaz MG, et al. Values and preferences for oral antithrombotic therapy in patients with atrial fibrillation: physician and patient perspectives. *Health Expectations.* 2014;IN PRESS.

28. Luong C, Barnes M, Tsang TM. Atrial Fibrillation and Heart Failure: Cause or Effect? *Curr Heart Fail Rep.* 2014/09/26 2014:1-8.

29. Miyasaka Y, Barnes ME, Bailey KR, et al. Mortality trends in patients diagnosed with first atrial fibrillation: a 21-year community-based study. *J Am Coll Cardiol.* Mar 6 2007;49(9):986-992.

30. Marijon E, Le Heuzey J-Y, Connolly S, et al. Causes of Death and Influencing Factors in Patients with Atrial Fibrillation: A Competing Risk Analysis from the Randomized Evaluation of Long-Term Anticoagulant Therapy Study. *Circulation.* September 9, 2013 2013.

31. Arnett DK, Goodman RA, Halperin JL, Anderson JL, Parekh AK, Zoghbi WA. AHA/ACC/HHS Strategies to Enhance Application of Clinical Practice Guidelines in Patients With Cardiovascular Disease and Comorbid Conditions: From the American Heart Association, American College of Cardiology, and US Department of Health and Human Services. *Circulation.* September 11, 2014 2014.

32. Colilla S, Crow A, Petkun W, Singer DE, Simon T, Liu X. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. *The American journal of cardiology.* Oct 15 2013;112(8):1142-1147.

33. Maisel WH, Stevenson LW. Atrial fibrillation in heart failure: epidemiology, pathophysiology, and rationale for therapy. *The American journal of cardiology.* Mar 20 2003;91(6a):2d-8d.

34. Desai AS, Stevenson LW. Rehospitalization for Heart Failure: Predict or Prevent? *Circulation.* July 24, 2012 2012;126(4):501-506.

35. Amin AN, Jhaveri M, Lin J. Hospital readmissions in US atrial fibrillation patients: occurrence and costs. *American journal of therapeutics.* Mar-Apr 2013;20(2):143-150.

36. Desai NK, Powell M, Skaf J, et al. ATRIAL FIBRILLATION AS AN INDEPENDENT PREDICTOR OF HEART FAILURE READMISSIONS: ANALYSIS OF "GET-WITH-THE-GUIDELINES" HEART FAILURE. *Journal of the American College of Cardiology.* 2014;63(12_S).

37. Ahmed A, Allman RM, Fonarow GC, et al. Incident heart failure hospitalization and subsequent mortality in chronic heart failure: a propensity-matched study. *Journal of cardiac failure.* Apr 2008;14(3):211-218.

38. Braunschweig F, Cowie MR, Auricchio A. What are the costs of heart failure? *Europace.* 2011;13:ii13-ii17.

39. Udell JA, Steg PG, Scirica BM, et al. Living alone and cardiovascular risk in outpatients at risk of or with atherothrombosis. *Arch Intern Med.* Jul 23 2012;172(14):1086-1095.

40. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *The Lancet.* 2013;381(9868):752-762.

41. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *The journals of gerontology. Series A, Biological sciences and medical sciences.* Mar 2001;56(3):M146-156.

42. Perera V, Bajorek BV, Matthews S, Hilmer SN. The impact of frailty on the utilisation of antithrombotic therapy in older patients with atrial fibrillation. *Age and Ageing.* 2009;38:156-162.

CHAPTER 8: CONCLUSION: IMPLICATIONS FOR PRACTICE, POLICY AND RESEARCH.

8.1. REVIEW AND DISCUSSION

This thesis has described the barriers and enablers to thromboprophylaxis in individuals at high risk of stroke in a population recently hospitalised with CHF. This work emphasizes the need for patient-centered approaches to decision making for thromboprophylaxis, to assist in judicious treatment and further, to optimise knowledge and adherence. The burden of CHF and AF are ever increasing. Given that AF begets CHF, as the numbers of individuals with AF increase this burden is only set to exponentially increase.

Chapter two of this thesis provided a review of the epidemiology of AF, the available validated risk schemes for stroke and bleeding, and pharmacological and non-pharmacological treatment options. This paper emphasized the need to consider a patient's circumstances and for tailored treatment, to meet the individual's needs, whilst balanced in the context of the best available evidence.

8.2. AF CLINICAL PRACTICE GUIDELINES

Chapter two described the lack of an Australian and New Zealand specific, multi-disciplinary AF management guideline. Our comprehensive review of electronic databases and search engines revealed no ANZ specific, multidisciplinary clinical management guideline for AF.[1] Clinical practice guidelines are vital to guide clinician and patient decisions about care based on the best available evidence for specific circumstances.[2] Clinical practice guidelines would likely assist to improve decision making, processes of care, and ultimately patient outcomes for individuals living with AF.[2] A comprehensive guideline exists in Australia for the prevention, detection and management of chronic heart failure.[3] These guidelines are wide-ranging across the spectrum of care, and take a multi-disciplinary approach to the management of CHF. There is urgent need for consensus and evidence based clinical practice guidelines for the management of AF in the ANZ context. Similar guidelines exist in the USA, UK and Europe for example, as produced and endorsed by the AHA, NICE and ESC groups.[4-6] Although these guidelines have been subject to recent criticism, as they have limited application in the context of complex comorbidity.[7] These are lacking in Australia and New Zealand. Minimum standard guidelines would provide a benchmark for clinical practice, and provide an overview of contemporary evidence based management in the ANZ setting tailored to approved medications and care models. A targeted and collaborative approach from the National Heart Foundation and the Cardiac Society of ANZ would deliver the most credible result. Guidelines would need to address the continuum of care from primary care, to acute and chronic care, including; prevention, diagnosis, and treatment.

Recommendation 1:

There is need for the development of a multi-disciplinary, ANZ Atrial Fibrillation clinical practice guideline.

8.3. CLINICAL ASSESSMENT AND DECISION MAKING FOR THROMBOPROPHYLAXIS

AF is the most commonly occurring cardiac arrhythmia in CHF. Both CHF and AF are burdensome, chronic conditions alone, and can be troublesome to manage concomitantly. Treatment is highly complex, and not risk-free. It is challenging to balance the benefits and risks of anticoagulation for stroke prevention. Nurses have a key role in the management of patients with CHF and AF, and will care for individuals across the spectrum of care from primary to acute care settings. Nurses must maintain a contemporary knowledge base to be adept in AF management. Nurses are well-placed throughout clinical practice to have meaningful conversations with patients about their treatment options, symptom management, lifestyle factors, and self-management strategies. Treatment must be personalized towards the individual's needs, and must be balanced within the context of the best available evidence. Assessment for thromboprophylaxis should include a comprehensive assessment.[8] Clinicians ought to use overly simplified stroke and bleeding risk prediction calculators with caution. A comprehensive assessment includes consideration of a number of factors such as; frailty, self-care behavior, likeliness for treatment adherence, cognitive ability, functional impairment, falls, stress and depression, literacy, caregiver support, polypharmacy etc. Whilst risk prediction tools such as the CHA_2DS_2VASc and HAS-BLED are highly useful in the clinical setting and simple to use, they fail to offer a holistic and patient-centered approach to thromboprophylaxis decision making. In addition, these tools provide complex risk-likelihood ratios, which many patients and their caregivers may not understand. This is likely to add to decision burden, from the perspective of the patient and their caregiver. Decision support tools and pictorial information that is easy to understand and digest, offer promise in this area. Expanding current validated and widely used risk prediction models to include other aforementioned factors, along with biochemical markers (including NT-ProBNP, Creatinine Clearance and eGFR), may assist in improving clinical decision making.[9,10] A novel scoring system named the R_2CHADS_2 has been recently proposed, which includes renal function assessment alongside traditional criteria in the

standard $CHADS_2$ metric. However, findings suggest that this does not improve the predictive ability of this tool. A recent study conducted by Chao and colleagues (2014) compared the new R_2CHADS_2 and the CHA_2DS_2VASc for predicting thromboembolic events in 526 patients receiving catheter ablation. This evaluation found no significant difference between the two scores in predicting thromboembolic events after AF. Yet, c-indices for both schemes were greater than 0.8, demonstrating good predictive ability. The authors advise that it may be inappropriate to add renal dysfunction to an existing score prediction system to estimate stroke risk.[11] Whilst this is true; renal function remains an important consideration in the chronic heart failure population with AF. Renal dysfunction is a significant risk factor for bleeding and many individuals with chronic heart failure may experience cardio-renal syndrome as evidenced by elevations in creatinine clearance and eGFR. Although renal function is a criteria in the HAS-BLED bleeding risk prediction tool, careful evaluation of such these biomarkers would benefit clinical decision making in HF with AF, and should be examined in future studies.

This thesis has generated new knowledge, and added to the understanding of the barriers and enablers to thromboprophylaxis. Data from the cohort study demonstrated that there are other important factors to decision making besides stroke and bleeding risk. Data identified that there were clinical differences in individuals who were prescribed anticoagulation, and those who were not at discharge. Increased morbidity, frailty and poor heart failure self-care behavior were clearly important factors in clinical decision making. Further, the review of medical records also provided data that support that homelessness, likeliness to adhere to therapy, multimorbidity, mental health, and end of life were also important considerations when making complex decisions related to thromboprophylaxis.

The problem of individuals being denied thromboprophylaxis is not new. Systematic review data demonstrates that in up to 30% of cases, individuals do not receive thromboprophylaxis for a number of reasons.[12] Where absolute contraindications exist, this is appropriate.

Chapter three highlighted some of the recognised barriers to thromboprophylaxis. This paper provided a solutions-based approach to problem solving some of the historical or perceived barriers to anticoagulation. This was framed within the World Health Organisation's multidimensional adherence model.[13] This provided a framework to examine issues of; socioeconomic; health system; condition related; treatment related; and patient related factors.

8.4. SHARED DECISION MAKING TO PROMOTE ADHERENCE

Shared decision making is a framework for improving the quality of communication of healthcare choices with individuals.[14] It is a process of building consensus, negotiation of goals, and finding agreement on care pathways.[15] In this study, warfarin was the most frequently used type of thromboprophylaxis, and 58% were prescribed this therapy. This remains a challenging drug for many clinicians, patients and caregivers. However, almost one third of participants were not prescribed thromboprophylaxis following their index hospitalisation. This suggests that many barriers remain to patients receiving thromboprophylaxis. Critical issues are falls and fear of bleeding events amongst clinicians. The barriers highlighted in this study include frailty, age, cognitive dysfunction, homelessness, mental illness, vision impairment, and depression. Facilitators to successful prescription and adherence were caregiver support, reminders and routine, self-testing and the use of technology. Perceived barriers to thromboprophylaxis need to be thoroughly scrutinized by clinicians to ascertain if prescription is possible. Patients and caregivers should be part of the process of close examination of the potential barriers. Clinicians must adopt patient-centered models of care, that ensures care is respectful and responsive and aligned to the patient's needs.[16] Shared decision-making allows clinicians to consider patients values, attitudes and beliefs towards thromboprophylaxis. Including these factors alongside risk versus benefit ratios, may assist in improving issues of adherence and also more effectively undertaking a comprehensive risk assessment. A well-documented barrier to physicians implementing shared decision making practices is the lack of time to provide information and options to patients.[17,18] Nurses are highly experienced communicators,

counsellors and educators. They are well situated to facilitate the shared decision making process.[19] Providing nurses with more opportunities, knowledge and skills in shared decision making will ultimately improve more patient-centered.[19]

Recommendation 2:

Enhancing shared decision making in AF should be a priority.

Improving nurses' knowledge and skills in SDM will likely improve PCC.

Decision support tools may offer support for shared decision making.

Chapter four provided a timely review of the role of the caregiver in thromboprophylaxis management in AF. This has provided valuable insight into the enabling attributes of the caregiver, explicitly in promoting adherence to treatment regimes. Further this review emphasized the important role of the caregiver in advocacy, family centered care and shared decision making. This paper highlighted the need to actively involve the caregiver throughout all aspects of care assessment and planning.

8.5. INCREASING ATTENTION TO THE CAREGIVER

Clinicians, educators and researchers must promote and support the caregiver role throughout all aspects of care.[20,21] The caregiver has a pivotal role in supporting individuals living with a chronic condition, and can positively influence behavior, issues of adherence and outcomes.[21] Individuals living with a chronic condition are more likely to require some level of caregiver assistance. Within clinical practice, it is essential that there is greater focus on inclusion of the caregiver when making treatment choices.[20] To date, there has been very limited research surrounding the role of the caregiver in AF, in comparison within other conditions. The literature review published in the *European Journal of Cardiovascular Nursing* (2014), we identified only two primary research studied that examined the role of the caregiver in AF. The first of the studies that we identified emphasized that patients living with AF, have a higher level of comorbidity, and are more likely to require caregiver assistance.[22] This need for caregiver assistance, should be assessed as part of a comprehensive clinical assessment, and may influence treatment choices. Secondly, it is important to recognise caregiver burden and burnout for caregivers of patients with AF. This burden occurs most commonly when caregivers experience a disrupted schedule, or is often seen in those providing > 4 hours/week care or when caring for frail, sick or disabled patients with a higher $CHAD_2$ score and requiring help with medications.[23] Assessment of caregiver needs and burden should be an integral part of any nursing assessment. There is scope for improvement on the integration of this aspect of care in contemporary practice. Further, caregivers must be recognised as key influencers in empowering patients to take responsibility for their own condition. Caregivers can also provide routine reminders, education and specific information that may have been omitted by the patient. Encouraging clinicians to work in partnership with caregivers can only stand to benefit patient outcomes. Clinicians must recognise the potential of caregivers in chronic care, and should adapt practices to best utilize their resources.

Recommendation 3:

The role of the caregiver in AF should be explored further, in research and practice.

The search of electronic databases and search engines revealed only two primary research studies examining the care role in AF. This paucity of original clinical research underpins the need for research programs that examine disparities and un-met needs of caregivers for those with non-malignant conditions, including CHF and AF. Further, there is urgent need for interventional studies that examine the impact of caregiver support in the setting of AF. A caregiver intervention study may include an educational arm, and tools that would facilitate enhanced decision support, medication adherence, along with improving knowledge of medications and their overall condition. A systematic review of systematic reviews published in 2014 highlights that education, support and information interventions warrant further research across chronic conditions.[24] In a large international survey, conducted during 2009 in 11 countries and including 825 patients, one in four patients were unable to explain AF.[25] Let alone why they are receiving the treatment and how this works. Similarly, 23% of patients reported in the survey that they did not know where to look, or whom to contact to get information on AF.[25] This further evidenced the need for improvement in this area of practice.

8.6. EVOLVING MODELS OF AF CARE

There is a need to target existing chronic care programs to increase attention on AF. Within the AFASTER study presented in this thesis, screening records demonstrated that 43% (209/365) of individuals with CHF also had concomitant AF. This prevalence of AF in CHF, justifies improving focus on AF within existing CHF programs. Future models of care should also formalize caregiver involvement. Clinicians must better understand the vital role of the caregiver in the management of chronic conditions, including CHF and AF.

Recent systematic review data were able to demonstrate that care driven by nurse-managed protocols is superior to that of standard care in the management of chronic conditions. Outcomes were improved in those with diabetes, hypertension and hyperlipidemia.[26] RCTs and meta-analyses have demonstrated that a multi-disciplinary approach to heart failure management is effective in reducing mortality, hospitalisation and improving quality of life.[27-30] Yet, to date there has been lesser focus on optimal model of management for individuals with AF. Recently, in Europe, Hendriks and colleagues (2012) were able to demonstrate nurse-led AF clinics to be superior to usual care with decreased rates of cardiovascular hospitalisation and cardiovascular mortality. Nurse-led care consisted of guideline base, software supported, integrated chronic care supervised by a cardiologist.[31] These are positive results. Future research may examine how to better embed shared decision making processes in this model of care.

The SAFETY (standard versus atrial fibrillation-specific management strategy) study was a multicenter RCT published in 2014, which examined the efficacy of a home-based disease-specific management strategy, delivered by cardiac nurses with multidisciplinary support.[32] This study found the SAFETY intervention prolonged the number of days alive and out of hospital, but did not to extend event-free survival. The study authors highlight that an AF-specific, nurse-led multidisciplinary program for older people with AF, similar to that seen in chronic heart failure management is feasible and will likely translate well into the wider population.[32]

Yet, disease based models of chronic care may be approached with some skepticism. Given AF more often than not exists alongside other cardiogeriatric conditions. Within this cohort the mean Charlson Comorbidity Index was 3.86 (SD 2.05), demonstrating a high level of associated comorbidity. This strengthens the rationale for an increased focus in existing chronic care programs, including heart failure programs, where AF may exist in up to 50% of patients seen in these services. This would negate the burden for an individual with complex multimorbidity having to manage a potential complex weekly timetable as outlined below.

TABLE 8.1 EXAMPLE OF AN INDIVIDUAL WITH HF & AF AND COMPLEX COMORBIDITY'S WEEKLY HEALTHCARE RELATED ACTIVITIES.

WEEKDAY	ACTIVITY	OTHER
MONDAY	Attend heart failure clinic at hospital to see cardiologist	Visit pharmacy at some stage to collect 10+ daily medications. Adhere to monitoring requirements for anticoagulation.
TUESDAY	AF nurse home visit	
WEDNESDAY	Appointment to see diabetes educator at community medical center about insulin	
THURSDAY	Visit to haematologist at private clinics	
FRIDAY	Make appointment to see GP for next week	

The burden placed on an individual or their caregiver to manage multiple chronic conditions is equivalent to that of full time paid employment. Regardless of the physical model of care or the care provider (*disease specific vs generalist clinic, clinic vs home based care, physician vs nurse-led or multidisciplinary approached*), there must be a strong focus on improvement in adherence to treatment regimes.

A proposed conceptual model to optimise adherence to anticoagulation is outlined in the paper presented in Chapter four published in the *European Journal of Cardiovascular Nursing.* The model proposed by Brown et al consists of key steps including; 1) condition knowledge; 2) motivation; 3) habit formation; 4) self-efficacy loop.[33] Further, findings from patient interviews and file note review in the AFASTER Study support this conceptual model, whereby facilitators to optimise adherence, identified by patient's included reminders and routine, and caregiver support. Physical assistance in medication taking, and reminders and 'having a system', including 'habit formation', were important facilitators of adherence. Models of care that place the patient and caregiver at the very center of care planning and assessment are integral to optimizing adherence. Coming to a mutual agreement on treatment decisions and care plans are fundamental to the shared decision making process.

Recommendation 4:

Improving focus on AF, within existing chronic care programs is justified.

Future models of care should formalize caregiver participation.

8.7. IMPROVING PATIENT EDUCATION AND SELF-MANAGEMENT

A recent international survey suggests that there is a lack of quality patient information on AF, and this may not be as readily available or accessible for patients, in comparison to other cardiac conditions.[18] Further, in a European survey, as little as one third of AF patients reported having been informed of potential medication side-effects.[34] The survey of cardiovascular nurses in ANZ presented in Chapter six draws attention to the need for improvement in cardiovascular nurses' knowledge of anticoagulation interactions, including drug-drug, drug-food and monitoring requirements. Due to the critical mass, nurses are well placed throughout clinical practice to provide education and counselling on many aspects of AF and anticoagulation. However, the quality of this intervention is strongly dependent on nurses maintaining a contemporary knowledge base. Cardiovascular nurses in particular, who care for individuals with AF frequently must be well-informed, and keep abreast with the advancements in care, to be able to deliver quality education to patients. McCabe and colleagues also emphasize that there are opportunities for improvement in patient education related to AF. Their qualitative study acknowledged that some patients may feel '*information overload*' at the time of diagnosis, and suggest that revisiting important information may be of value after diagnosis.[35]

There is a lot that patients living with AF need to know. It can be difficult to condense this volume of education into a standard 20 minute consultation with a physician in a primary care setting.[36,37] Important information to convey would include; the cause or trigger of AF; both the consequences and chronic illness trajectory of AF (*including functional and cognitive decline, stroke and heart failure*); treatment information including rate and rhythm, and thromboprophylaxis treatment; treatment action plans and goal setting (including self and family management); symptom management; managing psychosocial consequences of AF.[38]

Improving understanding of patient's experiences of living with AF may assist to develop interventions to enhance quality of life. McCabe and colleagues conducted interviews to gain

better insight into living with AF. They revealed themes including finding the meaning of symptoms; feeling uninformed and unsupported and managing unpredictable and function limiting symptoms.[39] This work is useful in gaining insight into the experience of patients living with AF. In today's technologically connected world, it is unacceptable that patients feel *'uninformed'* and *'unsupported'* when credible information is plentiful via the Internet. Researchers, educationalists, clinicians and policy makers ought to harness technologies including social media in developing innovative methods to deliver patient and caregiver education. Social media provides a platform for two-way conversation and can provide patients with instantaneous feedback and interaction with an expert clinician.[40] Further, social media may assist to improve a patient's knowledge of their condition and treatment. This may be beneficial in shared decision making processes.[40] There has been recent growth in the number of cardiovascular health professionals using platforms such as Twitter.[41] Cardiovascular nurses are challenged to adopt these platforms as validated tools to deliver educational interventions.[40,42,43] Non-government organisations and charities for other non-malignant chronic conditions have been highly successful in engaging with clinicians, consumers, and policy makers in the digital environment. The National Stroke Foundation in Australia has over 5,600 followers on Twitter and regularly engages with patients post stroke, reaching out and providing information and support when required. The AF Association has a similar service; however this has limited reach in Australia, due to the time limitations of live response and global times. It would be valuable to examine if a dedicated online AF service could be delivered in Australia, and the impact this would have in supporting individuals and their caregivers living with AF. It would also be helpful to examine if increasing the AF component in other online social media services already provided is helpful, given that AF is a cardiogeriatric condition. It may be a generalization that this intervention may not be as relevant for today's geriatric population; however it will be useful in planning for future generations with AF.

The optimal timing and method of an educational intervention warrants further research. Verbal discussions (both one-to-one, and group or peer support), explanations with images and drawings, videos, podcasts, and internet-based education platforms may all be tools in a clinician's toolbox as ways to deliver education. Further, it is important to recognise that '*one size does not fit all*' with AF education and it is important that this is individually tailored to meet the needs of patients and their caregivers.

Recommendation 5:

Future interventions should target improving patient education and self-management strategies.

Chapter five included analyses of data from patient interviews and retrieved from healthcare file reviews, as part of the cohort study (Chapter seven). This paper explored barriers and enablers from the patient, provider and health system perspective. This study elicited that patient choice and preference were two important factors in thromboprophylaxis decision making. This study complements Chapter three, and adds to a growing contemporary knowledge base in this area. This study revealed new and important factors including; homelessness, and the absence of a caregiver, and end of life considerations. Developing a routine or 'system', the use of technology and self-care interventions were highlighted as enablers to successful treatment.

