Medication Safety:

Exploring interventions to support vulnerable patients taking high-alert medications

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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 in the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are appropriately acknowledged within the thesis.

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Abstract

Ensuring patient safety around high-risk medications such as oral anticoagulants is a global challenge. Several patient-focused interventions have been used to support vulnerable patients such as older persons taking oral anticoagulants. However, limited research has been done to support those with limited health literacy, and those from cultural and linguistic diverse (CALD) backgrounds.

Qualitative and quantitative methods were used to identify the limitations in health literacy, warfarin knowledge gaps, patient's and carer's needs and preferences for medicine information about oral anticoagulants.

A double-sided A4 size Warfarin action Plan leaflet was developed, and feedback was obtained from patients and their carers. Several benefits of the action plan were highlighted such as its concise format and understandable content, the use of visuals and how it was interactive. The action plan also addressed the knowledge gaps of patients and carers who had been using warfarin for several years, highlighting the need for regular follow up and education. An unexpected finding was that the WAP had a positive impact on behaviour.

Based on the findings from the feedback on the WAP leaflet and knowledge gaps about NOACs, web-based education materials were assessed to see if they would also have a similar benefit in terms of understandability and actionability. The majority of materials were understandable, however, were not actionable. These findings suggest that there is a need for high quality NOAC medicines information that are actionable.

Overall, this thesis highlights the beneficial role of the written WAP leaflet in supporting older persons taking oral anticoagulants and their carers. The implications of this leaflet is that it could also be used for NOACs and be provided to patients and their carers in a variety of settings such as the hospital and home.

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List of Abbreviations

AF	Atrial Fibrillation
CALD	Cultural and linguistically diverse
DOACs	Direct-acting oral anticoagulants or Direct oral anticoagulants
HLQ	Health Literacy Questionnaire
HMR	Home Medicines Review
INR	International Normalised Ratio or International normalized ratio
MMP	Medicines Management Pathway
NSW	New South Wales
NOACs	Novel or new oral anticoagulants or Non-Vitamin K antagonists
NPS	National Prescribing Service
PEMAT	Patient Education Materials Assessment Tool
POC	Point of care
REALM	Rapid Estimate of Adult Literacy in Medicine
SDM	Shared Decision-Making
TTR	Time in Therapeutic Range
WAP	Warfarin action plan
WHO	World Health Organization

List of Definitions

Medication safety is defined as freedom from preventable harm with medication use (ISMP Canada, 2007).

People-centred care refers to an approach to care that consciously adopts the perspectives of individuals, carers, families and communities as participants in, and beneficiaries of, trusted health systems that are organised around the comprehensive needs of people rather than individual diseases, and respects social preferences. People-centred care also requires that patients receive the education and support they need to make decisions and to participate in their own care. Patient- and person-centred care should encompass both clinical encounters as well as attention to the health of people in their community and their crucial role in shaping policy and health services (World Health Organization Sixty-ninth world health assembly 2016).

Patient-centred care (the more widely used term) refers to the provision of care that is respectful of, and responsive to, individual patient preferences, needs and values, and that ensures that the patient's values guide all clinical decisions (Institute of Medicine 2001)

Person-centred care is a model in which healthcare systems are encouraged to partner with patients to co-design and deliver personalised care that provides people with the high-quality care they need and to improve healthcare system efficiency and effectiveness (Santana et al. 2018). Person-centred care is respectful of, and responsive to, the preferences, needs and values of patients and consumers. Key dimensions of person-centred care include respect, emotional

support, physical comfort, information and communication, continuity and transition, care coordination, involvement of carers and family, and access to care (Australian Commission on Safety and Quality in Health Care 2011). This is also known as patient-centred care or consumer-centred care (Australian Commission on Safety and Quality in Health Care (ACSQHC) 2017).

Consumer-centred care refers to the provision of care that is easy for patients to obtain when they need it and ensures that healthcare staff respect and respond to patient choices, needs and values. Partnerships are formed between patients, their family, carers and healthcare providers (Australian Commission on Safety and Quality in Health Care 2010).

Medication incidents refers to problems that occur in the prescription, dispensing and administration of medications (Roughead & Semple 2009).

Adverse drug events are defined as the proportion of medication incidents that result in patient harm (Roughead & Semple 2009)

High-alert medications are drugs that confer a heightened risk of causing significant patient harm when they are used inappropriately. Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients (Institute for Safe Medication Practices (ISMP) 2014).

Older persons are defined here as persons aged 65 years and older (Orimo et al. 2006; World Health Organization 2018a).

Limited health literacy is defined by the WHO as "the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health" (World Health Organization 2018b).

Culturally and linguistically diverse (CALD) is defined in Australia as those people born overseas, in countries other than those classified by the Australian Bureau of Statistics as "main English-speaking countries". The term CALD is also referred to as 'ethnic minorities' (Alhomoud et al. 2013; Mohammad, Saini & Chaar 2015), 'multicultural', 'migrants' and 'from a non-English speaking background (Smith V and Schaffer E. 2014).