There is great opportunity for improvement in how health professionals promote self-care and self-management for AF. Further, there is need for better access and quality AF self-management programs. There is an opportunity to improve definitions of what self-care is in AF, and what optimal self-care behavior would detail. To date, there has been much attention to self-care behavior in CHF, and how this relates to symptom management and outcomes (including mortality and hospitalisation). However, AF has received scant attention in this important area. Self-monitoring and self-management of oral anticoagulation must to be explored further. This provides an opportunity for individuals to become educated of their condition and treatment, and empower the patient to take ownership of their management within an 'expert patient' model of care. Self-monitoring and self-management may only be of benefit for a select group of individuals with AF, given that functional and cognitive impairment are common amongst this group. In terms of policy and practice implications in this area, there is need to adapt current models of care, funding and rebate to better support self-management interventions in AF. This may include improving time allocated that clinicians spend with patients and caregivers to counsel and educate on how to use self-monitoring devices. Funding and remuneration models would have to be flexible to accommodate these innovative interventions. Nurses are skillful in providing counseling and education for self-management in a range of other chronic conditions, including asthma, chronic heart failure and diabetes.[26] Given that AF is primarily a cardio-geriatric condition and rarely exists in isolation of other comorbidity, integration of AF self-care into existing chronic care programs is highly justified. Aside to self-monitoring and self-management of oral anticoagulation there is considerable scope for improving other aspects of AF self-management. This may include assessment of arrhythmia trigger patterns and symptom recognition and intervention, and may positively impact quality of life, reduce hospitalizations, and improve mortality.

8.8. REDEFINING AF NURSE EDUCATION

Chapter six revealed a knowledge gap around AF management for cardiovascular nurses in ANZ. This study demonstrated that cardiovascular nurses in Australia and New Zealand have insufficient knowledge on oral anticoagulant therapy, warfarin-diet, and warfarin-medication interactions. The findings presented in Chapter six are consistent with international research. The lack of knowledge on warfarin-medication interactions was alarming. It was of concern at the lack of knowledge on warfarin related advice, particularly relating to pregnancy and how alcohol affects INR. Our research was representative of a typically older, and more experienced cardiovascular nursing population, working in specialized positions with advanced qualifications. And as such, were more likely to be more knowledgeable on anticoagulation than other nurses. Given the overall poor results, it was feared that knowledge is likely to be even poorer in the broader nursing population. Clinician knowledge deficits may lead to inaccurate patient advice and impact adherence to therapy. Including a comprehensive education program pre-discharge may help to improve the quality and safety of anticoagulation. Due to the duration of therapy for this chronic condition, there is need for education refreshment and re-assessment of patients and clinicians knowledge, across all care settings. The education of patients on anticoagulation is not a role of a single health professional. A team approach must be taken and nurses have a key role in providing answers to questions and sound clinical advice across all care settings. Future research should address modes of delivery of AF and anticoagulation education for clinicians, individuals and their caregivers. There is need to explore the scope for professional organisations (including CSANZ or ACNC) to credential nurses on AF and anticoagulation. There is scope to revise nursing syllabus around AF into the 21st century. Innovative methods of cardiovascular nurse education for AF and stroke thromboprophylaxis should be explored in further detail, and evaluated in future research. This may include courses delivered fully online and open access.

Recommendation 6:

Nurse education for contemporary AF nursing care needs to be redefined.

This should go beyond cardiovascular nurses, and across all specialties and care settings.

Chapter seven underpins the importance of considering multimorbidity, frailty and self-care behavior in thromboprophylaxis decision making. The results of the cohort study demonstrate that in this frail, elderly and high-risk cohort, thromboprophylaxis was underused. All-cause rehospitalisation was frequent and 12-month all-cause mortality was high. Prescription of anticoagulation at discharge was significantly associated with improved mortality at 12 months, but was not associated with improved rates of rehospitalisation among individuals with CHF and concomitant AF. This study highlights that frailty, multimorbidity, and self-care behaviour to be important considerations in thromboprophylaxis decision making. Patients and caregivers must be central to thromboprophylaxis treatment choices. Whilst the CHA_2DS_2VASc and HAS-BLED schemata are useful in practice, it is problematic simply to use these tools in isolation to guide treatment decisions. Whilst helpful, they lack ability to provide a comprehensive assessment that includes key considerations including multimorbidity, frailty and self-care ability. Whilst preventing stroke is important in this high risk cohort of individuals, rates of rehospitalisation and mortality are very high and are often related to heart failure symptom management. Twelve month all-cause mortality was almost 30%. It is concerning that as few as 12% had a documented resuscitation status as 'not for CPR' at baseline. This highlights the need for improvement in advanced care planning and having conversations about end-of-life. Future research should explore clinicians fear and patient choice in thromboprophylaxis.

Optimising AF management needs to be considered in the context of multimorbidity, frailty, self-care ability, cognitive functioning, and caregiver support. There is need to target clinical interventions that improve self-care behavior and self-management of AF in the setting of CHF.

Recommendation 7:

All health professionals must recognise that AF commonly exists in the setting of multimorbidity, and how this adds to the complexity of care management.

8.9. BETTER UNDERSTANDING CHOICE, PREFERENCES, AND ATTITUDES

There is need to improve palliative approaches to the management of chronic heart failure with AF. A patient-centered approach to AF is about matching treatments to peoples goals. The AFASTER cohort study presented in this thesis demonstrated that 29% of individuals hospitalised with CHF and AF were not alive at 12 months and that only 5% experienced a stroke or TIA. Therefore, individuals were 6 times more likely to die than have a stroke. Although cause of death was not formally adjudicated, this demonstrates that individuals with CHF and AF are more likely to die from their CHF than to die from a stroke. Having deep and meaningful conversations with patients, particularly those with end-stage chronic heart failure is important to gain an understanding of what is important to them at end of life. For some, this may be not taking 'non-essential medications' or those that are not related to symptom control. Oral anticoagulation is not a medication that with cessation, would negatively impact symptoms in CHF and therefore, it may be a patient's choice to cease this medication towards end-of-life. What is important to an individual at end-of-life is likely to differ, for some; not taking handfuls of medications, multiple times a day may be an important consideration. It is important that clinicians respect this choice, when having conversations with patients around treatments. Frequently outcome is judged in terms of reduction in disability or improvement in function and not improved comfort at end of life. Death is frequently viewed as a failure of modern

healthcare and not as a due-course of life. If researchers are aiming to produce patient-centered research, perhaps a paradigm shift is needed toward the assessment of outcome.[44]

There is need for discrete choice experiments (DCEs) for anticoagulation in the AF population**.** DCEs have been highly useful in eliciting patient preference for different treatment options, whilst considering other demographics and clinical variables. Until recently, these experiments have focused on small cohorts of individuals with limited comorbidity. Ghijben and colleagues recently conducted a small DCE in Australia to examine patient preferences for attributes of warfarin and NOACs and to examine which attributes were most important. 67 participants completed this study identifying preference for NOACs over warfarin, as their cost decreased.[45] This study was quite small, and had several limitations.

However, a more recent DCE published in 2014, aimed to elicit patient preferences for different benefits and risks of anticoagulation in patients with CVD. Results highlighted that patients valued a 1% increased risk of death from bleeding, the same as a 3% increase in nonfatal stroke, a 2% increase in nonfatal myocardial infarction, a 3% increase in cardiovascular death, a 16% increase in minor bleeding, and a 6% increase in major bleeding. Further, that patients exhibited preferences for new drugs regardless of their relative risks and benefits.[46] This study supports that including patients values and preferences for treatment decisions may enhance the patient centered-ness of decision making. In order to gain greater understanding patient beliefs, attitudes and preferences to treatment choices, there is need conduct DCEs on larger cohorts of individuals with complex comorbidity in the ANZ setting.

Recommendation 8:

Patient preference, choice and attitudes must be considered in research and practice.

8.10. EIGHT KEY RECOMMENDATIONS GENERATED FROM THIS THESIS.

Recommendation 1: Clinical Guidelines
There is need for a multi-disciplinary ANZ Atrial Fibrillation clinical practice guideline.
Recommendation 2: Shared Decision Making
Developing shared decision making practices in AF should be a priority. Improving nurses' knowledge and skills in SDM will likely improve PCC. Decision support tools may offer support for shared decision making.
Recommendation 3: The Caregiver
The role of the caregiver in AF should be explored further, in research and practice.
Recommendation 4: Models of AF Care
Given the cardiogeriatic context of AF. Improving focus on AF, within existing chronic care programs is justified. Future models of care should formalize caregiver participation.
Recommendation 5: Patient Education & Self-Management
Future interventions should target improvement in patient education and self-management strategies.
Recommendation 6: Nurse Education
Nurse education for contemporary AF nursing care needs to be redefined. This should go beyond cardiovascular nurses, and across all specialties and care settings.
Recommendation 7: Multimorbidity
All health professionals must recognise that AF commonly exists in the setting of multimorbidity, and how this adds to the complexity of care management.
Recommendation 8: Patient Preference & Choice
Patient preference, choice and attitudes must be considered in research and practice.

8.11. CONCLUSIONS

The overall purpose of this thesis was to describe the barriers and enablers to thromboprophylaxis in individuals with CHF and concomitant AF. This was achieved through a series of discrete but linked studies. Key findings from this thesis include 1) knowledge and practice gaps of cardiovascular nurses; 2) the important role of the caregiver; 3) the need for a comprehensive clinical assessment when making thromboprophylaxis decisions; 4) the need for ANZ multidisciplinary AF management guidelines; 5) individuals with CHF and AF are a highly complex cohort, and it is important to consider self-care strategies to promote adherence to treatment regimes.

This thesis has demonstrated the need for patient centered approaches to the management of CHF and AF. This research evidences that there are many more components of patient-centered care than simple stroke and bleeding risk prediction. Shared decision making and patient-centered care hold promise for improving the quality of care and improving health outcomes. These processes create a meaningful dialogue with patients and help gain understanding of treatment options. This can help empower patients, whilst improving condition and treatment knowledge. Subsequently, this may lead to optimised treatment decisions, from both the perspective of the patient and the provider. Further, this may positively impact adherence to treatment regimes.

Stroke in the context of CHF and AF is devastating, yet many strokes are preventable. Empowering patients to be central to decisions making, may optimise treatment decisions. Many of the barriers detailed in this thesis can be overcome by working in partnership with patients and their caregivers. This can be achieved when healthcare providers adopt a solution-based approach and empower individuals with knowledge, skills and resources. Consequently, this may help to improve self-care and adherence and optimise patient outcome.

8.12. REFERENCES

1. Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. Atrial fibrillation: stroke prevention in focus. *Australian critical care : official journal of the Confederation of Australian Critical Care Nurses.* 2014;27(2):92-98.

2. Graham ID, Harrison MB. Chapter 26: Appraising and adapting clinical practice guidelines. In: Cullum N, Ciliska D, Haynes RB, Marks S, eds. *Evidenced-based Nursing*. 1st ed. Oxford, UK: Blackwell Publishing Ltd; 2008:219-230.

3. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand (Chronic Heart Failure Guidelines Expert Writing Panel). Guidelines for the prevention, detection and management of chronic heart failure in Australia. 2011.

4. Wann L, Curtis A, January C, et al. 2011 ACCF/ AHA/ HRS focused update on the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;123:104-123.

5. Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. *European Heart Journal.* 2012;33:2719-2747.

6. National Institute for Health Care Excellence. *Atrial fibrillation: the management of atrial fibrillation.* UK: NICE; June, 2014 2014.

7. Hughes LD, McMurdo MET, Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. *Age and Ageing.* January 1, 2013 2013;42(1):62-69.

8. Ferguson C, Inglis S, Newton P, Middleton S, Macdonald P, Davidson P. Atrial fibrillation and thromboprophylaxis in heart failure: the need for patient-centrered approaches to address adherence. *Vascular Health & Risk Management.* 2013;9:3-11.

9. Vanassche T, Connolly SJ, Eikelboom JW, et al. Abstract 18936: Can Biomarkers Improve Risk Stratification of Atrial Fibrillation Patients? Analysis of 3578 Aspirin-treated Patients in ACTIVE and AVERROES. *Circulation.* November 25, 2014 2014;130(Suppl 2):A18936.

10. Aspberg S, Chang Y, Singer D. Abstract 18538: The ATRIA Stroke Risk Score Predicts Ischemic Stroke Better than CHADS2 and CHA2DS2-VASc in a large Swedish Cohort of Patients with Atrial Fibrillation. *Circulation.* November 25, 2014 2014;130(Suppl 2):A18538.

11. Chao T-F, Lin Y-J, Chang S-L, et al. R2CHADS2 Score and Thromboembolic Events After Catheter Ablation of Atrial Fibrillation in Comparison With the CHA2DS2-VASc Score. *Canadian Journal of Cardiology.* 2014;30(4):405-412.

12. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GYH. Underuse of Oral Anticoagulants in Atrial Fibrillation: A Systematic Review. *The American Journal of Medicine.* 2010;123:638-645.

13. Organisation WH. *Adherence to Long Term Therapies: Evidence for Action.* Geneva, Switzerland: World Health Organisation;2003.

14. Hoffmann TC, Legare F, Simmons MB, et al. Shared decision making: what do clinicians need to know and why should they bother. *Medical Journal of Australia.* 2014;201(1):35-39.

15. Charles C, Gafni A, Whelan T. Shared decision-making in the medical encounter: What does it mean? (Or it takes at least two to tango). *Soc. Sci. Med.* Mar 1997;44(5):681-692.

16. Barry MJ, Edgman-Levitan S. Shared Decision Making — The Pinnacle of Patient-Centered Care. *New England Journal of Medicine.* 2012;366(9):780-781.

17. Gravel K, Legare F, Graham I. Barriers and facilitators to implementing shared decision-making in clinical practice: a systematic review of health professionals' perceptions. *Implementation Science.* 2006;1(1):16.

18. Aliot E, Breithardt G, Brugada J, et al. An international survey of physician and patient understanding, perception, and attitudes to atrial fibrillation and its contribution to cardiovascular disease morbidity and mortality. *Europace.* 2010;12(5):626-633.

19. Stacey D, Murray MA, Légaré F, Sandy D, Menard P, O'Connor A. Decision Coaching to Support Shared Decision Making: A Framework, Evidence, and Implications for Nursing Practice, Education, and Policy. *Worldviews on Evidence-Based Nursing.* 2008;5(1):25-35.

20. Ferguson C, Inglis SC, Newton PJ, Middleton S, Macdonald PS, Davidson PM. The caregiver role in thromboprophylaxis management in atrial fibrillation: a literature review. *European Journal of Cardiovascular Nursing.* 2014;INPRESS.

21. Strömberg A. The Situation of Caregivers in Heart Failure and Their Role in Improving Patient Outcomes. *Curr Heart Fail Rep.* 2013/09/01 2013;10(3):270-275.

22. Chen SY, Vanderpoel J, Mody S, et al. Caregiver assistance among Medicare beneficiaries with atrial fibrillation and factors associated with anticoagulant treatment. *The American journal of geriatric pharmacotherapy.* Oct 2012;10(5):273-283.

23. Coleman CI, Coleman SM, Vanderpoel J, et al. Factors associated with 'caregiver burden' for atrial fibrillation patients. *International journal of clinical practice.* Oct 2012;66(10):984-990.

24. Corry M, While A, Neenan K, Smith V. A systematic review of systematic reviews on interventions for caregivers of people with chronic conditions. *Journal of Advanced Nursing.* 2014:n/a-n/a.

25. Aliot E, Breithardt G, Brugada J, et al. An international survey of physician and patient understanding, perception, and attitudes to atrial fibrillation and its contribution to cardiovascular disease morbidity and mortality. *Europace.* May 2010;12(5):626-633.

26. Shaw RJ, McDuffie JR, Hendrix CC, et al. Effects of Nurse-Managed Protocols in the Outpatient Management of Adults With Chronic Conditions. *Annals of Internal Medicine.* 2014;161(2):113-121.

27. Stewart S, Carrington MJ, Marwick TH, et al. Impact of home versus clinic-based management of chronic heart failure: the WHICH? (Which Heart Failure Intervention Is Most Cost-Effective & Consumer Friendly in Reducing Hospital Care) multicenter, randomized trial. *Journal of the American College of Cardiology.* Oct 2 2012;60(14):1239-1248.

28. Rich MW, Beckham V, Wittenberg C, Leven CL, Freedland KE, Carney RM. A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure. *The New England journal of medicine.* Nov 2 1995;333(18):1190-1195.

29. McAlister F, Stewart S, Ferrua S, McMurray J. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. *J Am Coll Cardiol.* Aug 18 2004;44(4):810-819.

30. Blue L, Lang E, McMurray JJ, et al. Randomised controlled trial of specialist nurse intervention in heart failure. *BMJ (Clinical research ed.).* Sep 29 2001;323(7315):715-718.

31. Hendriks JML, deWit R, Crijns HJGM, et al. Nurse-led care vs usual care for patients with atrial fibrillation. *European Heart Journal.* 2012;33:2692-2699.

32. Stewart S, Ball J, Horowitz JD, et al. Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: pragmatic, multicentre, randomised controlled trial. *The Lancet.* 2014.

33. Brown T, Siu K, Walker D, Pladevall-vila M, Sander S, Mordin M. Development of a conceptual model of adherence to oral anticoagulants to reduce risk of stroke in patients with atrial fibrillation. *J Manag Care Pharm.* 2012;18(5):351-362.

34. Bakhai A, Sandberg A, Mittendorf T, et al. Patient perspective on the management of atrial fibrillation in five European countries. *BMC Cardiovascular Disorders.* 2013;13(1):108.

35. McCabe PJ, Rhudy LM, DeVon HA. Patients' experiences from symptom onset to initial treatment for atrial fibrillation. *Journal of Clinical Nursing.* 2014:n/a-n/a.

36. Martin CM, Banwell CL, Broom DH, Nisa M. Consultation length and chronic illness care in general practice: a qualitative study. *Med J Aust.* 1999/07// 1999;171(2):77-81.

37. Australian Government Department of Health. MBS Online, Medicare Benefits Schedule - Item 23,. 2014; http://www9.health.gov.au/mbs/fullDisplay.cfm?type=item&qt=ItemID&q=23. Accessed 09/12/2014, 2014.

38. McCabe PJ. What patients want and need to know about atrial fibrillation. *Journal of multidisciplinary healthcare.* 2011;4:413-419.

39. McCabe PJ, Schumacher K, Barnason SA. Living with atrial fibrillation: a qualitative study. *The Journal of cardiovascular nursing.* Jul-Aug 2011;26(4):336-344.

40. Ferguson C. It's time for the nursing profession to leverage social media. *J Adv Nurs.* Apr 2013;69(4):745-747.

41. Redfern J, Ingles J, Neubeck L, Johnston S, Semsarian C. Tweeting Our Way to Cardiovascular Health. *Journal of the American College of Cardiology*. 2013;61(15):1657-1658.

42. Jaarsma T. Developing the potential of social media in cardiovascular care. *European Journal of Cardiovascular Nursing.* October 1, 2014 2014;13(5):386-387.

43. Antheunis M, Tates K, Nieboer T. Patients' and health professionals' use of social media in health care: motives, barriers and expectations. *Patient Educ Couns.* Sep 2013;92(3):426-431. .

44. Glasgow RE, Brownson RC, Kessler RS. Thinking about Health-Related Outcomes: What Do We Need Evidence about? *Clinical and Translational Science.* 2013;6(4):286-291.

45. Ghijben P, Lancsar E, Zavarsek S. Preferences for Oral Anticoagulants in Atrial Fibrillation: a Best–Best Discrete Choice Experiment. *PharmacoEconomics*. 2014/11/01 2014;32(11):1115-1127.

46. Najafzadeh M, Gagne JJ, Choudhry NK, Polinski JM, Avorn J, Schneeweiss SS. Patients' Preferences in Anticoagulant Therapy: Discrete Choice Experiment. *Circulation: Cardiovascular Quality and Outcomes*. November 1, 2014 2014;7(6):912-919.

9 APPENDICES

APPENDIX 1: HREC APPROVAL

St Vincent's Hospital

A facility of St Vincents
& Mater Health Sydney

St Vincent's Hospital Sydney Ltd
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06 March 2013

Prof Peter MacDonald
Victor Chang Institute
St Vincent's Hospital
390 Victoria Street
Darlinghurst NSW 2010

Dear Peter

SVH File Number: 13/038
Project Title: Atrial Fibrillation and Stroke Thromboprophylaxis in Heart Failure – Barriers & Enablers to Treatment (THE AFASTER STUDY)
HREC Reference Number: (LNR/13/SVH/62)

Thank you for submitting the above project for review. Based on the information you have provided and in accordance with the NHMRC National Statement 2007 and NSW Health Policy Directive PD2010_055 Ethical and Scientific Review of Human Research in NSW Public Health Organisations, this project has been assessed as low/negligible risk and is therefore exempt from full HREC review.

This HREC has been accredited by NSW Ministry of Health as a Lead HREC under the model for single ethical and scientific review and Certified by the NHMRC under the National model for Harmonisation of Multicentre Ethical Review (HoMER).This lead HREC is constituted and operates in accordance with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research* and the *CPMP/ICH Note for Guidance on Good Clinical Practice*. No HREC members with a conflict of interest were present for review of this project.

I am pleased to advise that the HREC Executive at a meeting on **26 February 2013** has granted ethical and scientific approval of the above **single centre** project.

You are reminded that this letter constitutes *ETHICAL* and *SCIENTIFIC* approval only. You must not commence this research project at a site until a completed Site Specific Assessment Form and associated documentation have been submitted to the site Research Governance Officer and Authorised. A copy of this letter must be forwarded to all site investigators for submission to the relevant Research Governance Officer.

The project is approved to be conducted at **St Vincent's Hospital Sydney.**

If a new site(s) is to be added please inform the HREC in writing and submit a Site Specific Assessment Form (SSA) to the Research Governance Officer at the new site.

The following documents have been approved:

- Protocol Synopsis, Version 1 dated 15 February 2013
- Protocol, Version 1 dated 15 February 2013
- Participant Information Sheet and Consent Form – Study 1 (Patient), Version 1 dated 13 February 2013
- Participant Information Sheet and Consent Form – Study 2 (Patient/Carer), Version 1 dated 13 February 2013
- Participant Information Sheet and Consent Form – Study 2 (Clinician), Version 1 dated 13 February 2013
- Form 1 – Case Report Form – General Screening Log, Version 1 dated 15 February 2013
- Form 2 – Case Report Form – Index Admission Data Collection Form, Version 1 dated 15 February 2013
- Form 3 – Case Report Form – 3 Month Follow Up, Version 1 dated 15 February 2013
- Form 4 – Case Report Form – 6 Month Follow Up, Version 1 dated 15 February 2013
- Form 5 – Case Report Form – 12 Month Follow Up, Version 1 dated 15 February 2013
- Form 6 – Case Report Form – GP Notification and File Note, Version 1 dated 19 February 2013

- Interview and Focus Group Schedule, Version dated 19 February 2013
- CV – Professor Peter Simon MacDonald
- CV – Professor Patricia Mary Davidson
- CV – Doctor Sally C Inglis
- CV – Doctor Philip J Newton
- CV – Mr Caleb Ferguson

The Low and Negligible Risk Research Form (LNRF) reviewed by the HREC was LNRF **AU/6/8E41112**.

Please note the following conditions of approval:

- HREC approval is valid for **5 years** from the date of the HREC Executive Committee meeting and expires on **26 February 2018.** The Co-ordinating Investigator is required to notify the HREC 6 months prior to this date if the project is expected to extend beyond the original approval date at which time the HREC will advise of the requirements for ongoing approval of the study.

- The Co-ordinating Investigator will provide an annual progress report beginning in **February 2014**, to the HREC as well as a final study report at the completion of the project in the specified format.

- The Co-ordinating Investigator will immediately report anything which might warrant review of ethical approval of the project in the specified format, including unforeseen events that might affect continued ethical acceptability of the project and any complaints made by participants regarding the conduct of the project.

- Proposed changes to the research protocol, conduct of the research, or length of approval will be provided to the HREC Executive for review, in the specified format.

- The HREC Executive will be notified, giving reasons, if the project is discontinued before the expected date of completion.

- Projects that are undertaken by Investigators holding an academic appointment (including conjoint appointments) or by students as part of a University course are also required to contact the relevant University HREC to seek advice from the University regarding their requirements.

Should you have any queries about your project please contact the Research Office, Tel: 8382-2075, email research@stvincents.com.au. The HREC Terms of Reference, Standard Operating Procedures, *National Statement on Ethical Conduct in Human Research* (2007) and the *CPMP/ICH Note for Guidance on Good Clinical Practice* and standard forms are available on the Research Office website: www.stvincents.com.au/researchoffice or internal at http://exwwwsvh.stvincents.com.au/researchoffice

Please quote **SVH File Number: 13/038** in all correspondence.

The HREC wishes you every success in your research.

Yours sincerely

Production Note:

Signature removed prior to publication.

Maria Mury
Acting HREC Executive Officer
Research Office
L6 deLacy Building
CC: Caleb Ferguson
Trim File Ref: D/2013/12049

APPENDIX 2: AMENDMENT TO SURVEY DISTRIBUTION

St Vincent's Hospital

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17 February 2014

Prof. Peter MacDonald
Victor Chang Institute
St Vincent's Hospital
390 Victoria Street
Darlinghurst NSW 2010

Dear Peter

SVH File Number: 13/038
Project Title: Atrial Fibrillation and Stroke Thromboprophylaxis in Heart Failure - Barriers & Enablers to Treatment (THE AFASTER STUDY)
HREC Reference Number: LNR/13/SVH/62

Thank you for submitting a request for an amendment dated **07 February 2014** to the above project. This was considered by the St Vincent's Hospital HREC at its Executive meeting held on **11 February 2014.** This HREC has been accredited by NSW Ministry of Health as a Lead HREC under the model for single ethical and scientific review and Certified by the NHMRC under the National model for Harmonisation of Multicentre Ethical Review (HoMER). This lead HREC is constituted and operates in accordance with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research* and the *CPMP/ICH Note for Guidance on Good Clinical Practice*. No HREC members with a conflict of interest were present for review of this project.

I am pleased to advise that the document reviewed and approved at the meeting was:

- Clinician Survey version 1 dated 07 February 2014

This amendment has also been reviewed by the Research Governance Officer at St Vincent's Hospital. Further authorisation of the above approved documents is not required for any site that has the Research Governance conducted by St Vincent's Hospital Research Office. Implementation of this amendment can now proceed.

Should you have any queries about your project please contact the Research Office, Tel: 8382-2075, email research@stvincents.com.au. The HREC Terms of Reference, Standard Operating Procedures, *National Statement on Ethical Conduct in Human Research* (2007) and the *CPMP/ICH Note for Guidance on Good Clinical Practice* and standard forms are available on the Research Office website:
www.stvincents.com.au/researchoffice or internal at http://exwwwsvh.stvincents.com.au/researchoffice

Production Note:
Signature removed prior to publication.

Sarah Charlton
HREC Executive Officer
St Vincent's Research Office
Level 6 deLacy Building

cc. Caleb Ferguson
TRIM Ref: D/2014/8474

Continuing the Mission of the Sisters of Charity

APPENDIX 3: AMENDMENT TO METHOD OF CONSENT

St Vincent's Hospital

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6 August 2014

Prof. Peter Macdonald
Cardiopulmonary Transplant Unit
Xavier Building, Level 4
St Vincent's Hospital
390 Victoria Street
Darlinghurst NSW 2010

Dear Peter

SVH File Number: 13/038
Project Title: Atrial Fibrillation and Stroke Thromboprophylaxis in Heart Failure - Barriers & Enablers to Treatment (THE AFASTER STUDY)
HREC reference Number: LNR/13/SVH/62

Thank you for submitting a request for an amendment dated **02 July 2014, received by the Research Office 8 July 2014,** to the above project. This was considered by the St Vincent's Hospital HREC at its Executive meeting held on **21 July 2014.** This HREC has been accredited by NSW Ministry of Health as a Lead HREC under the model for single ethical and scientific review and Certified by the NHMRC under the National model for Harmonisation of Multicentre Ethical Review (HoMER). This lead HREC is constituted and operates in accordance with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research* and the *CPMP/ICH Note for Guidance on Good Clinical Practice*. No HREC members with a conflict of interest were present for review of this project.

I am pleased to advise that the Committee approved your request to conduct a 12 month follow-up telephone call on all participants initially recruited during index admission.

This amendment has also been reviewed by the Research Governance Officer at St Vincent's Hospital. Further authorisation of the above approved documents is not required for any site that has the Research Governance conducted by St Vincent's Hospital Research Office. Implementation of this amendment can now proceed.

Please note that only an electronic copy of this letter will be provided, if you require the original signed letter please contact the Research Office and we will be happy to provide this.

Should you have any queries about your project please contact the Research Office, Tel: 8382-2075, email SVHS.Research@svha.org.au. The HREC Terms of Reference, Standard Operating Procedures, *National Statement on Ethical Conduct in Human Research* (2007) and the *CPMP/ICH Note for Guidance on Good Clinical Practice* and standard forms are available on the Research Office website found at: www.stvincents.com.au/researchoffice or at http://exwwwsvh.stvincents.com.au/researchoffice (internally).

Production Note:
Signature removed prior to publication.

Sarah Charlton
HREC Executive Officer
St Vincent's Hospital Research Office
Level 6 de Lacy Building

cc: Caleb Ferguson
TRIM REF: D/2014/37173

Continuing the Mission of the Sisters of Charity

APPENDIX 4: SITE SPECIFIC AUTHORISATION

APPENDIX 5: PARTICIPANT CONSENT FORM

St Vincent's Hospital

Participant Information Sheet and Consent Form Guidance Document for a Non-Interventional Study

Participant Information Sheet and Consent Form Non-interventional Research

Title:	**Atrial Fibrillation and Stroke Thromboprophylaxis in Heart Failure (STUDY 1)**
Short Title:	**The AFASTER Study**
Principal Investigator:	**Mr Caleb Ferguson, University of Technology, Sydney**
Site:	**St Vincent's Hospital, Darlinghurst**
Protocol :	**v1**

Part I – What does my participation in the study involve?

1 Introduction

You are invited to take part in The AFASTER Study because you have been admitted to St Vincent's Hospital with heart failure and have atrial fibrillation. This Participant Information Sheet and Consent Form tells you about the study. It explains what is involved to help you decide if you want to take part in the study. Please read this information carefully. Ask questions about anything that you do not understand or want to know more about. Before deciding whether or not to take part you might want to talk about it with a relative, friend or local health worker.

Researchers are based at the Centre for Cardiovascular and Chronic Care at St Vincent's Hospital and the University of Technology, Sydney. This project is part of a PhD study being undertaken by Mr Caleb Ferguson at UTS who has received funding support from the University of Technology, Sydney (UTS) and the Australian College of Nursing. The project is principally supervised by Professor Peter Macdonald from St Vincent's Hospital, Sydney and Professor Patricia Davidson from the University of Technology, Sydney. Other Investigators on this study include Dr Sally Inglis, and Dr Phillip Newton.

2 What is the purpose of this research?

This study aims to:

1) Describe the rate and type of prescription of blood thinning medications in a group of patients aged 18 years and older with atrial fibrillation with a confirmed diagnosis of heart failure.
2) Explore what factors contribute to side effects such as stroke or bleeding that some people who take blood thinning medications may experience.
3) Investigate the factors that contribute to or hinder the use of blood thinning therapy to prevent strokes in patients with heart failure and atrial fibrillation.

Atrial fibrillation (AF) is a frequent abnormal heart beat in heart failure (HF) and a risk factor for stroke. Blood thinning therapy may be appropriate to prevent stroke in patients with heart failure and atrial fibrillation. However blood thinning therapy may not be commonly applied in practice for a variety of reasons such as older age, frailty, falls and the risk of bleeding. Medication usage is lower than desired in patients with heart failure. Current ways for doctors and nurses to risk assess patients are limited and do not consider medication adherence. There is need to extend current risk assessment tools. This study aims to obtain data to inform the development of a new risk assessment tool that includes assessment of patient adherence.

3 Why have I been chosen?

You have been chosen to participate in the study as you have been admitted to St Vincent's Hospital, Sydney with heart failure and have atrial fibrillation.

4 Do I have to take part in the research?

It is up to you to decide whether or not to take part in this study. If you do decide to take part you will be given this Participant Information Sheet and Consent Form to sign and you will be given a copy to keep. If you decide to take part you can change your mind later and withdraw from the study at any stage, for any reason.

5 Other relevant information

It is estimated 160 – 200 patients will take part in the study. This study is for only for patients admitted to St Vincent's Hospital, Sydney with heart failure and atrial fibrillation.

6 What will happen to me if I take part?

If you decide to join the study, the researcher will ask a few questions and you will require a telephone to participate in the follow up.

There are no costs associated with participating in this study, nor will you be paid.

7 What do I have to do?

If you decide to join the study, you will first be given a telephone call at 3 months after your admission to hospital. There will be further phone calls at 6 and 12 months after your admission. At each phone call we will ask about your general health since you were discharged from hospital, if you have been to hospital and a few questions about your medications and self care. Each phone call should take no longer than 15 minutes and will be made at a time convenient to you.

If we are unable to contact you, for instance you have changed telephone numbers, we may contact your next of kin, your GP, another hospital or State agencies if this is required. We will be identifying your next of kin from the hospital record. We will only contact this person if we are unable to find you, and if you nominated a next of kin when you were admitted to hospital. If you do not want us to keep details of your next of kin please let us know

8 What are the possible benefits of taking part?

There will be no clear benefit to you from your participation in this research.

9 What are the risks of taking part?

You may feel that some of the questions we ask are stressful or upsetting. If you do not wish to answer a question you may skip it and go to the next question, or you may stop immediately. If you become upset or distressed as a result of your participation in the study, the study coordinator is able to arrange for counselling or other appropriate support. Any counselling or support will be provided by staff who are not members of the study team.

10 What do I do if I wish to withdraw from the research?

Participation in any research project is voluntary. If you do not wish to take part you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at a later stage. If you wish to withdraw from this study please advise the study team. The study coordinator will inform you if there are any special requirements linked to withdrawing.

If you do consent to participate, you may only withdraw prior to the end of the telephone call.If you do withdraw you will be asked to complete and sign a 'Withdrawal of Consent' form. This will be provided to you by the study team.

If you decide to leave the project, the researchers would like to keep the personal and/or health information about you that has been collected. This is to help them make sure that the results of the research can be measured properly. If you do not want them to do this, you must tell them before you withdraw from the research project.

11 What happens when the study ends?

Once the study has finished and you have received all 3 telephone calls at 3, 6 and 12 months your participation will be complete. A summary of the results will be published and made available at the heart failure service at St Vincent's Hospital, Sydney. You will not be able to be identified in these publications.

Part II – How is the study being conducted?

12 What will happen to information about me?

By signing the consent form you consent to the study coordinator and relevant research staff collecting and using personal information about you for the study project. Any information obtained in connection with this study project that can identify you will remain confidential. Information will be confidential and de-identified by a code Information will be kept at St Vincent's Hospital, Sydney and the Centre for Cardiovascular & Chronic Care, University of Technology, Sydney. Information will be password protected if kept on a computer or locked in a secure filling cabinet if paper based. Your information will only be used for the purpose of this study project and it will only be disclosed with your permission, except as required by law.
The personal information we will collect and use for this study is medical and personal information including age, date of birth, gender and date of hospital admission including clinical and socio-demographic data.
Your information will be kept for 5 years after the study has completed. This is anticipated to be until 2020. After this date information will be destroyed via shredding of information.
Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this study.
It is anticipated that the results of this study will be published and or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your express permission.
In accordance with relevant Australian and/or NSW privacy and other relevant laws, you have the right to request access the information collected and stored by the study team about you. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.
This project is non-interventional. No adverse or unforeseen events are expected. Data will be collected by trained researchers who are familiar with the need to maintain patient privacy and confidentiality of information. The information will be stored at St Vincent's Hospital or the University of Technology, Sydney.
The information about groups of patients as a whole, not about individuals, is fed back to the hospital to help them improve the way they care about patients. In some cases, this information may be gathered together into a publication which will be disseminated to health care workers around Australia. You cannot be identified from any of these publications.

13 What if something goes wrong?

If you suffer any injuries or complications as a result of this study, you should contact the study team as soon as possible, who will assist you in arranging appropriate medical treatment.
If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital. You do not give up any legal rights to compensation by participating in this study. If you suffer any distress or psychological injury as a result of this study, you should contact the study team as soon as possible, who will assist you in arranging appropriate treatment and support.

14 Who is organising and funding the research?

This study is being conducted by Mr Caleb Ferguson at the Centre for Cardiovascular and Chronic Care, University of Technology, Sydney in part fulfilment of his PhD.

15 Who has reviewed the study?

All research in Australia involving humans is reviewed by an independent group of people, called a Human Research Ethics Committee (HREC). This study has been reviewed and given approval by St Vincent's Hospital, (Sydney) Human Research Ethics Committee.

The conduct of this study at St Vincent's Hospital, Sydney has been authorised by the St Vincent's and Mater Health Service and the University of Technology, Sydney.

16 Further information and who to contact

If you would like any further information on this study you may contact Caleb Ferguson

If you would like to talk to someone not directly involved with the study for any further information regarding your rights as a study participant or should you wish to make a complaint to people independent of the study team, you may contact the St Vincent's Hospital, Sydney Research Office on (02) 8382 2075 and quote the HREC reference number:

Question	Who to contact	Phone / Facsimile
General questions or concerns during the study	Study Coordinator Mr Caleb Ferguson Principal Investigator Professor Peter Macdonald	Tel: 02 8382 3569 Fax: 02 9514 4474 Phone: 02 9295 8600 Fax: 02 9295 8601
Questions about the way the research is being conducted	Professor Patricia Davidson Institutional Research Governance Officer	Tel: 02 9514 4822 Fax: 02 9514 4474 Tel: 02 8382 2075 Fax: 02 8382 3667

St Vincent's Hospital

PARTICIPANT CONSENT FORM

Title:	**Atrial Fibrillation and Stroke Thromboprophylaxis in Heart Failure (STUDY 1)**
Short Title:	**The AFASTER Study**
Principal Investigator:	**Mr Caleb Ferguson, University of Technology, Sydney**
Site:	**St Vincent's Hospital, Darlinghurst**
Protocol :	**v1**

Participant will be provided with a copy of the Participant Information Sheet and this Consent Form
All parties signing the Consent Form must date their own signature

1. I have read the attached Participant Information Sheet outlining the nature and purpose of the research study and I understand what I am being asked to do.

2. I have discussed my participation in this study with the member of the study team named below. I have had the opportunity to ask questions and I am satisfied with the answers I have received.

3. I have been informed about the possible risks of taking part in this study.

4. I consent to medical practitioners, other health professionals, hospitals or laboratories outside this institution releasing information concerning my condition and treatment which is needed for this study and understand that such information will remain confidential.

5. I freely consent to participate in the research project as described in the attached Participant Information Sheet.

6. I understand that my participation is voluntary and that I am free to withdraw at any time during the study.

Name of Participant	Signature of Participant	Date
Name of Witness to Participant's Signature	Signature of Witness	Date

*Witness is not to be the Investigator or member of the study team nor their delegate
* Please note that in the event that an Interpreter is used, the Interpreter is not a witness to the consent process

Witness to informed consent

A witness is required in the following circumstances as per the Note for Guidance on Good Clinical Practice (GCP) CPMP/ICH/135/95):
If a participant is unable to read. *By signing the consent form the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject, and that informed consent was freely given by the subject.*

ALL WITNESSES MUST BE OVER 18 YEARS OF AGE

Participant will be provided with a copy of the Participant Information Sheet and this Consent Form
All parties signing the Consent Form must date their own signature

Name of Witness to consent process (GCP Guidelines 4.8.9)	Signature of Witness	Date

*Witness is not to be the Investigator or member of the study team nor their delegate
* Please note that in the event that an Interpreter is used, the Interpreter is not a witness to the consent process

Name of Investigator	Signature of Investigator	Date

Participant will be provided with a copy of the Participant Information Sheet and this Consent Form
All parties signing the Consent Form must date their own signature

St Vincent's Hospital

WITHDRAWAL OF PARTICIPATION

Title:	**Atrial Fibrillation and Stroke Thromboprophylaxis in Heart Failure (STUDY 1)**
Short Title:	**The AFASTER Study**
Principal Investigator:	**Mr Caleb Ferguson, University of Technology, Sydney**
Site:	**St Vincent's Hospital, Darlinghurst**
Protocol :	**v1**

I hereby wish to WITHDRAW my intent to participate further in the above research project and understand that such withdrawal will not jeopardise my future health care.

Participant's Name (printed) .....

Signature .....

Date .....

Participant will be provided with a copy of this Withdrawal of Consent Form

St Vincent's Hospital

If a verbal withdrawal:

In the event the participant decided to withdraw verbally, please give a description of the circumstances. Coordinating Investigator to provide further information here:

Coordinating Investigator to sign the withdrawal of consent form on behalf of a participant if verbal withdrawal has been given:

Participant's Name (printed) .....

Signature of Investigator .....

Date .....

Participant will be provided with a copy of this Withdrawal of Consent Form

APPENDIX 6: PARTICIPANT SCREENING TOOL

AFASTER Study Screening Tool

Office use only

Subject ID | | | | |

Instructions: Shade circles like this: ● **Not like this: ⌀** **Please print in BLOCK STYLE in the boxes**

Section 1 General Screening Log

Date of Admission D D / M M / Y Y Y Y

Date of birth D D / M M / Y Y Y Y Age ___ ◯Female ◯Male

If < 18 years ineligible for study

Diagnosis of heart failure ◯NO ◯YES If NO > ineligible for study

NYHA class ◯ I ◯ II ◯ III ◯ IV

Confirmed AF ◯NO ◯YES If NO > ineligible for study

AF due to reversible causes? ◯NO ◯YES If YES > ineligible for study

AHA class of AF ◯Persistent ◯Permanent ◯Paroxysmal If paroxysmal > ineligible for study

Meets inclusion criteria? ◯Include ◯Exclude

Reason for exclusion _____

AFASTER Study: FORM 1: General Screening Log Page 1 of 1 Version 1 15th Feb, 2013

APPENDIX 7: CASE REPORT FORM

AFASTER Study Index Admission Data Collection Form

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Subject ID ☐☐☐☐

Instructions: Shade circles like this: ● Not like this: ⊘ Please print in BLOCK STYLE in the boxes

Section 1 Patient Profile / Sociodemographics

Date of birth D D / M M / Y Y Y Y Age ☐☐☐ ◯Female ◯Male

Admission status ◯ Planned ◯ Unplanned

Date of Admission D D / M M / Y Y Y Y Length of stay

Date of Discharge D D / M M / Y Y Y Y ☐☐☐ days

Cause of Admission _____ ◯ CV ◯ Non-CV If CV related, is it HF? ◯No ◯Yes

Marital Status ◯ Single ◯ Married/ Defacto ◯ Widowed Living Status ◯ Lives alone ◯ Cohabits

Resident in aged care facility ◯No ◯ Yes If yes, please state ◯ low level ◯ medium level ◯ high level

Nominated general practitioner? ◯ No ◯ Yes Nominated community pharmacist? ◯ No ◯ Yes

Postal Code of Residence ☐☐☐☐

Highest Educational Qualification ◯ HSC ◯ Degree ◯ Higher Degree ◯ Other

Primary Occupation _____ If other, please state: _____

Ethnicity ☐ **Ethnicity code:** 1=Caucasian, 2=Maori, 3=Pacific Islander, 4=Aboriginal, 5= Torres Strait Islander, 6=Asian, 7=Indian, 8=Other

Country of Birth ☐☐ **Country code:** 1=Australia, 2=UK, 3=New Zealand, 4=Italy, 5=China/HK, 6=Vietnam, 7=India, 8=Philippines, 9=Greece, 10=Germany, 11=South Africa, 12=Pacific Islands, 13=Other

Language Spoken at home ☐☐ **Language code:** 1=English, 2=Italian, 3=Greek, 4=Cantonese, 5=Arabic, 6=Mandarin, 7=Vietnamese, 8=Spanish, 9=German, 10=Hindi, 11=Maori, 12=Other

Section 2 Charlson Comobidity Index

(Complete the appropriate response for each condition (give only 1 answer per item)

AIDS	◯ No ◯ Yes	Dementia	◯ No ◯ Yes
Cerebrovascular disease	◯ No ◯ Yes	Hemiplegia	◯ No ◯ Yes
COAD	◯ No ◯ Yes	Leukaemia	◯ No ◯ Yes
Chronic heart failure	◯ No ◯ Yes	Mailgnant lymphoma	◯ No ◯ Yes
Connective tissue disease	◯ No ◯ Yes	Myocardial infarction	◯ No ◯ Yes
Peripheral vascular disease	◯ No ◯ Yes	Peptic ulcer disease	◯ No ◯ Yes
		Lymphoma	◯ No ◯ Yes

Diabetes mellitus ◯ None ◯ Without end organ damage ◯ With end organ damage

Liver disease ◯ None ◯ Mild ◯ Moderate ◯ Severe

Renal disease ◯ None ◯ Mild ◯ Moderate ◯ Severe

Malignant solid tumor ◯ None ◯ Non-metastatic ◯ Metastatic

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Section 3 Previous Medical History