Chapter 1: Introduction and overview of thesis

1.1. The global challenge: Medication safety

Given that almost everyone takes medicines at some point in their life (World Health Organization 2017) medication safety is, therefore, of significant interest to health systems, government policy and members of the public. The recent literature has noted that unsafe medication practices and medication errors are a leading cause of 'avoidable' harm in healthcare systems across the world (World Health Organization 2017). The cost associated with medication errors globally has been estimated at US $42 billion annually (World Health Organization 2017). In Australia, a literature review in 2013 reported that 2–3% of all hospital admissions are medication related and that the annual cost of medication-related admissions was $1.2 billion (Australian Commission on Safety and Quality in Health Care (ACSQHC) 2013). Overall, these medication-related problems have compromised patient health and safety.

The causes of medication errors may be explained by the 'Swiss cheese' model. 'This model states that adverse events or hazards may occur when holes in the many defensive layers of the Swiss cheese or barriers momentarily line up to permit a trajectory of accident opportunity, allowing a hazard to come into potentially damaging contact with the consumer or victims' (Reason 2000; Stowasser, Allinson & O'Leary 2004).

Strategies to minimise medication errors may involve targeting the different stages of the medication process, as indicated by the Medicines Management Pathway (MMP) (See Figure 1.1). This pathway describes the nine steps and three background processes that are involved in the use of medications, with a focus on the consumer (Stowasser, Allinson & O'Leary 2004).

This pathway offers a framework to identify weak or error-prone processes, pinpoint strategies to reduce the opportunity for error in previous steps, and proactively evaluate the potential limitations associated with proposed changes (Stowasser, Allinson & O'Leary 2004).

The medication safety principle of the MMP is relevant to high-alert medications, also known as high-risk medications, such as oral anticoagulants because they are associated with a high risk of severe harm if used improperly (ACSQHC 2013; Piazza et al. 2011; Runciman et al. 2003; World Health Organization 2017) (See Table 1.1). The Institute for Safe Medication Practices (ISMP) in the USA developed a list of high-alert medications in acute care settings (Institute for Safe Medication Practices 2014). In Australia, the high-risk medications are represented by the acronym 'A PINCH' and a category called 'Other' (Clinical Excellence Commission (CEC) 2015). The acronym is formed from the following categories: Anti-infective, Potassium and other electrolytes, Insulin, Narcotics (opioids) and other sedatives, Chemotherapeutic agents, Heparin and anticoagulants (including newer oral anticoagulants). More recently, other medications such as paracetamol have been added to the list.

Table 1.1 Examples of high-risk or high-alert medications

High-risk medicine groups	Examples of medicines
A. Anti-infective	amphotericin, aminoglycosides
P. Potassium and other electrolytes	Injections of potassium, magnesium, calcium, hypertonic sodium chloride
I. Insulin	all insulins
N. Narcotics (opioids) and other sedatives	hydromorphone, oxycodone, morphine, fentanyl, alfentanil, remifentanil and analgesic patches, benzodiazepines, thiopentone, propofol and other short-term anaesthetics
C. Chemotherapeutic agents	vincristine, methotrexate, etoposide, azathioprine
H. Heparin and anticoagulants	warfarin, enoxaparin, rivaroxaban, dabigatran, apixaban
Other	paracetamol

1.1.1 The importance of targeting anticoagulants

This thesis focused on anticoagulants for several reasons. Atrial fibrillation (AF) is considered to be a major global health burden because of its rising prevalence and its association with complications such as stroke and outcomes such as mortality (Fawzy & Lip 2019). Stroke can cause permanent and irreversible adverse effects, and is therefore a priority for action in the health sector (Australian Institute of Health and Welfare 2019). Stroke prevention is integral to the management of AF. Anticoagulants such as warfarin and the non-vitamin K antagonist oral anticoagulants (NOACs) are highly effective for life-long stroke prevention in patients with AF. However, they are high-alert medications because they are associated with a high risk of severe harm such as death and bleeding events, if used improperly (Piazza et al. 2011; Runciman et al. 2003; Sennesael et al. 2018).

The second reason why the oral anticoagulants are of particular interest is that they are one of the drug classes most often associated with potentially preventable medication-related hospital admissions (Leendertse et al. 2008).

Another reason for the focus on anticoagulants in this thesis was the recent availability of NOACs on the Australian market and the publication of Australian guidelines advocating their use (Brieger et al. 2018). Recent randomised trials have highlighted the benefits of NOACs over warfarin (Saraiva 2018). NOACs, such as dabigatran (direct thrombin inhibitor), apixaban (factor Xa inhibitor), edoxaban (factor Xa inhibitor), and rivaroxaban (factor Xa inhibitor), have been shown to be non-inferior (and in some cases superior) to warfarin in terms of reducing the risk of stroke. Some NOACs also have a lower risk of cerebrovascular bleeding among patients with AF who are at moderate to high risk of stroke (Saraiva 2018).

Finally, anticoagulants were selected due to clinical practice experience at a large teaching hospital in Sydney. During the ward rounds the research candidate noticed that:

- some patients felt overwhelmed with all of the information contained within the warfarin information booklet currently provided to them
- some patients who had taken warfarin for several years had gaps in their knowledge
- some patients stated they had received the information booklet in the past but had not read it.

Due to time restraints, sometimes it was challenging for the hospital pharmacist to communicate the critical information points about warfarin or NOAC therapy to patients and their carers in an efficient and effective way.

1.1.2 The importance of targeting vulnerable patient groups

Several patient groups were of interest in this thesis because they may be vulnerable or at risk of experiencing harm from anticoagulants. The patient populations included older persons, those with limited health literacy and those from cultural and linguistically diverse (CALD) backgrounds. A common problem for these patient groups identified in the literature is that they have knowledge gaps about the oral anticoagulants they are taking, which may lead to an increased risk of non-adherence and poor outcomes such as a stroke (Di Minno et al. 2014; Nasser, Mullan & Bajorek 2012). The identified knowledge gaps pertain to topics relating to their anticoagulant use such as the drugs' mechanisms of action, benefits and risks of therapy, treatment side effects, interactions with other drugs or foods, frequency of monitoring using the international normalized ratio (Fang et al. 2006; Nadar et al. 2003, Nasser, Mullan & Bajorek

2012; Wilson et al. 2003), ability to recognise an emergency situation such as stroke or bleeding complications (Maikranz et al. 2017; Vormfelde et al. 2014) and the need for renal function monitoring at least annually when taking a NOAC (Amara et al. 2016). These knowledge gaps may arise because the patients have received sub-optimal verbal education and/or written information that is not understandable or not culturally sensitive (Diamantouros, Bartle & Geerts 2013; Estrada et al. 2000; Nasser, Mullan & Bajorek 2012; Wilson et al. 2003).

The literature has also identified other problems specific to older people and those from CALD backgrounds. Older persons are at risk of anticoagulant-associated adverse drug reactions (Piazza et al. 2011), and those who have atrial fibrillation require anticoagulants to prevent stroke. Patients from CALD backgrounds may experience language barriers, have certain perceptions of warfarin therapy or respond differently to the anticoagulants because of genetic variability.

For several reasons, older persons are at risk of anticoagulant-associated adverse drug reactions such as potentially life-threatening bleeding complications. Older persons often have multiple comorbidities, such as severe chronic kidney disease, age-related functional and cognitive decline, and polypharmacy (Bajorek 2011; Forbes & Polasek 2017; Schneider et al. 2018). Polypharmacy increases the risk of potential drug–drug interactions (Schneider et al. 2018), is associated with medication non-adherence (Maher, Hanlon, & Hajjar 2014) and is one of the key risk factors for preventable medication-related hospital admissions (Leendertse et al. 2008). Furthermore, the need for anticoagulants to prevent stroke in older people is paramount because the prevalence of AF increases markedly with advancing age and age is an independent risk factor for stroke (Fawzy & Lip 2019). AF is responsible for 10–20% of all strokes, and for more than 25% of all strokes in people aged 80 to 89 years (Chen, Yi & Cheng 2018). The World

Health Organization (2018c) states the world's population is rapidly ageing. Between 2015 and 2050, it is expected that the percentage of the world's population aged over 60 years will nearly double from 12% to 22%. Systems of long-term care are required in all countries to meet the needs of older people with multiple chronic conditions (World Health Organization 2018c).

In addition to their knowledge gaps about anticoagulants, patients from CALD backgrounds may also have other medication-related problems. CALD patients such as Indo-Asians may face language barriers which may reduce physician–patient interaction (Lip et al. 2002). Indo-Asian patients may have difficulty understanding their anticoagulation management (Nadar et al. 2003) and may lack the motivation to be adherent because of their perceptions of warfarin therapy (Abdou et al 2016). In one study (Lip et al. 2002), Indo-Asian patients perceived that the locus of control for their health was God or "fate" rather than believing that they or their doctor had control of their health (Abdou et al. 2016). In addition to their poor understanding and perceptions of treatment, patients from CALD backgrounds may respond differently (in physiological terms) to warfarin and may be at risk of adverse effects and poor anticoagulation control (Apostolakis et al. 2013) depending on whether they have specific genetic variants (Verhoef et al. 2014). Furthermore, it was revealed that nearly half of the patients from ethnic minority groups took warfarin 'because their doctor told them to', without knowing the potential benefits of warfarin (Nadar et al. 2003). Indo-Asian communities, as well as women and older people, are most likely to leave their treatment in the hands of others and/or follow the doctor's advice rather than take responsibility of their own health (Nadar et al. 2003).

Another reason to include CALD population groups in this thesis was that the 2016 national census showed that Australia is a culturally diverse nation. This census showed that two-thirds (67%) of the Australian population was born in Australia. Nearly half (49%) of Australians had

either been born overseas (first generation Australian) or had one or both parents born overseas (Australian Bureau of Statistics 2017). In 2016, more than 300 separately identified languages were spoken in Australian homes and that about one-fifth (21%) of Australians spoke a language other than English at home (Australian Bureau of Statistics 2017). After English, the next most common languages spoken at home were Mandarin, Arabic, Cantonese and Vietnamese (Australian Bureau of Statistics 2017).