	Has the patient had any of the following conditions? No	Yes	How long (in years) was this diagnosed?
Myocardial Infarction	○	○	If yes →
Hypertension	○	○	If yes →
High blood cholesterol	○	○	If yes →
Type I Diabetes	○	○	If yes →
Type II Diabetes	○	○	If yes →
Heart Failure	○	○	If yes →
Stroke/ TIA	○	○	If yes →
Mental Illness ○ Depression	○	○	If yes →
Mental Illness ○ Other (eg Bi-polar, schizophrenia)	○	○	If yes →
Irregular Heart Beat / Atrial Fibrillation / Palpitations	○	○	If yes →
Angina	○	○	If yes →
Coronary Artery Disease	○	○	If yes →
Vascular disease ○ Peripheral arterial disease	○	○	If yes →
Vascular disease ○ Other - *Please specify* _____	○	○	If yes →
Aneurysm *(Abdominal, thoracic)*	○	○	If yes →
Heart Valve Condition	○	○	If yes →
Pacemaker	○	○	If yes →
Implanted Defibrillator	○	○	If yes →
Renal Disease	○	○	If yes →
Sleep Apnoea	○	○	If yes →
Asthma / Lung Disease *(eg. Emphysema, COPD)*	○	○	If yes →
Arthritis ○ Rheumatoid	○	○	If yes →
Arthritis ○ Osteoarthritis	○	○	If yes →
Eye disease / retinopathy	○	○	If yes →
Migraine	○	○	If yes →
Stomach ulcer	○	○	If yes →
Cancer	○	○	If yes →
Other serious condition Please specify _____	○	○	If yes →

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Section 4 Blood test results

Blood chemistries

Date of test D D / M M / Y Y Y Y

Are these bloods the last available results of admission? ◯NO ◯YES

Sodium		mmol/L	ALT		mmol/L
Potassium	.	mmol/L	AST		mmol/L
Urea	.	mmol/L	GGT		mmol/L
Creatinine		umol/L	Alkaline Phosphate		mmol/L
eGFR			Calcium	.	mmol/L
Total Bilirubin		umol/L	Magnesium	.	mmol/L
Albumin		g/L	Phosphate	.	mmol/L
Total Protein		g/L			

Haematology results

Red blood cells	.	$x10^{12}/L$	Haemoglobin		g/L
Haematocrit	.		White blood cells	.	$x10^{9}/L$
Platelets		$x10^{9}/L$			

Coagulation studies

PT		sec	INR	.	
APTT		sec			

AF ASTER Study

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Section 5 Clinical Data

Weight K G S

NYHA class ◯ I ◯ II ◯ III ◯ IV

AHA class of AF ◯ Persistent ◯ Permanent ◯ Paroxysmal

Type of AF ◯ Valvular ◯ Non-valvular

Rhythm ◯ Sinus Rhythm ◯ Atrial Fibrillation ◯ Paced Rhythm ◯ No data

CPR status ◯ For CPR ◯ Not for CPR

LV ejection fraction | | %

LV dysfunction ◯ None ◯ Mild ◯ Moderate ◯ Severe

LAA closure device ◯ NO ◯ YES

Previous cardioversion ◯ NO ◯ YES

Previous ablation ◯ NO ◯ YES

Previous pulmonary vein isolation ◯ NO ◯ YES

Section 6 Australian Modified Karnofsky Performance Scale

◯ 100 - Normal; no complaints; no evidence of disease
◯ 90 - Able to carry on normal activity; minor signs or symptoms
◯ 80 - Normal activity; minor signs or symptoms
◯ 70 - Cares for self; unable to carry on normal activity or to do normal activity
◯ 60 - Requires occassional assistance but is able to care for most of his needs
◯ 50 - Requires considerable assistance and medical care
◯ 40 - In bed more than 50% of the time
◯ 30 - Almost completely bedfast
◯ 20 - Totally bedfast and requiring extensive nursing care by professionals and/or family
◯ 10 - Comatose or barely rousable
◯ 0 - Dead

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Section 8 Medications on discharge

◯ ACE inhibitor	◯ Lipid lowering agent	◯ Antiplatelet
◯ Angiotensin Receptor Blocker	◯ Nitrate	◯ Anticoagulant
◯ Beta blocker	◯ Calcium channel blockers	◯ Warfarin
◯ Diuretic	◯ Other vasodilator	◯ Dabigatran
◯ Aldosterone antagonist	◯ Antiarrhythmic	◯ Rivaroxaban
◯ Digitalis	◯ NSAIDs	◯ Apixaban

Section 9 Past Admission History

	Number of admission (s) in the past 12 months:		Total length of stay	
Emergency		times		days
Elective		times		days
Emergency room presentations only		times		

Section 10 CHA2DS2VASC Score

Congestive Heart Failure/ LV dysfunction	◯ NO	◯ YES
Hypertension	◯ NO	◯ YES
Aged ≥ 75	◯ NO	◯ YES
Diabetes	◯ NO	◯ YES
Stroke/ TIA/ TE	◯ NO	◯ YES
Vascular Disease (MI, PAD or aortic plaque)	◯ NO	◯ YES
Aged 65-74	◯ NO	◯ YES
Female Sex	◯ NO	◯ YES

LV dysfunction = LV fractional shortening ≤25% on echo cardiography

Hypertension = SBP> 160mmHg

Section 11 HAS-BLED Score

Hypertension	◯ NO	◯ YES
Abnormal liver function	◯ NO	◯ YES
Abnormal kidney function	◯ NO	◯ YES
Stroke	◯ NO	◯ YES
Bleeding	◯ NO	◯ YES
Labile INRs	◯ NO	◯ YES
Elderly	◯ NO	◯ YES
Drugs	◯ NO	◯ YES
Alcohol	◯ NO	◯ YES

Hypertension = SBP> 160mmHg ; **Abnormal renal function** = dialysis / renal transplantion / serum creatinine >200mmol/L (>~2.3mg/dL); **Abnormal liver function** = chronic hepatic dysfunction (e.g. cirrhosis) or biochemical evidence of significant hepatic derangement (e.g. bilirubin 2 x upper limit of normal in association with AST/ALT/ALP > 3 x upper limit normal); **Bleeding** = history of bleeding or anemia or predisposition to bleeding; **Labile INRs** = unstable/ high INRs or poor TTR (eg <60%); **Age** = ≥ 65; **Drug Therapy** = concomitant use of anti-platelet or NSAIDS; **Alcohol Intake** = consuming 8 or more alcoholic drinks per week.

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Section 12 Morisky Self Reported Medication Adherence

1) Do you ever forget to take your medicine?	○ No	○ Yes	○ No data
2) Are you careless at times about taking your medicine?	○ No	○ Yes	○ No data
3) When you feel better do you sometimes stop taking your medicine?	○ No	○ Yes	○ No data
4) Sometimes if you feel worse when you take your medicine, do you stop taking it?	○ No	○ Yes	○ No data

Section 13 European Heart Failure Self Care Behaviour Scale

	I Completely Agree 1	2	3	4	I Completely Disagree 5
1) I weigh myself every day	○	○	○	○	○
2) If I get short of breath, I take it easy	○	○	○	○	○
3) If my shortness of breath increases, I contact my doctor or nurse	○	○	○	○	○
4) If my feet/ legs become more swollen than usual, I contact my doctor or nurse	○	○	○	○	○
5) If I gain 2kgs in 1 week, I contact my doctor or nurse	○	○	○	○	○
6) I limit the amount of fluids I drink (not more than 1.5 - 2L/day)	○	○	○	○	○
7) I take rest during the day	○	○	○	○	○
8) If I experience increasing fatigue, I contact my doctor or nurse	○	○	○	○	○
9) I eat a low salt diet	○	○	○	○	○
10) I take my medication as prescribed	○	○	○	○	○
11) I get a flu shot every year	○	○	○	○	○
12) I exercise regularly	○	○	○	○	○

○ Patient unavailable for assessment. Please state reason: _____

Section 14 Frailty Assessment

6.1 In the last month, have you had too little energy to do the things you wanted to do? ○ No ○ Yes

6.2 What has your appetite been like? ○ Diminution in desire for food ○ No diminution in desire for food ○ Non-specific or uncodeable response

If non-specific to Q6.2 above → 6.3 Have you been eating more or less than usual? ○ Less ○ More ○ Neither more nor less

6.4 Because of a health problem, do you have difficulty [expected to last more than 3 months] walking 100 metres? ○ No ○ Yes

6.5 Because of a health problem, do you have difficulty climbing one flight of stairs without resting? ○ No ○ Yes

6.6 How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car, or doing a walk?

○ More than once a week ○ Once a week ○ One to three times a month ○ Hardly ever or never

6.7 Hand grip strength Right hand First ☐☐ Kg Second ☐☐ Kg Left hand First ☐☐ Kg Second ☐☐ Kg

○ Patient unavailable for assessment. Please state reason: _____

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Section 15 Telephone follow up eligibility

Consents to telephone follow up ○ NO ○ YES If NO > withdrawn from study/ not enrolled in follow up

Telephone available? ○ NO ○ YES If NO > lost to follow up

END OF FORM

APPENDIX 8: ATRIAL FIBRILLATION: STROKE PREVENTION IN FOCUS.

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Atrial fibrillation: Stroke prevention in focus

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ABSTRACT

Introduction: Atrial fibrillation (AF) is a common arrhythmia and a risk factor for stroke and other, adverse events. Internationally there have been recent advancements in the therapies available for, stroke prevention in AF. Nurses will care for individuals with AF across a variety of primary and acute, care settings and should be familiar with evidence based therapies.
Aim: This paper provides a review of the epidemiology of AF and stroke, stroke and bleeding risk, assessment tools and evidence based treatments for the prevention of stroke in AF including the use of, novel anti-thrombin agents.
Method: A review of key databases was conducted from 2002 to 2012 using the key search terms 'atrial, fibrillation' 'anticoagulation' 'risk assessment' and 'clinical management'. The following electronic, databases were searched: CINAHL, Medline, Scopus, the Cochrane Library and Google Scholar., Reference lists were manually hand searched. Key clinical guidelines from National Institute for, Clinical Excellence (NICE, UK), American Heart Association (AHA, USA), American College of Cardiology, (ACC, USA) and the European Society of Cardiology (ESC) and key government policy documents were, also included. Articles were included in the review if they addressed nursing management with a focus, on Australia.
Results: Many treatment options exist for AF. Best practice guidelines make a variety of, recommendations which include cardioversion, ablation, pulmonary vein isolation, pharmacological, agents for rate or rhythm control approaches, and antithrombotic therapy (including anticoagulation, and antiplatelet therapy). Treatment should be patient centred and individualised based upon, persistency of the rhythm, causal nature, risk and co-morbid conditions.
Conclusion: AF is a common and burdensome condition where treatment is complex and not without, risk. Nurses will encounter individuals with AF across a variety of primary and acute care areas, understanding the risk of AF and appropriate therapies is important across all care settings. Treatment, must be individually tailored to the needs of the patient and balanced with the best available evidence.

Introduction

Atrial fibrillation (AF) is an emergent health concern,[1] described by some as an evolving epidemic.[2] AF is the most commonly occurring cardiac arrhythmia and is a risk factor for stroke. Factors contributing to thrombus formation, include abnormalities of the heart wall, abnormal blood stasis and blood constituents, are

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described as Virchow's Triad.[3] In AF structural heart disease, stasis of blood within the left appendage and atrium, and abnormalities of coagulation contribute to stroke risk.[3] A patient's stroke risk can be minimised through timely identification and diagnosis of AF and application of evidence-based treatment. Internationally, there have been recent advancements in therapies aimed at reducing stroke. These include novel anticoagulants, surgical procedures and implantable devices.[4–8] These innovative therapies are becoming more common in the Australian healthcare system. Therefore, it is imperative that nurses remain knowledgeable of the available therapies and risk factors for the prevention of stroke in AF.

Aims and objectives

This paper outlines stroke prediction and bleeding risk assessment tools and provides a review of evidence based therapies to manage stroke risk in AF.

Methods

A review of key databases was conducted from 2002 to 2012 using the key search terms '*atrial fibrillation*' '*anticoagulation*' '*risk assessment*' and '*clinical management*'. The following electronic databases were searched: CINAHL, Medline, Scopus and the Cochrane Library. Google Scholar was used to augment the search. Policy documents and clinical evidence based guidelines were also included. Reference lists were manually hand searched. Results were limited to English language and full text documents. Clinical guidelines from National Institute for Clinical Excellence (NICE, UK), American Heart Association (AHA, USA), American College of Cardiology (ACC, USA) and the European Society of Cardiology (ESC) along with key government reports were also included. Articles were included in the review, if they addressed clinical management with a focus on Australia.

Atrial fibrillation

AF is distinguished by chaotic electrical atrial activation and ineffective contraction. It is commonly observed on ECG by the substitution of regular P waves with rapid oscillations or fibrillatory waves that vary in amplitude, shape, and timing, associated with an irregular frequent ventricular response when AV conduction is intact.[9] Cardiac and non-cardiac risk factors for the development of AF including emergent risk factors are summarised in Table 1.

Definition and classification

AF can be classified as paroxysmal, *recurrent episodes that self-terminate, usually within 48* h, persistent, *recurrent episodes that last more than one week*, or permanent, *ongoing AF*. The normal progression of AF is from short, rare episodes increasing in duration to more frequent events and over time, most patients develop sustained episodes of AF.[10] Classification systems aim to provide an easier description of types of AF. The ACC/AHA/ESC Guidelines recommend a simplistic scheme for clinical relevance, as detailed in Fig. 1.

- **Paroxysmal AF**: self terminating within 7 days.[11]
- **Persistent**: requiring termination by pharmacological or electrical cardioversion.[11]
- **Permanent**: restoration to normal sinus rhythm is either impossible or unadvisable.[11]

Table 1
Cardiac and non cardiac risk factors for the development of AF.

Cardiac	Non-cardiac
Hypertension	Age
Heart failure	Gender: male
Valve disease	Diabetes
Ischaemic heart disease	Electrolyte abnormalities
Cardiomyopathy	Excessive alcohol intake
Cardiac surgery	Obesity
Atrial septal defects	Smoking
Ion channel disorders	Obstructive sleep apnoea
Myocarditis	COPD
Pericarditis	Pulmonary embolism
Left atrial enlargement	Thyroid dysfunction
Left ventricular hypertrophy	Altered metabolism
Congenital defects	Autonomic changes
	Environmental influences
	Excessive caffeine consumption

Novel & emergent risk factors	
Genetic influences & familial history	Parental history of AF doubled risk of AF in offspring[72]
Ethnic and socio-demographic differences	Blacks appear to be at a lower risk of AF than whites.[73] European ancestry in African Americans at an increased risk[74] Increased probability if Caucasian Increased probability if from a lower socio-economic background
Excessive endurance sports training[75]	Athletes may experience any arrhythmia during rest of exercise,[76] however AF is the most common cause of palpitations in athletes.[77] Possible association between anabolic steroid use and development of AF.[78,79]
Pericardial fat	Pericardial fat is associated with the prevalence of AF.[80]
Chronic kidney disease	Reduced kidney function and the presence of albumin-urea are strongly associated with the incidence of AF.[81]
Rheumatoid arthritis	Increased risk of developing AF.[82]
Coeliac disease	Increased risk of developing AF.[83]

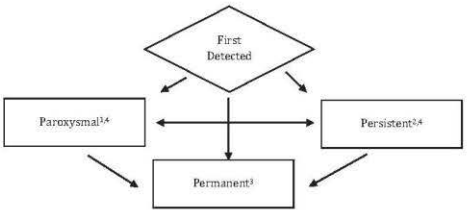

Fig. 1. Patterns of AF: (1) Episodes that generally last 7 days or less (most less than 24 h) (2) episodes that usually last longer than 7 days (3) cardioversion failed or not attempted (4) both paroxysmal and persistent AF may be recurrent.
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Stroke risk is similar with paroxysmal, persistent or permanent AF. Therefore, the selection of antithrombotic prophylaxis should be independent of the rate/rhythm control strategy.[12]

Screening and diagnosis

The screening and diagnosis of AF can be problematic. This is due to fluctuations in the presence of signs, particularly in paroxysmal AF many of which can be subtle and silent in nature. Signs and symptoms of AF are summarised in Table 2. An opportunistic manual palpation of a patient's radial pulse remains one of the most effective, feasible, and valid ways of checking for heart rate

Table 2
General signs and symptoms of AF.

General signs and symptoms[84]
Palpitations
Dyspnoea
Chest pain
Worsening angina
Hypotension
Reduced capacity to exercise
Fatigue
General malaise
Dizziness and light-headedness
Polyuria
Panic attacks
Syncope

and rhythm irregularity.[13] An ECG recording is gold standard in the diagnosis of AF. Any arrhythmia that has the hallmark characteristics of AF and is 30 s in duration on a rhythm strip or long enough to be captured on a 12 lead ECG is considered to be AF.[14]

Epidemiology of atrial fibrillation and stroke in Australia

AF affects 1–2% of the Australian population (equivalent to 240,000–400,000 Australians).[10] It is more commonly seen in the elderly with an estimated prevalence of 8% in people over the age of 80 years.[15] AF reduces an individual's capacity to exercise, and may lead to cognitive dysfunction and reduced quality of life.[16,17] Stroke is a major cause of death and disability and accounts for 9% of all-cause mortality worldwide. 20% of stroke survivors require institutional care after 3 months and 15–30% will be permanently disabled.[18,19] This highlights the need for a strong focus on primary stroke prevention.[20] A gradual reduction in mortality from stroke is attributed to the better control of modifiable risk factors, such as AF.[21]

Stroke prevention

It is estimated that 20–35% of all patients with ischaemic strokes have AF.[22] It is thought to be an aetiological factor in as many as 30% of strokes in the elderly.[23] This equates to 5% of all AF patients developing an embolic stroke every year.[24,25] Patients who experience an ischaemic stroke with AF as an existing condition are known to have substantially worse outcomes than patients without AF.[22] This may be due to increasing age and the greater likelihood of other comorbidities.[22] The risk of stroke was 5.6 times greater in patients with AF than that in comparably aged patients in sinus rhythm in the Framingham Cohort Study.[26] Predicting and treating the risk of stroke with definitive therapies, including antithrombotic therapies, is highly justified and recommended by best practice guidelines[20,27,28] and should be individually tailored, based on comorbidities and contraindications.[9,29–31] Hospitalisations

The burden of AF-related hospitalisation is set to increase rapidly over the next decade with the growing ageing population.[11,32] The prevalence of cardiovascular disease is likely to increase at least three-fold by 2050.[33] A large proportion of hospitalisations for arrhythmia are due to AF.[34] Wong and colleagues reported a 203% increase in the number of AF related hospitalisations in Australia between 1993 and 2007.[1] This may be largely due to technological advances and the increased availability and utilisation of hospital based therapies, such as electrical cardioversion, ablation and insertion of left atrial appendage closure devices.[35]

Stroke and bleeding risk assessment tools

Risk assessment tools are intended to guide clinical decision making in the allocation of thromboprophylactic therapies and are based on the evidence that certain risk factors increase the likelihood of clinical events.[36] Several risk stratification schemes have been established with the aim to quantify the risk of stroke in individual patients with AF and are summarised in Table 3.[25,37–40] The tool known as the congestive heart failure, hypertension, age >75 years, diabetes and prior stroke or TIA ($CHADS_2$) is a simple and well-validated tool. It allocates 1 point for a history of congestive heart failure, hypertension, age >75, or diabetes and 2 points for a history of stroke or TIA. Patients with 2 or more points on this scheme are predicted to have an annual stroke risk of over 4%, while those with no points have a predicted annual risk of less than 1–2%.[37] A score of 0 identifies patients at low stroke risk, a score of 1–2 identified patients at moderate stroke risk, and a score greater than 2 identified patients at high stroke risk.[37,41] It uses well-established independent stroke risk factors to assess patient risk.[42] The CHA_2DS_2-VASc scheme includes scoring categories for vascular disease, age between 65 and 74 years and sex, and provides greater sensitivity to predict thromboembolism than the original $CHADS_2$ score.[43]

Risk scores are used to estimate the absolute risk of an adverse event, which is helpful when advising patients and making complex treatment decisions.[44] However, these are limited within the context of complex cardiogeriatric syndromes as such models fail to consider frailty, cognitive and functional decline or non-adherence to therapy.[31] There is need to expand such risk prediction models to include a combination of these factors.[31] As part of a comprehensive patient assessment and prior to the commencement of oral anticoagulation it is important to undertake a bleeding risk assessment.[36] The HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR,

Table 3
Stroke risk stratification schemata.

SPAF (Stroke Prevention in Atrial Fibrillation) Acronym
Age, female sex, diabetes, previous stroke or TIA, hypertension, or elevated systolic BP
Framingham tool
Age, gender, systolic blood pressure, diabetes and prior stroke or TIA

$CHADS_2$ acronym[37]	Score	$CHADS_2$ score	Adjusted stroke rate (%/year)[36]
Congestive heart failure	1	0	1.9
Hypertension	1	1	2.8
Aged ≥75 yrs	1	2	4.0
Diabetes mellitus	1	3	5.9
Stroke/TIA	2	4	8.5
Max score	6	5	12.5
		6	18.2

CHA_2DS_2-VASc acronym[85]	Score	CHA_2DS_2-VASc score	Adjusted stroke rate (%/year)[36]
Congestive heart failure/LV dysfunction	1	0	0
Hypertension	1	1	0.7
Aged ≥75years	2	2	1.9
Diabetes mellitus	1	3	4.7
Stroke/TIA/TE	2	4	2.3
Vascular disease (prior to MI, PAD or aortic plaque)	1	5	3.9
Aged 65–74 years	1	6	4.5
Sex category (i.e. female gender)	1	7	10.1
Max score	10	8	14.2
		9	100

Reference: Lip YHG implications of the CHA2DS2-VASc and HAS-BLED scores for Thromboprophylaxis in Atrial Fibrillation.[36]

Elderly (>65), Drugs/alcohol concomitantly) bleeding risk score is a simple yet well-validated risk assessment tool, where a score of more than or equal to 3 indicates 'high risk'.[45] Treatment should be balanced within the context of the patient's individual circumstances, best available evidence, and clinical expertise (Refer to Table 4).[46]

Treatment and management of atrial fibrillation

Therapeutic recommendations include pharmacological management, electrical cardioversion, ablation, pulmonary vein isolation, pharmacological agents for rate or rhythm control approaches, and antithrombotic therapy including anticoagulation and antiplatelet therapy.[9,27] Treatment is dependent upon persistency of the rhythm, causal nature, risk and co-morbid conditions.[27] A range of pharmacotherapies used to prevent stroke in AF are summarised in Table 5.