These issues and statistics highlight the need for patient education about oral anticoagulants that is specific to each class of agent. Patient education should be comprehensive and comprehensible, especially to vulnerable patient groups (Amara et al. 2016; Maikranz et al. 2017).

1.1.3 The importance of heath literacy

This thesis incorporated the topic about health literacy due to the global call for healthcare organisations and healthcare professionals to take action in improving health literacy in policy and practice (Australian Commission on Safety and Quality in Health Care 2014; Brach et al. 2012; Sudore & Schillinger 2009; The Scottish Government 2017; U.S. Department of Health and Human Services 2010). At the 2016 Global Conference on Health Promotion, the World Health Organization (WHO) set 'improving health literacy' as a global priority for healthcare, disease prevention and health promotion (The Scottish Government 2017; World Health Organization and the United Nations Development Programme 2016). The United Nations Economic and Social Council Ministerial Declaration of 2009 provided a clear mandate for action: "*We stress that health literacy is an important factor in ensuring significant health outcomes and in this regard, call for the development of appropriate action plans to promote health literacy*" (World Health Organization and the United Nations Development Programme 2016).

1.1.4 The importance of a person-centred care approach

A person-centred care approach was used in this thesis. The World Health Organization advocates for the development of more integrated health services with a people-centred care approach in which people and communities, not diseases, are at the centre of healthcare systems (World Health Organization 2015). Other frameworks including a United Kingdom based model use the term person-centred care (Coulter A et al 2013; Health Education England 2017; Santana et al. 2017) or patient-centred care (Australian Commission on Safety and Quality in Health Care 2011; Berwick 2002).

However, the current preferred term is person-centred care because the word 'patient' tends to objectify and reduce the person to a mere recipient of medical services or to 'one who is acted on' rather than acknowledging that patients are persons with reason, will, feelings and needs who are able to engage as active partners with their healthcare providers (Ekman et al. 2011; Santana et al. 2017). In this thesis, the term person-centred care will be used.

Recent literature, policies and several international organisations, such as the WHO, have advocated the need to support people with a person-centred care approach because of its several benefits (Health Foundation 2014; Santana et al. 2017; World Health Organization 2015, 2016). These include improved access to care, improved health and clinical outcomes, better health literacy and self-care, increased satisfaction with care, improved job satisfaction for health workers, improved efficiency of services and reduced overall costs (World Health Organization 2016).

1.2. Key aspects examined

1.2.1 The Medicines Management Pathway (MMP) framework

The four chapters in this thesis focus on the 'Provision of medicine information' stage of the Medicines Management Pathway (MMP) framework as a person-centred approach for improving medication safety around anticoagulant use. Patient education and support may occur at different points on the MMP (Bajorek 2011; Stowasser, Allinson & O'Leary 2004).

The Medicines Management Pathway (MMP) describes the cognitive and physical steps involved in the use of medicines and has a focus on the consumer (Stowasser, Allinson & O'Leary 2004) (See Figure 1.1). The MMP comprises 9 steps and 3 background processes that are interdependent and influence each other. The 9 steps include: 1) Decision to treat and prescribe the most appropriate treatment by considering the best available evidence and consumer goals, 2) Record Medicine Order, 3) Review of Medicine Order, 4) Issue of Medicine, 5) Provision of medicines information specifically for the consumer such as how to store and correctly use the medicines, 6) Distribution and storage of Medicine, 7) Administration of medicine, 8) Monitor for any positive or negative (e.g., an adverse event) response to medicines, and 9) Transfer of Verified information such as medicines lists when another healthcare provider is involved in ongoing care (Stowasser, Allinson & O'Leary 2004).

There are 3 background processes, which can have effects across the whole pathway. These include 1) medicines procurement and materials management, 2) reporting and quality safety audit review, and 3) communication. The MMP offers a framework to identify weak or error-prone processes, pinpoint strategies to reduce the opportunity for error in previous steps and

evaluate the potential limitations associated with proposed changes (Stowasser, Allinson & O'Leary 2004).

The thesis focused mainly on 2 steps:

- patient education and support
- therapeutic drug monitoring

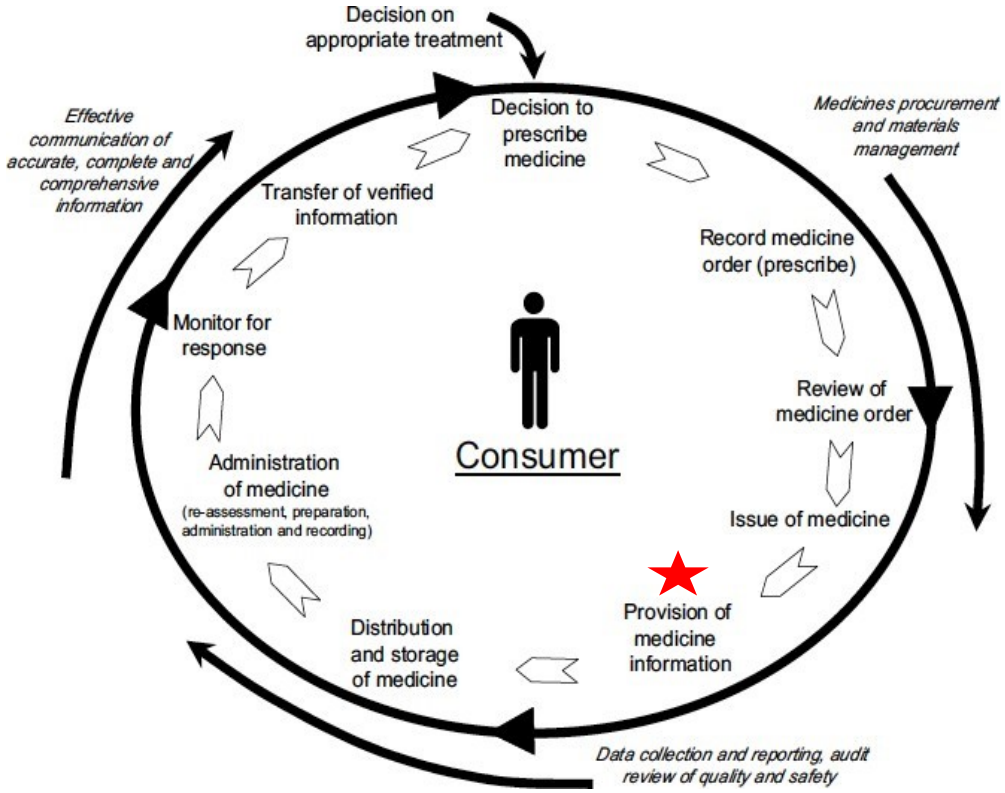
to assure medication safety and successful treatment for vulnerable patients taking high-alert medications such as oral anticoagulants.

The importance of patient education and support to increase patients' knowledge and understanding of their oral anticoagulants has been highlighted in several guidelines ((NICE) 2012; Brieger et al. 2018; Steffel et al. 2018). The provision of medicines information can assist the patient's ability to make informed decisions about the therapy, facilitate adherence to treatment and support patients with their day-to-day medication management (Bajorek 2011), which should help to optimise patient and medication safety. However, the literature shows that patient information may not be understandable, actionable or culturally sensitive (Aker et al. 2013; Diamantouros, Bartle & Geerts 2013; Estrada et al. 2000). The literature also shows some gaps in patients' and caregivers' knowledge about anticoagulants (Amara et al. 2016; Bajorek et al. 2009; Hernández Madrid et al. 2016; Nasser, Mullan & Bajorek 2012) and that there is a need to identify, target and develop educational and support resources to address these issues (Clarkesmith, Lip & Lane 2017; Nasser, Mullan & Bajorek 2012).

Figure 1.1 Medicines Management Pathway

(Stowasser, Allinson & O'Leary 2004)

A framework for assuring the safety of anticoagulants in patients and their carers, and for highlighting the importance of patient education/information ★



Several literature reviews have been published on the educational, behavioural, self-monitoring and self-management interventions to support patients taking oral anticoagulant medication (Clarkesmith et al. 2017; Clarkesmith, Pattison & Lane 2013; Heneghan et al. 2016; Stacey et al. 2017; Wofford, Wells & Singh 2008). This thesis was different because it used a narrative review approach to gather different types of evidence — both qualitative and quantitative — and explored the various types of patient-focused interventions available to support 3 vulnerable patient groups: older persons, those with limited health literacy and those from cultural and linguistically diverse backgrounds (CALD).

Although patient education can improve knowledge which may influence patient outcomes such as the time within therapeutic range for warfarin, other factors that can influence the effectiveness of patient education should also be considered. These factors include health literacy, patient engagement, patient empowerment, actionability, understandability and access to information such as website information via the internet.

Therefore, to address the above issues and encompass these different factors, this thesis includes the following chapters, which are linked to patient education and support on the MMP, with the emphasis of a person-centred approach that empowers the patient through effective interventions (Figure 1.1 and Figure 1.2):

Chapter 2: Patient-focused interventions to support vulnerable or special patient populations using oral anticoagulants

Chapter 3: Health literacy and knowledge in a cohort of Australian patients taking warfarin

Chapter 4: Patient Feedback on a Warfarin Action Plan used in a local Australian setting.

Chapter 5: An assessment of web-based patient education materials about oral anticoagulants in terms of actionability and understandability.