Pharmacological interventions to prevent stroke in AF

Warfarin

Warfarin is the first line pharmacotherapy for thromboprophylaxis[47] and reduces relative risk of recurrent stroke in patients with TIA or minor stroke by approximately 70% (hazard ratio 0.34, 95% CI 0.20–0.57).[48] Bleeding is a common risk with warfarin therapy. Poor treatment adherence, drug or diet interactions or the inconvenience of INR monitoring are causal factors of adverse events including haemorrhage and stroke. Warfarin requirements may be different according to a range of factors, such as; genetic factors, ethnicity, and cultural differences including food preferences.[49] The major concerns with warfarin therapy are the potential for catastrophic haemorrhage, predominantly intracranial haemorrhage which may lead to increased morbidity and mortality.[50–52] The optimal target therapeutic range for INR is between 2 and 3 for stroke prevention in AF.[53] A higher therapeutic range may be aimed for in patients with prosthetic heart valves or mitral heart disease.[54] Patients should maximise their time spent in their target range INR.[55,56] The relative contraindications to warfarin therapy include a past medical history of peptic ulcer disease, concomitant use of non-steroidal anti-inflammatory drugs, or advanced age (>85 years). Absolute contraindications to therapy include recent intracranial haemorrhage, cirrhotic liver disease, or advanced malignancy.[57] The burden of monitoring, and unpredictable pharmacokinetics of warfarin have prompted the search for more efficacious agents.[47]

Table 4
The HAS-BLED score.

Acronym	Scoring
Hypertension	1 point
Abnormal liver or kidney function	1 point each
Stroke	1 point
Bleeding	1 point
Labile INRs	1 point
Elderly	1 point
Drugs or alcohol	1 point each

Notes: Hypertension = systolic blood pressure > 160 mmHg. Abnormal renal function = dialysis/renal transplantion/serum creatinine > 200 mmol/L. Abnormal liver function = chronic hepatic dysfunction (e.g. cirrhosis) or biochemical evidence of significant hepatic derangement (e.g. bilirubin 2 × upper limit of normal in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase 3 × upper limit normal etc.). Bleeding = history of bleeding or a bleeding diathesis. Drugs = concomitant use of antiplatelet or non steroidal anti-inflammatory agent.

Table 5
Recommended pharmacological agents for stroke prevention in AF.

Drug	Class	Indication(s)	Pharmakineticsaction	Considerations
Warfarin	Anticoagulant	Prevention and management of thromboembolism in AF for high risk patients	Suppresses the vitamin-k dependent synthesis of prothrombin and factors VII, IX and X in the liver	Requires frequent checking of INR to maintain time within therapeutic range
	Vitamin K antagonist		Narrow therapeutic range	Use can be burdensome
Dabigatran	Anticoagulant	Prevention of stroke or systemic embolism in patients with non valvular AF at moderate to high risk of stroke	Novel anticoagulant	Requires less invasive and close serum coagulation level monitoring than warfarin
	Direct thrombin inhibitor		A potent direct competitive inhibitor of thrombin. Excreted by the kidneys. Serum half life is 14–17 h.	Concerns regarding a lack of an effective reversal agent
Rivaroxaban	Anticoagulant direct oral activated factor Xa inhibitor	Prevention of stroke or systemic embolism in patients with non valvular AF at moderate to high risk of stroke	Novel anticoagulant Oral factor Xa inhibitor Serum half life is 5–9 h	Requires less invasive and close serum coagulation level monitoring than warfarin Concerns regarding a lack of an effective reversal agent
Apixaban	Anticoagulant direct oral activated factor Xa inhibitors	Prevention of stroke or systemic embolism in patients with non valvular AF at moderate to high risk of stroke	Novel anticoagulant Oral factor Xa inhibitor	Not yet licensed in Australia for stroke prevention in AF
Clopidogrel	Antiplatelet	Prevention of vascular ischaemic associated with atherothrombotic events Prevention and management of thromboembolism in AF for low risk patients or those deemed unsuitable for traditional warfarin therapy	Inhibits platelet aggregation by irreversibly binding to ADP platelet receptors	May alter metabolism of warfarin Caution if administered with warfarin as may increase risk of bleeding
Aspirin	Antiplatelet	Prevention and management of thromboembolism in AF for low risk patients or those deemed unsuitable for traditional warfarin therapy	Inhibits thrombus formation by decreased platelet aggregation Antiplatelet due to the non-competitive inhibition of cyclo-oxygenase, which is needed for thromboxane synthesis	Advise to take with food Risk of GI complications with long term usage

Novel oral anticoagulants

Dabigatran is a novel oral direct thrombin inhibitor. Clinical trials have demonstrated that when given at a dose of 110 mg, it leads to lower rates of stroke when compared with warfarin.[4] Dabigatran was successfully listed on the Pharmaceutical Benefits Scheme in 2011 for stroke prevention in AF. However, considerable fears still exist amongst clinicians pertaining to the risk of bleeding.[58] The Therapeutic Goods Administration has announced a safety advisory notice regarding risk of bleeding with associated use.[59] Apixaban and rivaroxaban are both direct oral factor Xa inhibitors that are superior to warfarin in preventing strokes. Rivaroxaban is noted to have less frequent intracranial and fatal bleeding occurrence, whilst apixaban causes less bleeding and results in a lower mortality.[5,6] Apixaban is not yet licensed for use in stroke prevention for AF patients in Australia. Rivaroxaban was registered with the TGA in April 2012 in Australia for use in the prevention of stroke in patients with non-valvular AF and at least one additional risk factor for stroke.[60] The advantages these novel anticoagulants have over warfarin is that they have predictable pharmacokinetics and eliminate the burden of routine anticoagulation monitoring. A recent meta-analysis comparing the efficacy of new anticoagulants, including apixaban, dabigatran and rivaroxaban to warfarin therapy established that treatment with all three new anticoagulants was associated with lower risks of intracranial haemorrhage (RR 0.49, 95% CI 0.36–0.66) and appear to have a favourable safety profile.[61] Yet clinicians remain apprehensive prescribing novel anticoagulants due to the unavailability of any clinically proven reversal agent.[58] Recombinant factor VIIa, invasive renal dialysis or charcoal haemofiltration are highlighted as possible reversal strategies.[62] However such measures are expensive and may not be readily available.[58]

Rate and rhythm control

Ventricular rate control is a key aim in the management of AF. The aim is to maintain a ventricular rate within a haemodynamically acceptable range even though the atria continue to fibrillate. Ventricular rate is often controlled by treatment with betablockers, non-dihydropyridine calcium channel antagonists or digoxin. The selection of any rate control therapy should consider the pharmacological impact on any pre-existing comorbidities including hypertension, ischaemic heart disease and heart failure.[63] Rhythm control aims to restore and maintain normal sinus rhythm. This process is referred to as cardioversion and there are 2 treatment types; pharmacological and non-pharmacological. Pharmacological therapies include amiodarone, sotalol, flecainide and dronedarone.

The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial was a large multicentre RCT that compared cardioversion and adjunct use of anti-arrhythmic drugs verses rate controlling drugs. The investigators found that there was an increased risk of stroke in the rhythm control group. In addition, the rhythm control group were significantly at an increased risk of being hospitalised and developing adverse drug effects than those in the rate control group.[64]

Non pharmacological interventions to treat AF

Electrical cardioversion

Cardioversion aims to revert the arrhythmia back to normal sinus rhythm and therefore increase cardiac performance and lower the risk of stroke and should be considered as a first line treatment in all patients with AF.[65] Cardioversion is performed through a synchronous direct electric current discharge via an external cardioversion with a goal to repolarise the errant atrial conduction and to restore ordered conduction.[65] Success rates are influenced by any underlying aetiologies and vary between 20 and 90%.

Catheter ablation

Catheter ablation is routinely performed for patients with symptomatic AF.[7] It is normally reserved for those patients who are symptomatic despite treatment for both rate and rhythm control.[14] The procedure involves electrical isolation of the pulmonary veins through the application of radiofrequency ablation.[66] Success rates are dependent on variables, such as duration of AF, the presence of comorbidities including obesity and sleep apnoea and the duration of follow-up.[7] Ablation is primarily effective in reducing the recurrences of AF,[67] however multiple attempts of the procedure may be required for success in treatment.[68] The evidence demonstrates that catheter ablation is more effective than anti-arrhythmic drug therapy in controlling AF and may lead to improved quality of life.[7] The equipment and technical procedures used to perform ablation continues to rapidly evolve.[7]

Left atrial appendage (LAA) closure

Embolic stroke in patients with non-valvular AF is often associated with left atrial appendage thrombi.[8] It is estimated that up to 90% of thrombi in patients with non-valvular AF originate from the LAA.[69] Percutaneous closure devices are non-inferior to treatment with oral warfarin therapy and that it may be an effective alternative to anticoagulation.[8] The WATCHMAN© device is a self-expanding nickel titanium frame structure with fixation barbs and a permeable polyester fabric cover. It is implanted via a trans-septal approach by use of a catheter-based delivery system to seal the ostium of the LAA.[8] The main benefit to implantation is the cessation of any oral anticoagulant therapy shortly after implant thus eliminating the need for burdensome monitoring and associated coagulopathic complications. Whilst this device shows particular promise in clinical trials and practice overseas, it is not yet available on PBS in Australia and not yet registered as a prosthetic implant with many private health insurance companies.[70] It is important to highlight that such devices are in the very early stages of implantation in Australia and further investigation into the long-term efficacy and safety is warranted.

Lifestyle advice and patient education

Patient education is essential to ensure optimal adherence to any prescribed pharmacological therapy. A patient's knowledge of therapy is often a determinant of adherence, and has consequential effects to anticoagulant control and a lack of perception of the importance of medications.[71] A lack of awareness of risk-to-benefit threshold may cause altered coagulation and ultimately lead to adverse events.[71] Patient education is challenging due to AF primarily affecting the older population, where functional and cognitive impairment are common. Educational interventions must take account of this complexity and be individualised to meet the patient's needs.

Future research

Additional research is required in Australia to advance healthcare that is available for AF patients in the 21st century. The burden of AF is set to increase with the burgeoning ageing population. AF often coexists with concomitant cardiovascular conditions and future research needs to take account of such complexity. Attention should be drawn to the need for newer cross-condition models of AF care, and the need for more holistic approaches to stroke risk

APPENDIX 9: ATRIAL FIBRILLATION AND THROMBOPROPHYLAXIS IN HEART FAILURE: THE NEED FOR PATIENT-CENTERED APPROACHES TO ADDRESS ADHERENCE

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REVIEW

Atrial fibrillation and thromboprophylaxis in heart failure: the need for patient-centered approaches to address adherence

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Abstract: Atrial fibrillation is a common arrhythmia in heart failure and a risk factor for stroke. Risk assessment tools can assist clinicians with decision making in the allocation of thromboprophylaxis. This review provides an overview of current validated risk assessment tools for atrial fibrillation and emphasizes the importance of tailoring individual risk and the importance of weighing the benefits of treatment. Further, this review provides details of innovative and patient-centered methods for ensuring optimal adherence to prescribed therapy. Prior to initiating oral anticoagulant therapy, a comprehensive risk assessment should include evaluation of associated cardiogeriatric conditions, potential for adherence to prescribed therapy, frailty, and functional and cognitive ability.

Keywords: stroke risk, heart failure, atrial fibrillation, anticoagulation, risk stratification, medication adherence

Introduction

Heart failure (HF) is a complex and primarily cardiogeriatric syndrome.[1] One-third of patients with HF are likely to have atrial fibrillation (AF) as a concomitant condition.[2] AF is a predictor of stroke in patients with HF.[3] Therefore, predicting and treating the risk of stroke with definitive therapies, including antithrombotics, is highly justified and recommended by best practice guidelines.[4–6] Yet, commonly these therapies are not applied in practice.[7] Under 70% of estimated eligible patients receive anticoagulation therapy.[7]

Although the use of anticoagulants has increased in the past 2 decades,[8] those individuals considered to be at an increased risk of bleeding are less likely to be prescribed anticoagulation therapy.[8] As a consequence, patients may not be receiving therapy based purely upon their predicted stroke risk alone. Many factors contribute to clinical decision making amongst physicians that influence prescription.[9,10] Factors such as cognitive impairment and frailty are common reasons for clinicians choosing not to prescribe thromboprophylaxis.[11,12]

This is a clinical conundrum for health professionals in prescribing evidence-based therapy and deciding if the risk of treatment outweighs the risk of nontreatment.[13] The Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) trial compared dose-adjusted warfarin with 75 mg aspirin in elderly patients over 75 years. The investigators found that warfarin was associated with a significant reduction in stroke with no difference in the risk of significant hemorrhage.[14] However, the Warfarin and Aspirin in Patients with Heart Failure and Sinus Rhythm (WARCEF) study,[15] although conducted in people with sinus rhythm and not AF, showed that the benefit of warfarin

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in reducing ischemic stroke was offset by an increased risk of major hemorrhage.[15] Underpinning the choice to prescribe thromboprophylaxis should be one that is individualized to the risk of the patient.

This review provides a critique of current risk assessment tools for the evaluation of stroke and bleeding risk in AF. Further, it identifies the need to extend these assessments to factors that impact treatment adherence and to consider risks for adverse events, particularly bleeding. Strategies for promoting adherence to prescribed therapy are also included.

Stroke and bleeding risk assessment schemata in AF

Risk classification schemata are intended to guide treatment decisions in AF by defining the likelihood of future clinical events based on independent risk factors.[13] Risk scores can be used to estimate the absolute risk of an adverse event. This may be helpful in counseling patients and informing treatment decisions.[16] These metrics do not consider the balance of risk of adverse events and potential nonadherence. The $CHADS_2$ (congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke, transient ischemic attack, or thromboembolism) score (Table 1) was derived from the Atrial Fibrillation Investigators' and Stroke Prevention in Atrial Fibrillation Investigators' schemata. This was validated in a retrospective cohort of hospitalized patients with AF. A score of zero identified patients at low stroke risk. A score of one to two identified patients at moderate stroke risk. A score greater than two identified patients at high stroke risk.[17,18] Patients with two or more points are predicted to have an annual stroke risk of over 4%, whereas those scoring no points have a predicted annual risk of less than 1%–2%.[18]

Table 1 Stroke risk stratification with $CHADS_2$ and CHA_2DS_2-VASc assessment tools

	Score	$CHADS_2$ score	Adjusted stroke rate (%/year)
$CHADS_2$ acronym			
Congestive heart failure	1	0	1.9%
Hypertension	1	1	2.8%
Aged ≥ 75 years	1	2	4.0%
Diabetes mellitus	1	3	5.9%
Stroke/TIA	2	4	8.5%
Max score	6	5	12.5%
		6	18.2%
CHA_2DS_2-VASc acronym			
Congestive heart failure/ LV dysfunction	1	0	0%
Hypertension	1	1	0.7%
Aged ≥ 75 years	2	2	1.9%
Diabetes mellitus	1	3	4.7%
Stroke/TIA/TE	2	4	2.3%
Vascular disease (prior to MI, PAD, or aortic plaque)	1	5	3.9%
Aged 65–74 years	1	6	4.5%
Sex category (ie, female gender)	1	7	10.1%
Max score	10	8	14.2%
		9	100%

Abbreviations: LV, left ventricular; MI, myocardial infarction; PAD, peripheral artery disease; TE, thromboembolism; TIA, transient ischemic attack.

The Stroke Prevention in Atrial Fibrillation (SPAF) scheme estimates risk based upon the presence of the following risk factors alone or in combination: age, female sex, diabetes, previous stroke or transient ischemic attack, hypertension, or elevated systolic blood pressure.[19,20] Similarly, the Framingham scheme can be used to risk assess stroke risk through the assignment of values to each of the following well-established independent risk factors: age, gender, systolic blood pressure, diabetes, and prior stroke or transient ischemic attack.[16,20] The $CHADS_2$, SPAF, and Framingham schemes have demonstrated greater predictive accuracy than chance.[20] This predictive ability may allow clinicians to target high-risk patients for more aggressive therapeutic intervention.[20] The CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke, transient ischemic attack, or thromboembolism, vascular disease, age 65–74 years, sex category) score, provides the highest sensitivity of all schemes to predict thromboembolism (Table 1).[21]

A number of bleeding risk stratification tools exist. Amongst these are the $HEMORR_2HAGES$ (hepatic or renal disease, ethanol abuse, malignancy, older age, reduced platelet count, rebleeding risk, anemia, genetic factors, excessive falls risk, stroke)[22] and the HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio [INR], elderly, drug/alcohol concomitantly)[23] tools, yet these are not often used in clinical practice and use is cumbersome. Many use complex scoring systems, and few have been validated in patients with AF and HF. The HAS-BLED bleeding risk tool originated in 2011 and was validated in a European cohort of 3978 participants with AF (Table 2). In a comparative validation, the HAS-BLED tool displayed an increased predictive ability than four other bleeding risk stratification methods[22,24–26] among patients in the combined Stroke Prevention Using Oral Thrombin Inhibitor in Atrial Fibrillation (SPORTIF) III and V cohort.[23] Following validation, the HAS-BLED tool was suggested as a simple, yet easy to calculate tool

Table 2 The HAS-BLED score

Clinical characteristic	Score	HAS-BLED score	Bleeds per 100 patient-years
Hypertension	1 point	0	1.13
Abnormal liver or kidney function	1 point each (1 or 2)	1	1.02
Stroke	1 point	2	1.88
Bleeding	1 point	3	3.74
Liable international normalized ratios	1 point	4	8.70
Elderly	1 point		
Drugs or alcohol	1 point each (1 or 2); max 9 points		

Notes: Hypertension = systolic blood pressure > 160 mmHg; abnormal renal function = dialysis/renal transplantation/serum creatinine > 200 mmol/L; abnormal liver function = chronic hepatic dysfunction (eg, cirrhosis) or biochemical evidence of significant hepatic derangement (eg, bilirubin twice the upper limit of normal in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase three times the upper limit of normal); bleeding = history of bleeding or a bleeding diathesis; drugs = concomitant use of antiplatelet or nonsteroidal antiinflammatory drugs.

that can be used to assess bleeding risk in AF patients within everyday clinical practice.[13] A HAS-BLED score of at least three indicates high risk and the developers of the tool suggest the need for regular review and some caution following the initiation of oral anticoagulant or aspirin therapy.[13]

Adherence

Failing to adhere to recommendations is a major reason for adverse events.[27] Adherence is a multidimensional phenomenon determined by the relationship of five series of factors or dimensions. There are five dimensions within the World Health Organization's multidimensional adherence model, which incorporate socioeconomic-, health care system-, condition-, treatment-, and patient-related factors;[28] this model assists in providing a framework for the organization of barriers to anticoagulant therapy (Table 3). Implications for practice including strategies that may be employed to improve adherence are also provided.

Once the need for oral anticoagulation is identified, several additional factors must be considered. Despite the evidence demonstrating the benefits of anticoagulation therapy in AF and HF, adherence to these recommendations is far from optimal.[10,29,30] The hesitation to anticoagulate patients is often based upon fear of adverse effects and poor adherence with monitoring, and this is most pronounced in the elderly.[12] The need for monitoring and titration as well as the adverse effect profile likely contributes to this reticence.[31] Although the use of newer agents such as oral direct thrombin inhibitors (eg, dabigatran) and oral factor Xa inhibitors (eg, rivaroxaban and apixaban) show particular promise in decreasing monitoring, concerns regarding adherence and adverse events remain high.[13] Despite data describing the barriers and facilitators to thromboprophylaxis in the elderly, there has been a lesser focus on individuals with HF who are at high risk.[12] New approaches, that are patient centered, are required to enhance evidence-based use of therapy to prevent thromboembolism and identify risk of bleeding.[32]

Health system-related factors

Clinical trials and meta-analyses have demonstrated the effect of anticoagulation in reducing the risk of ischemic stroke in patients with AF.[33–37] Yet, a large proportion of patients with AF are not treated with anticoagulant therapy. Despite the well-recognized association between AF and prevention of ischemic stroke and the benefits of therapy, anticoagulant therapy remains underused in AF patients.[7] There are numerous reasons why anticoagulant therapy is not initiated, but it is largely due to clinician and patient concerns about the risk of falls and hemorrhagic complications.[7] Clinicians may be apprehensive about initially prescribing oral anticoagulants to elderly patients given the concerns about a higher risk of oral anticoagulant-associated hemorrhage.[38]

Table 3 Barriers to thromboprophylaxis

Health system-related factors	Clinician apprehension
	Fear of intracranial hemorrhage and falls
	Lack of multidisciplinary approach
	Urban versus rural resource barriers
Treatment-related factors	International normalized ratio monitoring
	Dietary restrictions
	Risk of hemorrhage
Socioeconomic-related factors	Cost of medication
	Cost of visiting clinics
	Ability to attend clinics
Patient-related factors	Level of cognition
	Medication and condition knowledge
	Language difficulties
	Inadequate patient education
Condition-related factors	Polypharmacy
	Frailty
	Cognitive and functional impairment
	Stress and depression

Of 4188 patients in the Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study with AF who were newly commenced on warfarin therapy, more than one-quarter of patients had discontinued treatment after 1 year.[39] The study authors hypothesized that this may have been due to difficulty in INR control or concerns from clinicians or patients about bleeding risk.[39] More recently, in a Swedish atrial fibrillation cohort study, in almost all patients within a large cohort of 182,678 patients with AF, the risk of ischemic stroke without anticoagulant treatment was higher than the risk of intracranial bleeding with anticoagulant treatment.[40]

Solution to health system-related factors

Clinician apprehension may be reduced through providing training and education and practical clinical practice guidelines that provide support for clinical decision making.[41–43] The additional use of a bleeding prediction tool (eg, HAS-BLED) with the stroke risk prediction tool (eg, CHA_2DS_2-VASc) may also assist in clinical decision making.[13] Undertaking chart reviews and clinical audits and excluding patients with documented contraindications to therapy may assist in the identification of patients who are eligible for oral anticoagulant therapy; however, this is not prescribed as a method to increase uptake.[44] From a wider health systems perspective, having access to a state or national surveillance system or the development of a national AF and anticoagulation registry is advocated.[41,45] Clinician adherence to guidelines is a complex issue.[46] Cabana et al offer a range of barriers why clinicians don't follow guidelines. They include barriers affected by clinician knowledge (eg, lack of awareness or lack of familiarity), attitudes (lack of agreement, lack of self-efficacy, lack of outcome expectancy, or the inertia of previous practice), or behavior.[47] A way to improve clinician adherence to guidelines may include developing specialized anticoagulation clinics with expert nurses and doctors as a way to reduce clinician apprehension when commencing patients on oral anticoagulant therapy.[48] This warrants further exploration.