Figure 1.2 Thesis chapters mapped against the educational interventions

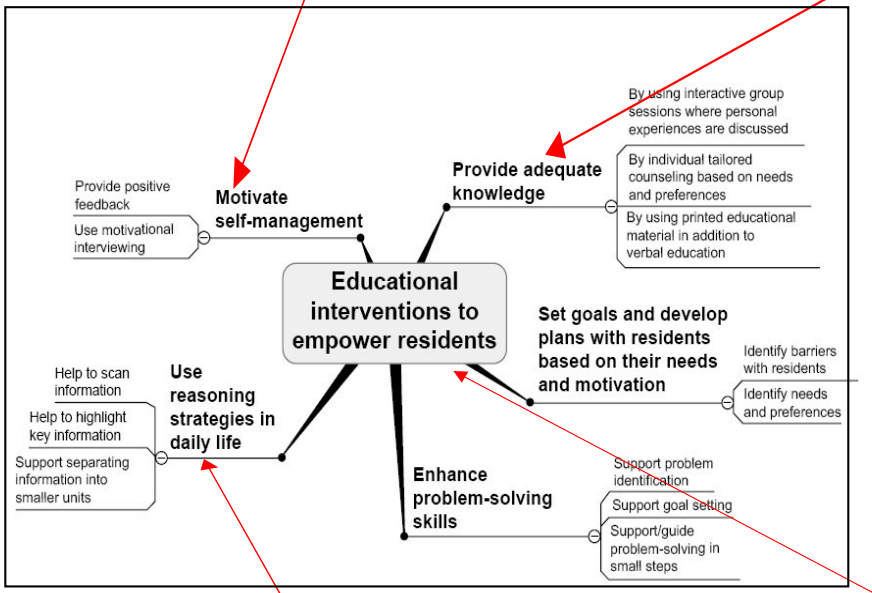
(adapted from Schoberer et al. 2016)

THESIS PAPER 3
Patient Feedback on a Warfarin Action Plan (WAP) leaflet used in a local Australian setting (CHAPTER 4)

THESIS PAPER 2
Health literacy and warfarin knowledge in a cohort of Australian persons (CHAPTER 3)

Medicines Management Pathway:

FOCUS ON the Provision of Medicines Information



THESIS PAPER 4 Evaluating the understandability and actionability of web based education materials for patients taking non-vitamin K oral anticoagulants (NOACs) (CHAPTER 5)

THESIS PAPER 1 Patient-focused interventions to support vulnerable people using oral anticoagulants (CHAPTER 2)

1.3. Research questions

The overall aim of this thesis was to investigate medication safety strategies for patients taking high-alert medications, focusing on the provision of information. The specific objectives entailed:

- to describe the range of patient-focused interventions developed, implemented and/or evaluated to support vulnerable patients using anticoagulant therapies (i.e., warfarin or one of the NOACs) (Paper 1)
- to report on the impact of these interventions on outcomes relevant to the use of anticoagulant therapy (Paper 1).
- to characterise older patients taking warfarin (Paper 2)
- to assess these patients' level of knowledge about warfarin (Paper 2)
- to describe their strengths and limitations in terms of health literacy and
- to explore relationships between participants' characteristics, warfarin knowledge and health literacy (Paper 2).
- to report patient feedback on a double-sided A4 size Warfarin Action Plan (WAP) leaflet and identify patient's preferences regarding the WAP's content (specific information and detail) and format (presentation and appearance) (Part A, Paper 3).
- to canvass in-depth feedback regarding the participants information needs and current information-seeking practices with respect to warfarin therapy (Part B, Paper 3).
- to identify patients' preferences for the types of information provided in terms of format and to identify patient's education needs (Paper 3)
- to evaluate the understandability and actionability of web-based education materials for patients taking non-vitamin K oral anticoagulants (NOACs) (Paper 4).

1.4. List of Publications

1.4.1 Paper 1

Angela Yiu. Beata V. Bajorek. Patient-focused interventions to support vulnerable people using oral anticoagulants: A narrative review. *Therapeutic Advances in Drug Safety* (submitted August 2018) (Chapter 2).

Candidate was the primary author, wrote and organised manuscript. Beata V. Bajorek contributed to the idea, manuscript drafting, critical review and editing of the manuscript

1.4.2 Paper 2

Angela Yiu, Beata V. Bajorek. Health Literacy and knowledge in a cohort of Australian patients taking warfarin. *Pharmacy* Practice. Vol 16, no.1, pp1-10.
DOI:10.18549/PharmPract.2018.01.1080
(published March 2018) (Chapter 3).

Candidate was the primary author, wrote and organised manuscript. Beata V. Bajorek contributed to the idea, manuscript drafting, critical review and editing of the manuscript.

1.4.3 Paper 3

Angela Yiu, Beata V. Bajorek, Dr. Vincent Lee and Kingsley Ng, Patient Feedback on a Warfarin Action Plan used in a local Australian setting. *Therapeutic Innovation and Regulatory Science* (Submitted February 2019) (Chapter 4).

Candidate was the primary author, wrote and organised manuscript. Beata V. Bajorek, Dr. Vincent Lee and Kingsley Ng contributed to the idea, manuscript drafting, critical review and editing of the manuscript.

1.4.4 Paper 4

Angela Yiu, Beata V. Bajorek, Kingsley Ng and Dr. Vincent Lee, Evaluating the understandability and actionability of web-based education materials for patients taking non-vitamin K oral anticoagulants (NOACs). *Therapeutic Innovation and Regulatory Science (*Submitted February 2019) (Chapter 5).

Candidate was the primary author, wrote and organised manuscript. Beata V. Bajorek, Kingsley Ng and Dr. Vincent Lee contributed to the idea, manuscript drafting, critical review and editing of the manuscript.

1.5. Content of Thesis

Four papers from Chapters 2,3,4, and 5, were completed in this thesis regarding medication safety with patients as the center of focus, such as patients taking high-risk oral anticoagulants.