Treatment-related factors

Both the efficacy and safety of warfarin therapy are strongly correlated with therapeutic dosages.[49] An INR of 2.0–3.0 is well established as a therapeutic target range for stroke prevention in AF;[50,51] therefore, time that a patient spends within their range of target INR should be maximized.[50,52] A major concern is intracranial hemorrhage, which is associated with high morbidity and mortality.[53,54] Novel anticoagulants appear to have a more favorable safety profile than warfarin, as evident through large clinical trials.[55–57] One of the foremost attractions of such novel agents including oral direct thrombin inhibitors and factor Xa inhibitors over warfarin is that they have predictable pharmacokinetics, therefore reducing or eliminating the burden of routine anticoagulation monitoring. Nevertheless, reversal of such newer agents can be complex and problematic.[58]

Solutions to treatment-related factors

In patients with normal kidney function and an estimated glomerular filtration rate > 30 mL/minute, thromboprophylaxis should be selected accordingly after a comprehensive clinical assessment. Dabigatran and rivaroxaban are excreted by the kidneys (dabigatran 80% and rivaroxaban 66%), therefore dosage may require adjustment according to estimated glomerular filtration rate.[59]

Many patients continue to be prescribed warfarin therapy, requiring them to have their INR monitored, which can be burdensome.[7] Health infrastructure must be supportive and enabling of this need for surveillance. Ensuring regular INR monitoring to maintain therapeutic targets and avoid adverse events is critical.[38] Rural outreach or metropolitan hospital liaison services and dedicated anticoagulation clinics are one such approach to achieve these goals.[41] INR self-check kits are an effective strategy to encourage patients with self-care.[60] However, patients must be able, well-informed, and be supplied with a coagulometer.[60] Although providing financial incentives to patients to attend clinics or visit clinicians to increase attendance rates is novel, uptake is low.[61]

Socioeconomic-related factors

The annual cost of anticoagulation with warfarin is estimated to be £207.30 in comparison to £1573.50 with the novel anticoagulant dabigatran (per patient; excluding the cost of INR monitoring).[62] The high cost of medication can prohibit initial purchase and continuation of therapy. In some instances this may lead to doses skipped in order to save money.[63] Costs associated with visiting a primary care physician or other member of the multidisciplinary health care team may discourage essential follow-up visits. It is essential to monitor the effectiveness of therapy. These factors may prohibit optimal care and outcomes of oral anticoagulation therapy.

Solutions to socioeconomic-related factors

Several suggested solutions have been offered to deal with such barriers. These include the use of innovative

technologies like self-check INR kits to undertake self-care at home. This limits the need for frequent visits to primary care, though this may be an expensive appliance which the patient may have to purchase and maintain.[60] A level of cognitive capacity and knowledge is required to interpret results and respond to these in an appropriate manner.[64] Point of care and health rebate systems as well as monitoring pharmacy refill records may assist in the uptake and maintenance of therapy.[41]

Patient-related factors

Medication adherence in HF is a poorly understood yet fundamental aspect of patient care.[65] Medication adherence rates within the HF population vary widely.[66] Patients are required to balance the need for prescribed medication against any perceived adverse drug event, which may lead to nonadherence or permanent discontinuation of use of oral anticoagulant medications.[67] Such suboptimal drug use is associated with an increase in unplanned hospital admissions, increased mortality and morbidity rates, and accompanied by additional health care-related costs.[68] It has been estimated that patients who do not take their medications as prescribed costs the US health care system $290 billion in avoidable health-related spending every year.[69]

Solutions to patient-related barriers

The World Health Organization emphasizes that despite the vast amount of knowledge that exists around adherence issues, efforts to address the problems have been divided and – with a few exceptions – have failed to encapsulate the potential contributions of the diverse health disciplines.[28] The World Health Organization advocates that a stronger buy-in and commitment to a multidisciplinary model is required in order to make progress in the area of poor adherence.[28]

Poor patient education is a commonly cited problem contributing to poor adherence.[43] Patient knowledge is a determinant of anticoagulation control.[43] A lack of the perception of medication importance, risk of adverse events, irregular monitoring of serum INR, or a lack of the perception of risk-to-benefit threshold may lead to adverse events.[43] Inadequate self-management counseling and language difficulties also contribute to this multifaceted issue.[70] Bajorek et al advocate that a pharmacist-led multidisciplinary process within the hospital setting may increase overall antithrombolytic therapy use.[71] Simplified drug regimes and improved case management comprising of patient education and discharge counseling may be of value.[71] This must address the behaviors and preferences of individual patients. Interventions that target the elderly and those with poor literacy are vital.[72] Such strategies may include providing pamphlets and printed materials with colors, pictures, and visual aids, the enlargement of materials, compact disc read-only memory (CD-ROM) or spoken materials, structured educational programs, the mailing of educational materials, or even online resources and social media patient education interventions.[41] Explicit instructions to primary care providers at patient discharge from acute care, patient reminder cards, and patient forums that provide peer support may be of help.[41] Telemonitoring may prove an effective method to improve medication adherence for HF patients at home. It was recently reported that HF patients using structured telephone support and telemonitoring experienced improvement in the use of evidence-based pharmacotherapy.[73]

Condition-related factors

Polypharmacy and falls

Polypharmacy and comorbidity are fundamental factors that affect medication adherence. Patients with HF and AF may be using antiplatelet therapy[74] or are likely to have concurrent use of multiple medications with antihypertensive properties that predispose patients to symptomatic orthostatic hypotension, syncope, or falls.[75] Being at an increased risk of falling may inevitably lead to an increased risk of hemorrhage, particularly intracranial if a head injury is sustained during a fall due to syncope. There are many explanations for an increased risk of falling. This may only be perceived by the clinician because of age.[75] However, this may be attributable to gait,[76] cognitive impairment, or dementia.[43] Anticoagulant therapy should not be denied based on age alone.[75]

Dietary restrictions

Patients may have dietary restrictions or preferences. This may affect pharmacokinetics and may lead to suboptimal coagulation and impact time spent in a therapeutic range.[67]

Associated condition burden

Frailty,[12] cognitive and functional impairment,[11] stress,[70] and depression[77] are all conditions associated with HF and AF. These conditions may lead to failure to adhere to appropriate INR monitoring or reduced adherence through the cognitive or physical inability to self-administer oral medications. Comparable to patients with cognitive decline, there is evidence that patients with mental health conditions and AF are less likely than those without mental health conditions to have adequate AF management.[78] Depression has been identified as a moderately common condition in HF,[79] and

was associated with poor medication compliance in the Heart and Soul Study.[77]

Solutions to condition-related factors

Polypharmacy and falls

Clinicians ought to assess the risk of falls using reliable and valid methods. Planning fall minimization interventions should be in collaboration with the multidisciplinary team.[44] Assessment of any underlying conditions including neuropathy, frailty, and cognitive concerns should be investigated.[80] Cognitive ability can be evaluated using reliable and validated and readily accessible measures such as the Mini Mental State Examination or The Montreal Cognitive Assessment.[81]

The use of once-daily medication formulations or polypills may aid improved adherence.[82] Whilst this may be achievable with HF treatments where doses of many medications remain consistent once up-titrated, this may present difficulties in AF with varying dosages of certain anticoagulants and the need to regularly adjust dosage according to the INR.

Dietary restrictions

Clinicians must ensure that a dietician consultation with specific dietary advice regarding vitamin K intake occurs. This may occur via telephone consultations or clinic visits. This is a simple yet imperative strategy that may reduce the risk of inadequate anticoagulation. Patients altering their dietary intake of green leafy vegetables should be encouraged to notify their clinician as their dosage of warfarin may require adjustment.[83]

Monitoring adherence

Patient self-reporting is a useful method of assessing medication adherence. Self-reporting offers reliable predictors of a broad array of cardiovascular health outcomes – including blood pressure control, hospitalization for HF, and serum drug concentrations – that are highly applicable to this group of patients.[77] There are a number of tools available to measure self-reported adherence. The Morisky Scale provides good predictive ability and can be easily integrated as part of a comprehensive patient assessment prior to the commencement of any oral anticoagulant therapy.[84]

Associated condition burden

Although there are numerous risk stratification tools available to assist clinicians in allocating treatments, they do not consider frailty, which impacts adversely on health outcomes.[12] Cognitive and functional decline are significant consequences of both HF and AF.[85] Undertaking a formal frailty assessment may assist in the guidance of prescribing of oral anticoagulants and may help clinicians identify patients who are at increased risk of adverse events from anticoagulant therapy.[12] Further investigation is warranted to examine the causal relationship between depression and adherence particularly in the HF and AF patient population. Where depression exists, the inclusion of a mental health clinician in the multidisciplinary care model providing care to the patient may be of benefit.[74]

Enhanced models for stratifying bleeding risk particularly in the frail population are required.[45] Frailty assessment tools that currently exist could be used as an adjunct to any stroke risk prediction tool. Any new models or frailty assessment criteria should additionally be incorporated into clinical practice guidelines.[45] Strategies that aim to reduce or manage falls including assistance from family, relatives, informal caregivers, or the provision of home help should not be overlooked.

Implications for clinical practice

Further research is required to examine the issue of anticoagulant therapy in patients with HF and AF. This is driven by population growth in the elderly and the increasing burden of the cardiogeriatric population.[86,87] Available data suggest it may be useful to include a risk assessment of other aspects of a patient's life as opposed to the restrictive tools that currently exist. Nonadherence with medication and other lifestyle recommendations is a major problem in patients with HF and has severe consequences for individual patients as well as for the health care system.[88] Treatment and care should take into account patients' individual needs and preferences. However, most people with AF should be considered for treatment with oral anticoagulants based on their risk of stroke, ability to tolerate anticoagulation without bleeding, and access to adequate anticoagulation monitoring.

Although there are robust stroke prediction tools, they cannot be considered external to a cardiogeriatric assessment. Extending and developing these tools to consider the risk of nonadherence to prescribed therapy and poor adherence are warranted. Currently, there is no comprehensive risk assessment tool that includes criteria that assesses or addresses the psychosocial aspects of a patient's ability to comply with anticoagulant therapy as well as the risk of stroke. Although novel agents offer promise, they still

confer risk and do not negate the importance of individual monitoring.

Conclusion

Current stroke risk prediction tools are useful, yet limited, within the context of complex cardiogeriatric syndromes. Expanding these to consider frailty, cognitive and functional decline, or nonadherence to therapy is warranted. Although avoiding stroke is an important consideration, the potential adverse effects of treatment needs to be balanced within the context of best available evidence, clinical expertise, and the individual patient's circumstances.[89] Developing metrics that consider the combination of these factors are likely to shed light on the issues of adherence in this population.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Krum H, Jelinek MV, Stewart S, Sindone A, Atherton JJ. 2011 Update to National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006. *Med J Aust*. 2011;194(8):405–409.
2. Gheorghiade M, Filippatos G. Reassessing treatment of acute heart failure syndromes: the ADHERE Registry. *Eur Heart J Suppl*. 2005;7(Suppl B):B13–B19.
3. Pullicino P, Homma S. Stroke in heart failure: atrial fibrillation revisited? *J Stroke Cerebrovasc Dis*. 2010;19(1):1–2.
4. Atrial fibrillation [webpage on the Internet]. Atrial fibrillation (CG36): the management of atrial fibrillation. National Institute for Health and Clinical Excellence; 2006 [updated July 10, 2012]. Available from: http://www.nice.org.uk/cg36. Accessed December 17, 2012.
5. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011;123(1):104–123.
6. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines. *Circulation*. 2006;114(7):e257–e354.
7. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GY. Underuse of oral anticoagulants in atrial fibrillation: a systematic review. *Am J Med*. 2010;123(7):638–645.
8. Singer DE, Albers GW, Dalen JE, et al. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, 8th ed. *Chest*. 2008;133(Suppl 6):546S–592S.
9. Gattellari M, Worthington J, Zwar N, Middleton S. Barriers to the use of anticoagulation for nonvalvular atrial fibrillation: a representative survey of Australian family physicians. *Stroke*. 2008;39(1):227–230.
10. Baczek VTL, Chen WT, Kluger J, Coleman CI. Predictors of warfarin use in atrial fibrillation in the United States: a systematic review and meta-analysis. *BMC Fam Pract*. 2012;13(1):5.
11. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. 2008;2:CD000011.
12. Perera V, Bajorek BV, Matthews S, Hilmer SN. The impact of frailty on the utilisation of antithrombotic therapy in older patients with atrial fibrillation. *Age Ageing*. 2009;38(2):156–162.
13. Lip GY. Implications of the CHA_2DS_2-VASc and HAS-BLED scores for thromboprophylaxis in atrial fibrillation. *Am J Med*. 2011;124(2):111–114.
14. Mant J, Hobbs FD, Fletcher K, et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet*. 2007;370(9586):493–503.
15. Homma S, Thompson JLP, Pullicino PM, et al. Warfarin and aspirin in patients with heart failure and sinus rhythm. *New Engl J Med*. Epub May 2, 2012.
16. Wang TJ, Massaro JM, Levy D, et al. A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community: the Framingham Heart Study. *JAMA*. 2003;290(8):1049–1056.
17. Lip GY, Halperin JL. Improving stroke risk stratification in atrial fibrillation. *Am J Med*. 2010;123(6):484–488.
18. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA*. 2001;285(22):2864–2870.
19. Hart RG, Pearce LA, McBride R, Rothbart RM, Asinger RW. Factors associated with ischemic stroke during aspirin therapy in atrial fibrillation: analysis of 2012 participants in the SPAF I–III clinical trials. *Stroke*. 1999;30(6):1223–1229.
20. Baruch L, Gage BF, Horrow J, et al. Can patients at elevated risk of stroke treated with anticoagulants be further risk stratified? *Stroke*. 2007;38(9):2459–2463.
21. Boriani G, Botto GL, Padeletti L, et al. Improving stroke risk stratification using the $CHADS_2$ and CHA_2DS_2VASc risk scores in patients with paroxysmal atrial fibrillation by continuous arrhythmia burden monitoring. *Stroke*. 2011;42(6):1768–1770.
22. Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF). *Am Heart J*. 2006;151(3):713–719.
23. Lip GY, Frison L, Halperin JL, Lane DA. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. *J Am Coll Cardiol*. 2011;57(2):173–180.
24. Shireman TI, Howard PA, Kresowik TF, Ellerbeck EF. Combined anticoagulant–antiplatelet use and major bleeding events in elderly atrial fibrillation patients. *Stroke*. 2004;35(10):2362–2367.
25. Beyth RJ, Quinn LM, Landefeld CS. Prospective evaluation of an index for predicting the risk of major bleeding in outpatients treated with warfarin. *Am J Med*. 1998;105(2):91–99.
26. Kuijer PM, Hutten BA, Prins MH, Buller HR. Prediction of the risk of bleeding during anticoagulant treatment for venous thromboembolism. *Arch Intern Med*. 1999;159(5):457–460.
27. Komajda M, Lapuerta P, Hermans N, et al. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey. *Eur Heart J*. 2005;26(16):1653–1659.
28. World Health Organization. *Adherence to Long Term Therapies: Evidence for Action*. Geneva: World Health Organization; 2003. Available from: http://whqlibdoc.who.int/publications/2003/9241545992.pdf. Accessed December 17, 2012.
29. Piccini JP, Hernandez AF, Zhao X, et al. Quality of care for atrial fibrillation among patients hospitalized for heart failure. *J Am Coll Cardiol*. 2009;54(14):1280–1289.
30. Nieuwlaat R, Eurlings LW, Cleland JG, et al. Atrial fibrillation and heart failure in cardiology practice: reciprocal impact and combined management from the perspective of atrial fibrillation: results of the Euro Heart Survey on atrial fibrillation. *J Am Coll Cardiol*. 2009;53(18):1690–1698.
31. Lip GY. Stroke in atrial fibrillation: epidemiology and thromboprophylaxis. *J Thromb Haemost*. 2011;9(Suppl 1):S344–S351.

32. Go AS. Efficacy of anticoagulation for stroke prevention and risk stratification in atrial fibrillation: translating trials into clinical practice. *Am J Manag Care*. 2004;10(Suppl 3):S58–S65.
33. Ezekowitz M, Bridgers SL, James KE, et al. Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Investigators. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. *New Engl J Med*. 1992;327(20):1406–1412.
34. Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. *Arch Intern Med*. 1994;154(13):1449–1457.
35. Stroke Prevention In Atrial Fibrillation Investigators. Stroke prevention in atrial fibrillation trial. Final results. *Circulation*. 1991;84(2):527–539.
36. Miller CS, Grandi SM, Shimony A, Filion KB, Eisenberg MJ. Meta-analysis of efficacy and safety of new oral anticoagulants (dabigatran, rivaroxaban, apixaban) versus warfarin in patients with atrial fibrillation. *Am J Cardiol*. 2012;110(3):453–460.
37. Agarwal S, Hachamovitch R, Menon V. Current trial-associated outcomes with warfarin in prevention of stroke in patients with nonvalvular atrial fibrillation: a meta-analysis. *Arch Intern Med*. 2012;172(8):623–631.
38. Marinigh R, Lip GY, Fiotti N, Giansante C, Lane DA. Age as a risk factor for stroke in atrial fibrillation patients: implications for thrombophrophylaxis. *J Am Coll Cardiol*. 2010;56(11):827–837.
39. Fang MC, Go AS, Chang Y, et al. Warfarin discontinuation after starting warfarin for atrial fibrillation. *Circ Cardiovasc Qual Outcomes*. 2010;3(6):624–631.
40. Friberg L, Rosenqvist M, Lip GY. Net clinical benefit of warfarin in patients with atrial fibrillation: a report from the Swedish atrial fibrillation cohort study. *Circulation*. 2012;125(19):2298–2307.
41. Bajorek BV, Ogle SJ, Duguid MJ, Shenfield GM, Krass I. Management of warfarin in atrial fibrillation: views of health professionals, older patienst and their carers. *Med J Aust*. 2007;186(4):175–180.
42. Bo S, Valpreda S, Scaglione L, et al. Implementing hospital guidelines improves warfarin use in non-valvular atrial fibrillation: a before–after study. *BMC Public Health*. 2007;7(1):203.
43. Brophy MT, Snyder KE, Gaehde S, Ives C, Gagnon D, Fiore LD. Anticoagulant use for atrial fibrillation in the elderly. *J Am Geriatr Soc*. 2004;52(7):1151–1156.
44. Srivastava A, Hudson M, Hamoud I, Cavalcante J, Pai C, Kaatz S. Examining warfarin underutilization rates in patients with atrial fibrillation: detailed chart review essential to capture contraindications to warfarin therapy. *Thromb J*. 2008;6:6.
45. Tulner LR, Van Campen JP, Kuper IM, et al. Reasons for undertreatment with oral anticoagulants in frail geriatric outpatients with atrial fibrillation. *Drugs Aging*. 2010;27(1):39–50.
46. Grimshaw JM, Russell IT. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet*. 1993;342(8883):1317–1322.
47. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA*. 1999;282(15):1458–1465.
48. Rewiuk K, Wizner B, Fedyk-Lukasik M, et al. Heart failure and atrial fibrillation – does practice meet the anticoagulation guidelines? *Int J Cardiol*. 2012;157(2):274–275.
49. Ansell J, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, 8th ed. *Chest*. 2008;133(6 Suppl):160S–198S.
50. Connolly SJ, Laupacis A, Gent M, Roberts RS, Cairns JA, Joyner C. Canadian Atrial Fibrillation Anticoagulation (CAFA) study. *J Am Coll Cardiol*. 1991;18(2):349–355.
51. Albers GW, Diener HC, Frison L, et al. Ximelagatran vs warfarin for stroke prevention in patients with nonvalvular atrial fibrillation: a randomized trial. *JAMA*. 2005;293(6):690–698.
52. Stroke Prevention In Atrial Fibrillation Investigators. Adjusted-dose warfarin versus low-intensity, fixed-dose warfarin plus aspirin for high-risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial. *Lancet*. 1996;348(9028):633–638.
53. Appelboam R, Thomas EO. Warfarin and intracranial haemmorhage. *Blood Rev*. 2009;23(1):1–9.
54. Sjoblom L, Hardemark HG, Lindgren A, et al. Management and prognostic features of intracerebral hemmorhage during anticoagulant therapy: a Swedish multicenter study. *Stroke*. 2001;32(11):2567–2574.
55. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. *New Engl J Med*. 2011;365(11):981–992.
56. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *New Engl J Med*. 2011;365(10):883–891.
57. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *New Engl J Med*. 2009;361(12):1139–1151.
58. Battinelli EM. Reversal of new oral anticoagulants. *Circulation*. 2011;124(14):1508–1510.
59. Mussigbrodt A, Hindricks G. Clinical implications from recent trials and new guidelines for stroke prevention in atrial fibrillation. *Eur Cardiol*. 2012;8(3):174–178.
60. Horstkotte D, Piper C. Improvement of oral anticoagulation therapy by INR self-management. *J Heart Valve Dis*. 2004;13(3):335–338.
61. Giuffrida A, Torgerson D. Should we pay the patient? Review of financial incentives to enhance patient compliance. *BMJ*. 1997;315(7110):703–707.
62. Ali A, Bailey C, Abdelhafiz AH. Stroke prophylaxis with warfarin or dabigatran for patients with non-valvular atrial fibrillation-cost analysis. *Age Ageing*. 2012;41(5):681–684.
63. Dunlay SM, Eveleth JM, Shah ND, McNallan SM, Roger VL. Medication adherence among community-dwelling patients with heart failure. *Mayo Clin Proc*. 2011;86(4):273–281.
64. Dolor RJ, Ruybalid RL, Uyeda L, et al. An evaluation of patient self-testing competency of prothrombin time for managing anticoagulation: pre-randomization results of VA Cooperative Study #481 – The Home INR Study (THINRS). *J Thromb Thrombolysis*. 2010;30(3):263–275.
65. Wu JR, Moser DK, Chung ML, Lennie TA. Predictors of medication adherence using a multidimensional adherence model in patients with heart failure. *J Card Fail*. 2008;14(7):603–614.
66. Brown SB, Shannon RP. Improving medication compliance in patients with heart failure. *Am J Cardiol*. 2008;101(2):274–277.
67. van der Wal MH, Jaarsma T. Adherence in heart failure in the elderly: problem and possible solutions. *Int J Cardiol*. 2008;125(2):203–208.
68. De Smedt RH, Denig P, van der Meer K, Haaijer-Ruskamp FM, Jaarsma T. Self-reported adverse drug events and the role of illness perception and medication beliefs in ambulatory heart failure patients: a cross-sectional survey. *Int J Nurs Stud*. 2011;48(12):1540–1550.
69. NEHI. Thinking outside the pillbox: a system-wide approach to improving patient medication adherence for chronic disease. Cambridge, MA: NEHI; 2009. Available from: http://www.nehi.net/publications/44/thinking_outside_the_pillbox_a_systemwide_approach_to_improving_patient_medication_adherence_for_chronic_disease. Accessed December 6, 2012.
70. McCabe PJ, Schumacher K, Barnason SA. Living with atrial fibrillation: a qualitative study. *J Cardiovasc Nurs*. 2011;26(4):336–344.
71. Bajorek BV, Krass I, Ogle SJ, Duguid MJ, Shenfield GM. Optimizing the use of antithrombotic therapy for atrial fibrillation in older people: a pharmacist-led multidisciplinary intervention. *J Am Geriatr Soc*. 2005;53(11):1912–1920.
72. Tang EO, Lai CS, Lee KK, Wong RS, Cheng G, Chan TY. Relationship between patients' warfarin knowledge and anticoagulation control. *Ann Pharmacother*. 2003;37(1):34–39.
73. Inglis SC, Cark RA, McAlister FA, et al. Structured telephone support or telemonitoring programmes for patients with chronic heart failure. *Cochrane Database Syst Rev*. 2010;8:CD007228.