1.5.1 Chapter 2: Patient-focused interventions for vulnerable people

The first paper was a narrative review that focused on exploring what patient-focused interventions have been reported in the literature to support certain patient populations, such as older persons, those with limited health literacy and those from CALD backgrounds.

Knowing what interventions in the literature have been useful to these patient populations with regard to the medication safety of oral anticoagulants and what has supported them is important so that they are less likely to experience medication problems, errors or harm.

A narrative review methodology was chosen to gather different types of evidence through qualitative and quantitative research (Mays, Pope & Popay 2005), to synthesize, be inclusive and provide an overview of a broad area of research.

One of the findings from this review was that written medicines information may be a useful strategy to support older persons in terms of knowledge about oral anticoagulants, however, the health literacy of the patient should be considered. Another finding was that limited research has been done to support vulnerable people taking NOACs.

1.5.2 Chapter 3: Assessing warfarin knowledge and health literacy

In the second paper, based on the findings from the narrative review, a descriptive, questionnaire-based pilot study comprising older persons was conducted in a primary care setting to assess participants' (patients' and carers') warfarin knowledge using a questionnaire based on previous literature and health literacy using the Health Literacy Questionnaire (HLQ) tool. Quantitative data were analysed using the software program IBM SPSS™ version 23.0 (SPSS Incorporation, Chicago, II, USA), and Microsoft Excel™.

The findings of this paper revealed gaps in warfarin knowledge, and the limitations of health literacy suggested that there was a need for participants to receive standardised warfarin information in an understandable format. To address this issue, a Warfarin Action Plan (WAP) leaflet was developed.

1.5.3 Chapter 4: Patient Feedback on a Warfarin Action Plan

Based on the health literacy and knowledge gaps identified from Paper 3, a WAP leaflet was developed. Patient feedback was obtained from patients and carers. The WAP promoted patient engagement and empowered patients and carers to act on the new information.

In the third paper, a concise, double-sided, A4 size written Warfarin Action Plan leaflet (WAP) was developed as an intervention which could potentially be used to support patients taking warfarin and their carers. A qualitative research design based on thematic analysis and a

pragmatic approach were used to obtain participant feedback on the WAP leaflet. This design was chosen to elicit more detailed, in-depth feedback than would have been possible through a quantitative data approach (Bradshaw, Atkinson & Doody 2017). In addition, thematic analysis has several advantages because it can be useful for examining the similarities and differences in participants' perspectives, generating unanticipated insights (Nowell et al. 2017).

One main finding of this paper was that some participants became empowered to take action using the WAP leaflet by completing the dosing record table. In addition, participants overall found the leaflet useful and liked its format. Gaps in knowledge were addressed, such as the need to carry identification about warfarin, using a card or a medic-alert bracelet. A few participants suggested other modes of communicating the key points about warfarin through the use of technology such as applications (apps) and websites.

Overall these findings confirmed that the WAP leaflet was understandable and empowered patients and carers to take action.

1.5.4 Chapter 5: Evaluating NOAC web-based materials

In response to the findings from Paper 1 and 3 and increasing trend for the use of other anticoagulants such as the NOACs, we were keen to explore whether written materials about NOACs from the World Wide Web would be understandable and actionable.\