74. Robert-Ebadi H, Le Gal G, Righini M. Use of anticogulants in elderly patients: practical recommendations. *Clin Interv Aging*. 2009;4:165–177.
75. Sansossian S, Ovbiagele B. Prevention and management of stroke in very elderly patients. *Lancet Neurol*. 2009;8(11):1031–1041.
76. Krass I, Ogle SJ, Duguid MJ, Shenfield GM, Bajorek BV. The impact of age on antithrombotic use in elderly patients with non-valvular atrial fibrillation. *Australas J Ageing*. 2002;21(1):36–41.
77. Gehi A, Haas D, Pipkin S, Whooley MA. Depression and medication adherence in outpatients with coronary heart disease: findings from the Heart and Soul Study. *Arch Intern Med*. 2005;165(21):2508–2513.
78. Walker GA, Heidenreich PA, Phibbs CS, et al. Mental illness and warfarin use in atrial fibrillation. *Am J Manag Care*. 2011;17(9):617–624.
79. Vaccarino V, Kasl SV, Abramson J, Krumholz HM. Depressive symptoms and risk of functional decline and death in patients with heart failure. *J Am Coll Cardiol*. 2001;38(1):199–205.
80. Forman DE, Rich MW, Alexander KP, et al. Cardiac care for older adults. Time for a new paradigm. *J Am Coll Cardiol*. 2011;57(18):1801–1810.
81. Flaker GC, Pogue J, Yusuf S, et al. Cognitive function and anticoagulation control in patients with atrial fibrillation. *Circ Cardiovasc Qual Outcomes*. 2010;3(3):277–283.
82. Hauptman PJ. Medication adherence in heart failure. *Heart Fail Rev*. 2008;13(1):99–106.
83. Hylek EM. Oral anticoagulants. Pharmacologic issues for use in the elderly. *Clin Geriatr Med*. 2001;17(1):1–13.
84. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24(1):67–74.
85. Marzona I, O'Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with atrial fibrillation: results of the ONTARGET and TRANSCEND studies. *CMAJ*. 2012;184(6):E329–E336.
86. Wong CX, Brooks AG, Leong DP, Roberts-Thomson KC, Sanders P. The increasing burden of atrial fibrillation compared with heart failure and myocardial infarction: a 15 year study of all hospitalizations in Australia. *Arch Intern Med*. 2012;172(9):739–741.
87. Stewart S. Epidemiology and economic impact of atrial fibrillation. *J Cardiovasc Nurs*. 2004;19(2):94–102.
88. McEntee ML, Cuomo LR, Dennison CR. Patient-, provider-, and system-level barriers to heart failure care. *J Cardiovasc Nurs*. 2009;24(4):290–298.
89. Sackett DL, Rosenberg WM, Muir Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ*. 1996;312(7023):71–72.

APPENDIX 10: THE CAREGIVER ROLE IN THROMBOPROPHYLAXIS MANAGEMENT IN ATRIAL FIBRILLATION: A LITERATURE REVIEW

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Review Article

The caregiver role in thromboprophylaxis management in atrial fibrillation: A literature review

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Abstract

Background: Atrial fibrillation is a common arrhythmia and a risk factor for adverse events including stroke. People living with atrial fibrillation are commonly elderly and have multiple comorbidities. The role of a caregiver in supporting the individual to manage a chronic and complex condition has received limited attention.

Objectives: This review aims to summarize available information on the caregiver role in atrial fibrillation, specifically in promoting adherence to thromboprophylaxis and evidence for strategies to support and enable the caregiver.

Data sources: A review of electronic databases and search engines was undertaken including Medline, Scopus and CINAHL. The search terms 'atrial fibrillation', 'anticoagulation', 'carer', 'caregiver', 'family support' were used. Dates searched were from January 1990 to November 2012.

Results: The review found limited original clinical research studies. The majority of the literature identified in the initial search included review papers and work which recommends the inclusion of the caregiver in the care of patients with atrial fibrillation but limited empirical evidence.

Conclusions: Caregivers have an essential role to play in advocacy, family centred care and shared decision-making. This may influence thromboprophylaxis treatment choices and potentially adherence. Assessment of caregiver needs and support should be central to patient assessment and care planning. There is a need for clinical intervention studies which more target and address the caregiver role.

Keywords

Atrial fibrillation, stroke prevention, caregiver, caregiver role, caregiver education, family support, thromboprophylaxis

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Background

It is estimated that 3 million people in the United States (US) are affected by atrial fibrillation (AF).[1] Hospitalization for AF is common and costly.[2] Stroke is a major complication of AF and is associated with a three- to five-fold increased risk.[3] AF is likely to be an aetiological factor in approximately 30% of strokes in the elderly.[4] Patients with AF post stroke will have significantly worse outcomes.[5] Patients with AF who experience a stroke are often cared for in the community by caregivers with little healthcare support. There is also a need to explore the role of caregiving in people living with AF in the community. Interventions should be targeted to support caregivers.[6] Chronic conditions, including AF, create the need for self-care strategies. Numerous examples of inadequate self-management emphasize the importance of looking at innovative models.

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Commonly, self-care models target the individual and, although implicit, the role of the caregiver is less well described.

Who is a caregiver?

The nomenclature of care giving can be confusing, as the word caregiver may sometimes be used synonymously with family caregiver, carer, support or family support. For the purposes of this paper we have defined a caregiver as 'a spouse, adult child, other relative, partner or friend who has a personal relationship with, and provides a wide range of unpaid care for, an adult with a chronic condition'. There are diverse and heterogeneous models of care giving as well as caregiver needs and resources.[7] There are many different cultural nuances to care giving. This paper is approached from an Anglo-Western-Caucasian perspective.

It is recognized that in a Western, primarily Caucasian, context, feelings and emotions of responsibility for family members may be associated with feelings of guilt or inadequacy for some caregivers. This may be due to caregiving responsibilities placing restrictions on personal and parental autonomy and independence that run counter to dominant Western ideals.[8]

There are more than 65 million people (29% of the US population) who provide care for a chronically ill, disabled or elderly family member or friend during any given year and spend an average of 20 hours per week providing care.[9] The typical caregiver is a 49-year-old woman who cares for her widowed 69-year-old mother, who does not live with her; she is married and employed.[9] The economic value of caregiving in the context of today's society must not be underestimated. Whilst the value of services provided by caregivers is 'free', it is estimated to be US$375bn per year. This is more than twice as much as what is actually spent on home care and nursing home services (US$158bn).[10] Caregivers may provide care and assistance with a wide range of activities of daily living. These may include bathing, dressing, feeding, toileting, helping with incontinence, assisting with mobility, cooking, house cleaning, handling finances, transport to health professional appointments and overseeing or assisting with medications.[10] These trends are replicated around the world.[11] Examples of caregiving activities in individuals with AF may include: opening medication packaging and assisting or confirming correct dosage to be taken; driving patients to the primary care GP or anticoagulation clinic to have venous blood samples taken; assisting with activities of daily living due to tiredness experienced due to AF; monitoring for signs of bleeding; ensuring adherence to any dietary restrictions.

In spite of the importance of caregivers, most multidisciplinary clinical practice guidelines fail to recommend the inclusion of the caregiver throughout the spectrum of care. This may be due to limited data supporting their role or potentially their lack of visibility in the policy context. Enhancing caregiver support to enable better self and family management may lead to favourable patient outcomes.[12] Moreover, many discussions of caregivers highlight that they are commonly unrecognized and underemphasized.

Although management of all chronic illness is complex, the use of thromboprophylaxis in AF increases the risk of adverse events and the complexity of caregiving. The most worrisome from the perspective of the clinician is that of stroke and bleeding risk.[13] Most clinical practice guidelines recommend thromboprophylaxis for patients with AF with congestive heart failure, hypertension, age ≥75 years, diabetes, prior stroke or transient ischaemic attack (TIA), vascular disease, age 65–74, sex category (CHA_2DS_2-VASc) score of > 1.[14–19] Thromboprophylaxis may come in the form of traditional vitamin K antagonists (VKAs) (warfarin) or novel anticoagulants including dabigatran, rivaroxaban and apixaban that have a lower need for need for haematological monitoring. Warfarin may be burdensome due to the requirements of regular INR monitoring to ensure optimal time spent in the therapeutic range.[20] The attraction of novel agents such as direct thrombin inhibitors (e.g. dabigatran, rivaroxaban and apixaban) is the simplified dosing regimens and reduction in the need for routine monitoring.[21]

Adverse events can occur because of failure to adhere to management recommendations. Adherence is defined as 'the extent to which a person's behaviour taking medication corresponds with agreed recommendations from a clinician'.[22] Non-adherence to oral medications is common and complex, particularly in chronic diseases, including AF.[23] It is estimated to cost the US healthcare system in excess of US$100bn per year.[24] Poor adherence may lead to suboptimal patient outcomes including increased hospitalization, morbidity and mortality.[22,23] It is estimated 40–60% of patients fail to take their medications as prescribed by their physician.[25] In a US longitudinal cohort study one-third of the AF population who were initially prescribed warfarin for stroke prevention had discontinued treatment after 30 months.[26] Similarly, a study by Fang et al. identified that more than a quarter of patients newly commenced on warfarin for AF were found to have discontinued treatment within the first year.[27] The World Health Organization recognizes that there are five domains that impact medication adherence: socio-economic, patient related, treatment related, health system related and condition related factors.[22]

Frailty and functional and cognitive dysfunction occur commonly in this population.[28] Within the context of this paper, frailty may be present in both caregiver and patient. These factors may impact adversely on non-adherence to prescribed therapy. Patients who are frail or are unable to self-care are less likely to receive anticoagulant therapy.[29] This may be due to clinician apprehension due to the fear of patient falls. Consequently, this may lead to increased

morbidity and mortality.[30,31] Functional and cognitive decline are commonly associated with a diagnosis of AF,[28] demanding additional caregiver support, formally and informally.[32] Potentially involving the caregiver may result in more individuals receiving prophylactic treatment and fewer adverse events.

Many interventions focus on optimizing adherence to therapy. Most interventions include combinations of reminders (including reminder packaging),[25] aid devices, self-monitoring strategies, reinforcement, counselling, and telephone support or tele-health.[23] Many of the interventions recommend involvement of caregivers. A caregiver can provide ongoing support, encouragement and reminders on a frequent basis.[23] The assistance of caregivers is often required due to the complex nature of anticoagulant therapy, including altered dosing requirements, the need for frequent monitoring and medication costs.[20,33] Caregivers may also have a role in physical assistance to administer oral medication to more disabled and frail patients with AF.[33]

Objectives

This review aims to:

1. Discuss the role of caregivers and their role in supporting thromboprophylaxis in AF.
2. Identify strategies for developing the caregiver role in AF management, specifically in promoting adherence.

Methods

A review of electronic databases and search engines was undertaken including Medline, Scopus and CINAHL. The search terms 'atrial fibrillation' 'anticoagulation' 'carer' 'caregiver' 'family support' were used. Dates searched were from January 1990 to November 2012. Literature prior to 1990 was not searched in order to provide a contemporary perspective of the caregiver role over the last decade. Reference lists of retrieved articles were hand searched. Papers were included that addressed the role and responsibilities of the caregiver in patients with AF. Review papers, correspondence, letters to editors and abstracts of conference proceedings were excluded. Only primary research papers were included.

Results

There was a limited description of the role of the caregiver in patients with AF. The volume of primary research undertaken in the area is poor. Refer to Figure 1. The majority of the literature reviewed through our search included review papers and work which recommends the inclusion of the caregiver in the care of patients with AF. However, there was limited original clinical research work. The papers included in this review are discussed below and are provided in Table 1.

In a prospective, cross-sectional survey in 80 AF caregiver-dyads (average age was 66 years, mostly married and of female gender) caregiving responsibilities were usually for greater than one year when caring for someone with AF and out of pocket payment for healthcare was required by 55%. Most participants described that they were required often to eliminate things from their schedule and experienced less time to visit family and friends. However, 61% strongly agreed that caring was important to them, and 52% strongly disagreed that they resented having to care. Coleman and colleagues' study suggest that the greatest burden is placed on caregivers due to the disruption of schedules and followed by financial problems. Particularly highlighted is the finding that medication, particularly thromboprophylaxis medication, problems appeared to be a notable source of burden. And patients that required help in managing their medications have a greater predicator of burden due to disrupted schedules and health problems. 'Financial problems' burden scores were significantly associated with caring for frail patients and those requiring more frequent clinician follow-up. 'Lack of family support' scores were inversely associated with having somebody else to help provide care and increased as patients $CHADS_2$ score increased. Lower 'Health problem' burden scores were associated with female gender and higher scores with the need to spend > 4 h/week providing care.[33]

Discussion

In light of the paucity of primary research in this area, findings from the broader literature search have been framed and augmented within existing caregiver literature. Special attention has been drawn to how the caregiver role can be best enabled to promote optimal adherence to thromboprophylaxis.

Models of AF management

C Everett Koop, MD is famously quoted as saying 'Drugs don't work in patients who don't take them.' Adherence can be defined as the 'active, voluntary, and collaborative involvement of the patient in a mutually acceptable course of behaviour to produce a therapeutic result.'[34] Poor adherence to thromboprophylactic therapies is common and complex and not fully understood. This contributes to worsening of disease, increases stroke and haemorrhagic risk and leads to increased healthcare costs.[35] In the majority of cases, patients with AF who are prescribed thromboprophylaxis may be on therapy for lifetime duration. This duration of treatment adds to the complexity of issues of adherence. There are different models of management for

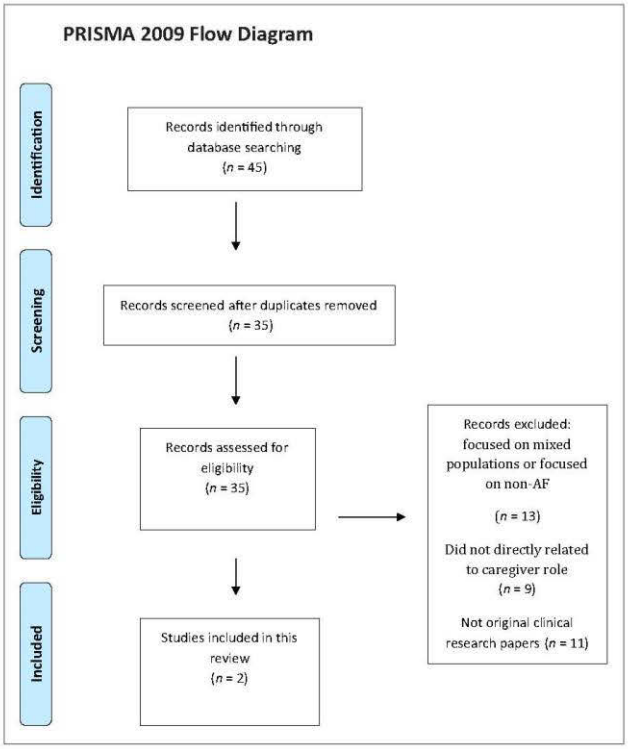

Figure 1. PRISMA flow chart.

AF to facilitate optimal adherence. These are affected by personal factors, including socio-demographic influences, psychosocial, cognitive and functional abilities. Although models emphasize the socio-cultural context of the individual the role of the caregiver receives scant attention.

Methods of facilitating adherence to anticoagulant therapy are outlined in a conceptual model proposed by Brown and colleagues.[36] These include:

1. Knowledge about the condition and continuous reinforcement by clinicians through regular visits and interaction;
2. Short-term and long-term motivation (e.g. avoidance of negative health consequences);
3. Development of a personalized system, habit formation and system adaptation (e.g. developing a routine or external reminders, i.e. text messaging, smart-phone apps or alarms for medication reminders);
4. Self-efficacy loop (i.e. reinforcement of the personalized system and its adaptability as patients become more consistent, confident and adherent).

In each of the key steps identified above, the caregiver can play a critical role in providing both physical and psychosocial support.

Nurse-led clinics have been successful in the management of other chronic conditions, including heart failure, asthma and diabetes. Such models of care for patients with AF may be worthwhile to explore further in practice. A recent randomized controlled trial was conducted by Hendriks et al. which included 712 patients with AF assigned to nurse-led care versus usual care. Nurse-led care intervention consisted of guidelines-based, software-supported, integrated chronic care supervised by a cardiologist. Nurse-led care of patients with AF proved superior to usual care, with decreased rates of cardiovascular hospitalization and cardiovascular mortality.[37]

Table 1. Summary of studies.

Authors	Study design and purpose	Sample characteristics and setting	Results	Limitations	Implications
Chen et al.[29] USA	**Design** Cross-sectional study to compare Medicare beneficiaries with AF with beneficiaries without AF. **Purpose** To describe patients' characteristics and caregiver assistance among Medicare beneficiaries with AF and examine factors associated with receiving anticoagulant treatment.	2990 patients with AF and 5980 control patients were included in the burden of disease analysis and 1481 patients with AF were included in the anticoagulant predictor analysis. Multistage, stratified sampling design. Allowing for analysis of a nationally representative sample of all Medicare beneficiaries.	Patients with AF had a higher level of comorbidity, worse self perceived health status, a greater level of disability than their matched counterparts. A greater proportion of patients with AF require caregiver assistance (62.8% vs. 51.5%, $p<0.01$). A greater need for caregiver assistance was observed in patients with AF. Logistic regression found that a higher Charlson Comorbidity Index score, difficulty in obtaining necessary healthcare, older ages, being widowed, a history of psychiatric disorders, and being underweight decreased the likelihood of receiving anticoagulant therapy. Subgroups characterized by frailty, inability to self care were identified as being less likely to receive anticoagulant therapy.	Medicare claims data sets are subject to underreporting and miscoding of diagnoses. Several proxies were used to assess caregiver assistance. Study findings are associations and not causal, so they may not be generalizable to institutionalized Medicare beneficiaries or non-Medicare patients.	Patients with AF have a greater need for caregiver assistance ($p<0.01$). Individuals with AF who are not able to self care are identified as being less likely to receive anticoagulant therapy. The need for caregiver assistance must be considered when making thromboprophylaxis treatment decisions.
Coleman et al.[33] USA, pharmacy	Design Cross sectional survey of AF patient–caregiver dyads recruited from cardiology clinics at an urban teaching hospital. Purpose To examine the interrelationship between unpaid caregiver, patient and thromboprophylaxis characteristics and caregiver burden in AF.	80 patient caregiver dyads were surveyed	The need for caregiver assistance should be considered when making treatment decisions. Significantly greater caregiver burden due to 'disrupted schedule' was seen in those spending >4 h/week providing care and when caring for frail, sick or disabled patients with higher $CHADS_2$ scores and requiring help with their medications. Financial problems burden scores were significantly associated with caring for frail patients and those requiring more frequent office follow-up. Lack of family support scores were inversely associated with having somebody else help provide care and increased as patients' $CHADS_2$ score increased. Lower health problem scores were associated with female gender and higher scores with the need to spend > 4 h/week providing care. The greatest burden to caregivers of AF patients occurs due to schedule disruption.	Small study population. Small sample size may have resulted in type 2 error in analysis. Caregiver dyads were recruited from only a handful of arrhythmia clinics affiliated with a single urban teaching hospital in the USA. All participants had healthcare insurance. Caregivers were younger than the patients they cared for; they were still relatively old, few were still working and most were women. Very few patients received alternative treatment strategies to warfarin or aspirin.	Individuals with AF and higher $CHADS_2$ scores who require help with their medication may impose greater caregiver burden. The greatest burden to caregivers of AF patients occurs due to schedule disruption.

AF: atrial fibrillation

A new, emergent care model is that of interdisciplinary, nurse coordinated AF expert programmes. This model aims to reduce symptom burden and prevent severe complications, including stroke. This model appears to be a pragmatic way to optimize patients' access to clinicians, given time restraints imposed on physicians, whereby patients are educated and empowered, and trained and counselled on self-management, which would contribute to improved outcomes in mortality and hospitalization. Such models hold hope as innovative methods to improve self-management, education and adherence to treatment regimes. Importantly these approaches enable the caregiver and involve them in the education and decision-making processes.[38]

Caregiver education

There are many factors that influence a patient's time in therapeutic range. These may include diet, alcohol consumption, medication and health service cost and availability.[39] A patient's knowledge of their condition and treatment plan are often determinants of their overall quality of anticoagulation control.[40] Patients with low health literacy or cognitive impairment may be more likely to require caregiver assistance. This may be an impacting factor in their understanding of medication importance. Therefore, caregiver education should be a core element of routine anticoagulation management. It is essential that the patient's primary caregiver receive adequate anticoagulant counselling that is individually tailored to meet their needs.[41]

Clinicians, patients and their caregivers are increasingly demanding customized resources to support anticoagulant use and management.[42] This may include educational material translated into languages other than English for a culturally diverse population. Promoting adherence requires educational approaches involving patients and caregivers in the management of their therapy (e.g. self-monitoring).[43] Successful home monitoring of prothrombin time (PT) with a self-testing device requires adequate levels of cognition, health literacy and manual dexterity. Whilst cognitive impairment and functional decline are common in AF,[28] training a caregiver can modestly increase the proportion of patients who are able to perform home monitoring.[44] The ability of patients to undertake home monitoring can improve a patient's time in the therapeutic range (TTR) and may lead to improved outcomes and decrease the prevalence of stroke and other adverse events.[45]

A caregiver may also be trained in how to undertake a simple manual radial pulse check, to ascertain whether a patient is in a regular or irregular rhythm. This education may be particularly useful for elderly patients with recurrent episodic paroxysmal AF and those who are greatly affected by burdensome symptoms. This may help to assist in identifying potential triggers and coping mechanisms, and help form the basis of treatment plans.

Medication management

A study of patients attending an anticoagulation clinic identified that nearly 20% of those participating identified another person as responsible for their medication.[46] Given that AF often coexists with multiple comorbidities[47] and therefore poly-pharmacy is likely,[48] clinicians must be responsive to this additional complexity. Complex dosing regimens should be reduced where possible. In the VARIA (Veterans AffaiRs Study to Improve Anticoagulation) study, patients receiving 16 or more medications were predicted a 4.3% lower TTR than that of patients receiving 0–7 medications.[49] Therefore reducing the number of medications prescribed where possible is highly justified. However, judgement as to whether there are many (i.e. appropriate poly-pharmacy) or too many (i.e. inappropriate poly-pharmacy) medications is complex.[50] The hospital pharmacist plays a key role in the assessment for medication aids upon discharge. The issue of altered cognition in this population adds a layer of complexity to dosing regimens. Caregiver assistance may be of help in the community setting to assist with dosing regimens and in understanding medication packing for those individuals with poor health literacy.

Advocacy and shared decision-making

The decision to anticoagulate a patient with AF is multifaceted. Stroke and bleeding risk must be considered.[51] Views between clinicians and patients when weighing up outcomes of thromboprophylaxis in AF vary considerably.[52] Therefore patient preferences must be central to decisions to anticoagulate. Treatment must be patient-centred and individualized.[53] Clinicians who fail to include the patient and their caregivers in decisions about commencing thromboprophylaxis risk disengaging with those whose care they are trying to improve.[52] Patients and caregivers should have an active role in treatment decisions, as this may prove helpful in achieving favourable outcomes of therapy.[54] Previous studies have highlighted that the absence of a caregiver may bias against initial prescription of anticoagulation.[55] The need for caregiver assistance should be considered when making treatment decisions.[29] Patients may be perplexed by complicated stroke and bleeding risk information such as risk–benefit ratios. Whilst clinicians may be aware of patient limitations they should not use this to influence clinician desired treatment choices.[56] Caregivers play a vital role in advocacy and shared decision-making. Shared decision-making with frail older adults where cognitive impairment can influence competency may be challenging. Such consultations may involve lengthy detailed discussions that take time.[57]

Support from healthcare

Arrhythmia nurse specialists or consultants act as a designated clinical contact to provide specialized care. They may support patients who are newly diagnosed with AF, and their caregivers, through the provision of education.[58] This may include: timely provision of health information, counselling and advice on medications, and reassurance. Nurse specialists may also coordinate AF support groups. Support groups are identified as adding value to caregiver support as they can provide platforms for patients and caregivers to meet, engage and exchange health information and stories.[58] This may encourage supportive community networks and reduce caregiver burden. Support for coping and adjusting with the emotional aspects of burden in AF are generally lacking.[59] And there is growing demand for newer educational programmes to be developed to address the emotional burden of AF.[59]

Caregiver burden

Whilst thromboprophylaxis remains chronically underutilized,[60] it could be assumed that more patients are receiving oral anticoagulation than ever before. Such factors likely result in a greater reliance on caregivers.

Patients with AF have a greater need for caregiver assistance.[29] However this assistance may come at a cost, in forms of both physical and emotional stress. An early definition by Townsend in the 1950s describes a phenomenon of 'strain of illness'. 'This strain can be a change of employment as a result of caring for a family member, or excessive physical or mental demands imposed on the entire family structure.' Turner and Catania provide a more up to date (1997) broader definition of caregiver burden as a 'caregiver's subjective experience of problems or strains that were linked to the caregiver's role'.[61] Caregivers who report emotional or mental strain associated with caregiving are more likely to die than non-caregivers.[62] Amongst elderly spousal caregivers, experiencing psychological or emotional strain is an independent risk factor for mortality.[62]

There is significantly greater caregiver burden due to 'disrupted schedule' in those spending >4 h/week providing care and when caring for frail, sick or disabled patients with higher $CHADS_2$ scores and requiring help with their medications.[33] The greatest burden to caregivers of AF patients occurs due to schedule disruption.[33] Patients living in rural and remote regions may have to endure lengthy travel to a healthcare professional for INR checking. Point of care INR testing may be a strategy which can be implemented by caregivers to reduce unnecessary expensive medical travel.[63] Additionally, point of care testing may lead to increased time in TTR and improved outcomes if successfully integrated into a caregiver's routine.[63] The impact of caregiver burden may lead to less adequate patient support, physical and emotional stress, caregiver burnout and suboptimal patient outcomes. It is therefore vital for health professionals to recognize and support caregivers in their role. There is a need for studies that examine interventions that reduce caregiver burden in AF. Higher burden scores were significantly associated with caring for frail patients who require frequent office follow-up.[33] Therefore, clinical interventions that target the frail AF population should be developed further.

Limitations

There is a scarce amount of original research in the area of the role of the caregiver in AF. This review is limited by only including primary research studies available via the identified databases. Studies were only included if published in the English language. In spite of these limitations, there is a robust literature that identifies issues germane to caregiving. This review casts the spotlight on specific issues in AF research which will facilitate the development of effective caregiver support.

Underrepresentation in research

The role of the caregiver and the relationship to health outcomes in AF is underrepresented in clinical research.[64] Data suggest that living alone and poor social support are associated with adverse outcomes. This emphasizes the need to look at elements of caregiver support.[65,66]

AF is associated with functional decline.[28] Frail patients are less likely to be prescribed anticoagulation than non-frail patients.[29,67] Similarly, patients with poor self-care are less likely to receive anticoagulation.[29] The need for caregiver assistance in frail patients and those with poor self-care must be carefully considered when making decisions about thromboprophylaxis. Whilst useful in clinical practice, the $CHADS_2$ and CHA_2DS_2-VASc models of risk assessment are limited. Such models do not consider frailty, ability to self-care or the need for caregiver assistance.[39] The need for caregiver assistance must be carefully assessed when making complex treatment decisions. The lack of a caregiver may be a factor that influences clinician's behaviour when prescribing thromboprophylaxis. Treatment choices must be individualized and best balanced to consider the abilities of the caregiver. Involving the caregiver at the outset in education is essential.

Implications for clinical practice and research

Health professionals must recognize the pivotal role of caregivers across all care settings. Support strategies for caregivers must be implemented and routinely reviewed to avoid burnout. Many barriers exist for caregivers who seek support. However, caregivers may not always be

aware of the various support services on offer. They may not regard the services offered as relevant to meet their needs or the needs of their spouse. Or they may not think that the services are of sufficient quality. Health professionals must recognise the vital role of the caregiver in AF. The caregiver has an essential role to play in advocacy, family-centred care and shared decision-making around thromboprophylaxis treatment choices. Urgent research is required that examines the role of the caregiver in AF and patient outcomes in greater detail. This will inform recommendations in multidisciplinary clinical practice guidelines in the future which must move to value the role of the caregiver.

AF is a primarily cardio-geriatric condition affecting an elderly population with comorbidities and health disparities.[68] AF frequently co-exists with other chronic conditions including hypertension, heart failure and diabetes.[3,69] It is also associated with cognitive dysfunction, reduced functional abilities[28] and frailty.[67] This population is more likely to need caregiver assistance.[29] Medication regimens are routinely complex, whereby poly-pharmacy is problematic.[48] Managing these multiple medications can be particularly difficult for those who experience functional and cognitive decline as a consequence of AF.

Caregiving is a complex experience. It is important to assess the individual's needs, social circumstances, networks and community support.[11] Recent research conducted on caregiving in the heart failure population identified disparities for caregivers in access of support services for caregivers of non-malignant conditions, compared with that of those dying from other conditions, such as cancer. The disparities and un-met needs in caregiver support for those with non-malignant conditions, including AF, should be examined further.[11]

Conclusion

There is a limited amount of original clinical research that examines the role of the caregiver in individuals with AF. This review highlights that whilst the caregiver role seems to be important, how this role is best utilized has not been well studied and evidence is lacking. Furthermore, patients with AF have a greater need for caregiver assistance and this need must be considered when making complex decisions on thromboprophylaxis. Patients without caregiver support are less likely to receive anticoagulation. Assessment of caregiver support should be central to patient assessment and care planning. Support from a caregiver may help to improve adherence to treatment regimes. There is an ongoing need to include the caregiver in treatment decisions in a paradigm shift towards shared decision-making and promotion of adherence.

Implications for practice

- To date, the role of the caregiver in AF is poorly described.
- Support for adherence with thromboprophylaxis may be enhanced by caregiver support and involvement in care planning.
- There is need for the systematic development of models for AF management that formalize caregiver participation.

Conflict of interest

There are no conflicts of interest.

Ethical approval

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References

1. Naccarelli G, Varker H, Lin J, et al. Increasing prevalence of atrial fibrillation and flutter in the United States. *Am J Cardiol* 2009; 104: 1534–1539.
2. Wong CX, Brooks AG, Leong DP, et al. The increasing burden of atrial fibrillation compared with heart failure and myocardial infarction: A 15 year study of all hospitalisations in Australia. *Arch Intern Med* 2012; 172: 739–740.
3. Ball J, Carrington M, McMurray JJV, et al. Atrial fibrillation: Profile and burden of an evolving epidemic in the 21st century. *Int J Cardiol* 2013; 167: 1807–24.
4. Kannel WB, Wolf PA, McGee DL, et al. Systolic blood pressure, arterial rigidity, and risk of stroke: The Framingham Study. *JAMA* 1981; 245: 1225–1229.
5. Gattellari M, Goumas C, Aitken R, et al. Outcomes for patients with ischaemic stroke and atrial fibrillation: The PRIMS Study (A Program of Research Informing Stroke Management). *Cerebrovasc Dis* 2011; 32: 370–382.
6. Khan M, Ahmed B, Ahmed M, et al. Functional, cognitive and psychological outcomes, and recurrent vascular events in Pakistani stroke survivors: A cross sectional study. *BMC Res Notes* 2012; 5: 89.
7. Kang X, Li Z and Nolan M. Informal caregivers' experiences of caring for patients with chronic heart failure. *J Cardiovasc Nurs* 2011; 26: 386–394.
8. Funk L, Chappell N and Liu G. Associations between filial responsibility and caregiver well-being: Are there differences by cultural group? *Res Aging* 2013; 35: 78–95.
9. The National Alliance for Caregiving in collaboration with AARP. Caregiving in the US. http://www.caregiving.org/data/Caregiving_in_the_US_2009_full_report.pdf2009:1–79 (2009, accessed)
10. Evercare by United Healthcare. *The Evercare Survey of the economic downturn and its impact on family caregiv-*

ing: Report of findings. http://www.caregiving.org/data/EVC_Caregivers_Economy_Report%20FINAL_4-28-09.pdf (2009, accessed 1st Nov 2012).
11. Davidson PM, Abernethy AP, Newton PJ, et al. The caregiving perspective in heart failure: A population based study. *BMC Health Serv Res*. 2013; 13: 342.
12. Grey M, Knafl K and McCorkle R. A framework for the study of self- and family management of chronic conditions. *Nurs Outlook* 2006; 54: 278–286.
13. Lip GYH. Implications of the CHA2DS2-VASc and HAS-BLED scores for thromboprophylaxis in atrial fibrillation. *Am J Med* 2011; 124: 111–114.
14. Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation. *Circulation* 2006; 114: e257–e354.
15. European Society of Cardiology. Guidelines for the management of atrial fibrillation. *Eur Heart J* 2010; 31: 2369–2429.
16. National Institute for Clinical Excellence. *Atrial fibrillation. The management of atrial fibrillation*. National Institute for Clinical Excellence, 2006, UK.
17. Singer D, Albers G, Dalen J, et al. Antithrombotic therapy in atrial fibrillation: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; 126: 429S.
18. Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2011; 123: 104–123.
19. Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC guidelines for the management of atrial fibrillation. *Eur Heart J* 2012; 33: 2719–2747.
20. Ansell J, Hirsh J, Hylek E, et al. Pharmacology and management of the vitamin K antagonists. *Chest* 2008; 133(6 Suppl.): 160S-198S.
21. Ferguson C, Inglis SC, Newton PJ, et al. Atrial fibrillation: Stroke prevention in focus. *Aust Crit Care* 2014; 27: 92–98.
22. World Health Organization. *Adherence to long term therapies: Evidence for action*. Geneva, Switzerland: World Health Organization, 2003.
23. Haynes R, Ackloo E, Sahota N, et al. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2008; 2: 1–158.
24. O'Connor PJ. Improving medication adherence: Challenges for physicians, payers and policy makers. *Arch Intern Med* 2006; 166: 1802–1804.
25. Mahtani K, Heneghan C, Glasziou P, et al. Reminder packaging for improving adherence to self-administered long-term medications. *Cochrane Database Syst Rev*. 2011; 9: 1–62.
26. Reynolds MR, Shah J, Essebag V, et al. Patterns and predictors of warfarin use in patients with new-onset atrial fibrillation from the FRACTAL Registry. *Am J Cardiol* 2006; 97: 538–543.
27. Fang MC, Go AS, Chang Y, et al. Warfarin discontinuation after starting warfarin for atrial fibrillation. *Circ Cardiovasc Qual Outcomes* 2010; 3: 624–631.
28. Marzona I, O'Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with atrial fibrillation: Results of the ONTARGET and TRANSCEND studies. *Can Med Assoc J* 2012; 184: E329–36.
29. Chen S-Y, Vanderpoel J, Mody S, et al. Caregiver assistance among Medicare beneficiaries with atrial fibrillation and factors associated with anticoagulant treatment. *Am J Geriatr Pharmacother* 2012; 10: 273–283.
30. Appelboam R and Thomas EO. Warfarin and intracranial haemorrhage. *Blood Rev* 2009; 23: 1–9.
31. Sjoblom L, Hardemark HG, Lindgren A, et al. Management and prognostic features of intracerebral hemorrhage during anticoagulant therapy: A Swedish multicentre study. *Stroke* 2001; 32: 2567–2574.
32. Lackie CL, Garbarino KA and Pruetz JA. Warfarin therapy for atrial fibrillation in the elderly. *Ann Pharmacother* 2002; 36: 200–204.
33. Coleman CI, Coleman SM, Vanderpoel J, et al. Factors associated with 'caregiver burden' for atrial fibrillation patients. *Int J Clin Pract* 2012; 66: 984–990.
34. Ho P, Bryson C and Rumsfeld J. Medication adherence. *Circulation* 2009; 119: 3028–3035.
35. Osterberg L and Blaschke T. Adherence to medication. *N Engl J Med* 2005; 353: 487–497.
36. Brown T, Siu K, Walker D, et al. Development of a conceptual model of adherence to oral anticoagulants to reduce risk of stroke in patients with atrial fibrillation. *J Manag Care Pharm* 2012; 18: 351–362.
37. Hendriks JML, deWit R, Crijns HJGM, et al. Nurse-led care vs usual care for patients with atrial fibrillation. *European Heart Journal*. 2012; 33: 2692–2699.
38. Berti D, Hendriks JML, Brandes A, et al. A proposal for interdisciplinary, nurse-coordinated atrial fibrillation expert programmes as a way to structure daily practice. *Eur Heart J* 2013; 34: 2725–2730.
39. Ferguson C, Inglis S, Newton P, et al. Atrial fibrillation and thromboprophylaxis in heart failure: The need for patient-centered approaches to address adherence. *Vasc Health Risk Manag* 2013; 9: 3–11.
40. Tang E, Lai C, Lee K, et al. Relationship between patient's warfarin knowledge and anticoagulation control *Ann Pharmacother* 2003; 37: 34–39.
41. Bockwoldt D. Antithrombosis management in community-dwelling elderly: Improving safety. *Geriatr Nurs* 2010; 31: 28–36.
42. Bajorek BV, Ogle SJ, Duguid MJ, et al. Management of warfarin in atrial fibrillation: Views of health professionals, older patients and their carers. *Med J Aust* 2007; 186: 175–180.
43. Bereznicki LR, Peterson GM, Jackson SL, et al. The risks of warfarin use in the elderly. *Expert Opin Drug Saf* 2006; 5: 417–431.
44. Dolor RJ, Ruybalid RL, Uyeda L, et al. An evaluation of patient self-testing competency of prothrombin time for managing anticoagulation: Pre-randomization results of VA Cooperative Study #481 – The Home INR Study (THINRS). *J Thromb Thrombolysis* 2010; 30: 263–75.
45. Horstkotte D and Piper C. Improvement of oral anticoagulation therapy by INR self-management. *J Heart Valve Dis* 2004; 13: 335–338.
46. Hylek E. Oral anticoagulants: Pharmacological issues for use in the elderly. *Clin Geriatr Med* 2001; 17: 1–13.

47. Lip GYH and Tse H. Management of atrial fibrillation. *Lancet* 2007; 370: 604–618.
48. Murray MD, Morrow DG, Weiner M, et al. A conceptual framework to study medication adherence in older adults. *Am J Geriatr Pharmacother* 2004; 2: 36–43.
49. Rose AJ, Hylek EM, Ozonoff A, et al. Patient characteristics associated with oral anticoagulation control: Results of the Veterans AffaiRs Study to Improve Anticoagulation (VARIA). *J Thromb Haemost* 2010; 8: 2182–2191.
50. Patterson S, Hughes C, Kerse N, et al. Interventions to improve the appropriate use of polypharmacy for older people (Review). *Cochrane Database Syst Rev* 2012; 5: 1–81.
51. Lip GYH. The balance between stroke prevention and bleeding risk in atrial fibrillation: A delicate balance revisited. *Stroke* 2008; 39: 1406–1409.
52. Devereaux PJ, Fahey T, Anderson DR, et al. Differences between perspectives of physicians and patients on anticoagulation in patients with atrial fibrillation: Observational study commentary: Varied preferences reflect the reality of clinical practice. *BMJ* 2001; 323: 1218.
53. Forman DE, Rich MW, Alexander KP, et al. Cardiac care for older adults: Time for a new paradigm. *J Am Coll Cardiol* 2011; 57: 1801–1810.
54. Abdelhafiz AH. A review of anticoagulation with warfarin in patients with nonvalvular atrial fibrillation. *Clin Ther* 2001; 23: 1628–1636.
55. Johnston JA, Cluxton Jr RJ, Heaton PC, et al. Predictors of warfarin use among Ohio Medicaid patients with new-onset nonvalvular atrial fibrillation. *Arch Intern Med* 2003; 163: 1705–1710.
56. Dudley N. Importance of risk communication and decision making in cardiovascular conditions in older patients: A discussion paper. *Qual Health Care* 2001; 10(Suppl. 1): i19–i22.
57. Milte CM, Ratcliffe J, Davies O, et al. Family meetings for older adults in intermediate care settings: The impact of patient cognitive impairment and other characteristics on shared decision making. *Health Expect* 2013. Epub ahead of print 20 May 2014. DOI: 10.1111/hex.12076.
58. Ismail H and Lewin RJ. The role of a new arrhythmia specialist nurse in providing support to patients and caregivers. *Eur J Cardiovasc Nurs* 2013; 12: 177–183.
59. McCabe PJ, Schumacher K and Barnason SA. Living with atrial fibrillation: A qualitative study. *J Cardiovasc Nurs* 2011; 26: 336–344.
60. Ogilvie IM, Newton N, Welner SA, et al. Underuse of oral anticoagulants in atrial fibrillation: A systematic review. *Am J Med* 2010; 123: 638–645.
61. Turner H and Catania J. Informal Caregiving to Persons with AIDS in the United States: Caregiver Burden Among Central Cities Residents Eighteen to Forty-Nine Years Old. *Am J Community Psychol* 1997; 25: 35–59.
62. Schulz R and Beach SR. Caregiving as a risk factor for mortality: The caregiver health effects study. *JAMA* 1999; 282: 23.
63. James M. An analysis of the use of a point-of-care system for international normalized ratio testing in remote areas of Canada: A literature review. *Point Care* 2008; 7: 34–37.
64. Berg AM. Dabigatran compared with warfarin for stroke prevention in atrial fibrillation. *Ann Intern Med* 2011; 154: 570.
65. Perissinotto CM, Cenzer IS and Covinsky KE. Loneliness in older persons. *Arch Intern Med* 2012; 172: 1078–1083.
66. Udell JA, Steg PG, Scirica BM, et al. Living alone and cardiovascular risk in outpatients at risk of or with atherothrombosis. *Arch Intern Med* 2012; 172: 1086–1095.
67. Perera V, Bajorek BV, Matthews S, et al. The impact of frailty on the utilisation of antithrombotic therapy in older patients with atrial fibrillation. *Age Ageing* 2009; 38: 156–162.
68. Murphy NF, Simpson CR, Jhund PS, et al. A national survey of the prevalence, incidence, primary care burden and treatment of atrial fibrillation in Scotland. *Heart* 2007; 93: 606–612.
69. Smit MD, Moes ML, Maass AH, et al. The importance of whether atrial fibrillation or heart failure develops first. *Eur J Heart Fail* 2012; 14: 1030–40.

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Permission to use the Morisky Scale in a PhD Student Project

Caleb Ferguson

Sent: 18 January 2013 14:07
To: dmorisky@ucla.edu
Attachments: Untitled (65 B)

Attachments: Morisky Agreement Form.pdf (60 KB)

Dear Dr Morisky,

My name is Caleb Ferguson and I am a PhD Student at the Centre for Cardiovascular & Chronic Care, University of Technology, Sydney. I am currently planning a PhD project entitled The AFASTER Study (Atrial Fibrillation and Stroke Thromboprophylaxis in Heart Failure) and I would like to apply for permissions to use your instrument - the Morisky Medication Adherence Scale (MMAS-8) to measure self-reported medication adherence in patients with heart failure. We are aiming to collect data from 2013 - 2014 for a duration of 12 months.

I have attached a completed copyright and licensure agreement form,

Kind regards, Caleb Ferguson

Mr. Caleb Ferguson RN, MHlth, BScN, MACN
PhD Candidate - Centre for Cardiovascular & Chronic Care
Lecturer - Faculty of Health
University of Technology, Sydney
PO Box 123, Broadway, NSW 2007
S: caleb.ferguson
E: caleb.ferguson@uts.edu.au
W: http://www.nmh.uts.edu.au/

Permissions for use of the EHFScBS

Caleb Ferguson

Sent: 11 February 2013 13:26
To: t.jaarsma@thorax.azg.nl

Dear Professor Jaarsma,

I am currently a PhD student at the Centre for Cardiovascular & Chronic Care at UTS studying with Professor Davidson. I am writing seek permissions to use the European Heart Failure Self-Care Behaviour Scale in my upcoming PhD project. The project is entitled The AFASTER Study: Atrial Fibrillation and Stroke Thromboprophylaxis in Heart Failure. We expect to recruit participants from 2013 – 2014 and anticipate use of the scale in 12 month follow up.

Kind regards, Caleb Ferguson

SV: Permission to reproduce knowledge test survey from Euro J Cardiovasc Nurs

Oterhals, Kjersti [kjersti.oterhals@helse-bergen.no]

You replied on 13/02/2014 17:51.

Sent: 12 February 2014 20:01
To: Caleb Ferguson
Attachments: Untitled (65 B)

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further questions.

Kind regards,

Kjersti Oterhals
Nurse researcher / PhD student

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April 2, 2013

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