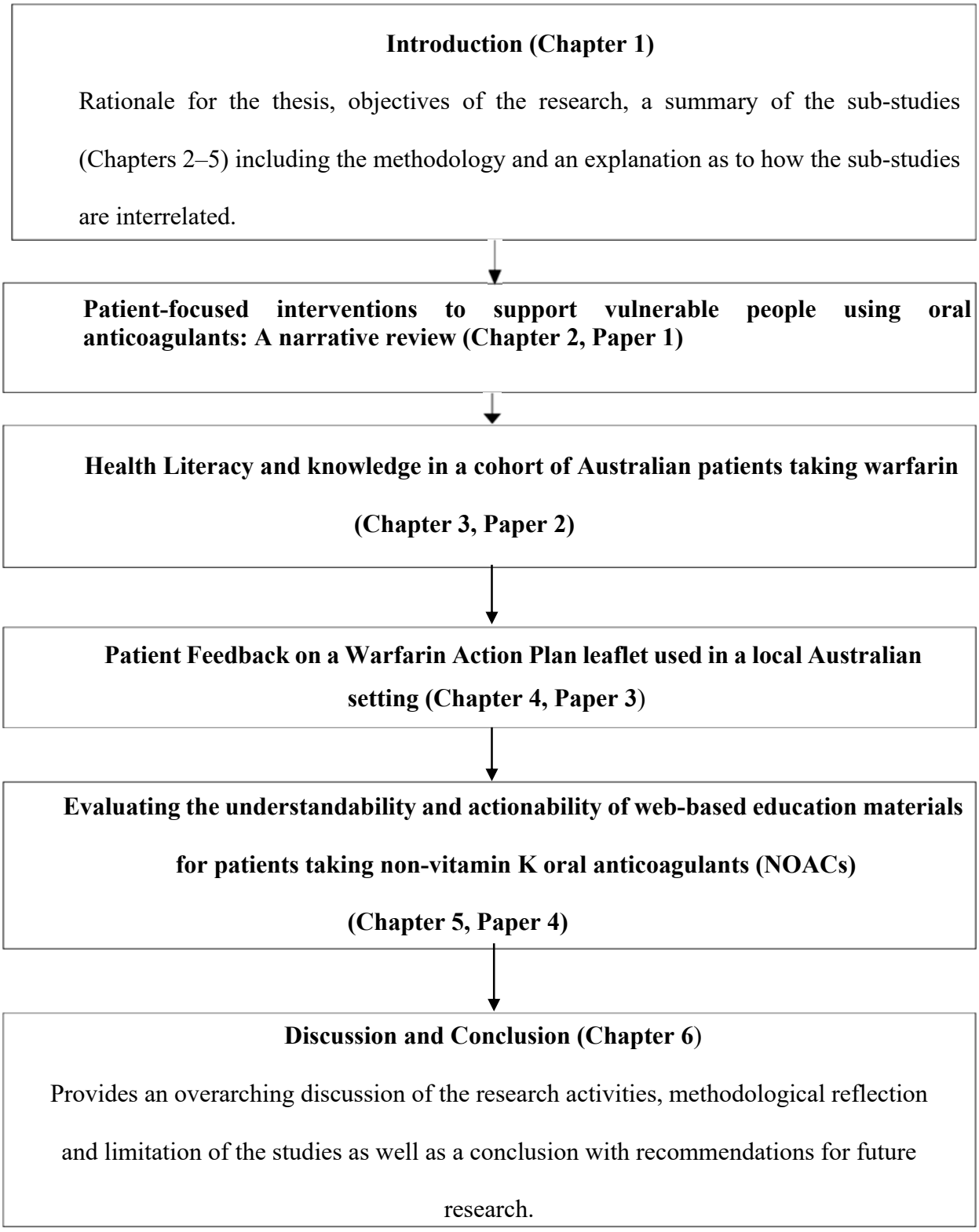
The fourth paper assessed actionability and understandability of information available on the internet about the high-alert medications, NOACs. In Australia, 88% of people aged 18-75 own or have access to a smartphone, and 78% of adults use the internet to find health-related information (Australian Institute of Health and Welfare 2018b).

Therefore, it is important to evaluate if the medicine information about the NOACs that is available on the internet is understandable, so that the patient can feel empowered to act on, and respond to, the knowledge they have acquired, to prevent medication problems or errors.

The Patient Education Materials Assessment Tool (PEMAT) was used, as it has been shown to be a reliable tool to assess the understandability and actionability of both printable material (e.g. brochures or pamphlets, or materials that can be printed from websites, such as PDFs) and audio-visual patient education materials (Shoemaker, Wolf & Brach 2014).

1.6. Organisation of the thesis

Figure 1.3 Organisation of this Thesis



Chapter 2: Patient-focused interventions

Patient-focused interventions to support vulnerable people using oral anticoagulants: A narrative review (Paper 1)

Angela Yiu and Beata V. Bajorek

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2.1. Abstract

The aim of this review was to identify patient-focused interventions that have been trialled to support vulnerable patient populations taking oral anticoagulants (warfarin and the direct-acting oral anticoagulants (DOACs)) such as older persons (65 years and over), those with limited health literacy, and those from culturally and linguistically diverse (CALD) backgrounds. This review also aimed to report on the effects of these interventions on outcomes relevant to the use of anticoagulant therapy. Original articles published between 1 January 1995 and 30 June 2017 were identified using several electronic databases such as Medline, Ovid, Embase, Scopus, Cochrane, and Google Scholar. The following terms were used for the three-tiered search: Tier 1, elderly, aged, older adult, geriatrics; Tier 2, health literacy, literacy, low health literacy, low English proficiency, patient literacy; and Tier 3, ethnicity, ethnic, ethnic groups, CALD, culturally and linguistically diverse, NESB, non-English speaking background, race, racial groups, religion, religious groups, and minority groups. The terms for each tier were combined with the following terms: anticoagulants, anticoagulation, warfarin, apixaban, dabigatran,

rivaroxaban, DOACS, new oral anticoagulants, novel oral anticoagulants, patient care, patient knowledge, comprehension, patient education, patient participation, and communication. A total of 41 studies were identified. Most of the interventions identified included older persons taking warfarin who were monitored using the international normalized ratio (INR) and who received patient education. Many interventions reported a significant positive impact on patients' knowledge, reduction in the number of adverse events caused by hemorrhage, and better INR control. More research on patient-focused interventions is needed that includes patients with limited health literacy, those from CALD backgrounds, and family members and caregivers of patients taking oral anticoagulants.

Key words:
anticoagulants, warfarin, DOACS, medication safety, elderly, health literacy, culturally and linguistically diverse, CALD, patient education, patient knowledge.

2.2. Introduction

Medication-related problems, such as unsafe medication practices and medication errors, are leading causes of avoidable harm in health-care systems throughout the world and may be serious enough to cause disability or death (World Health Organization 2017). Medication problems can occur when patients take high-alert medications, such as oral anticoagulants, which have a high risk of severe harm if used improperly (Piazza et al. 2011; Runciman et al. 2003; World Health Organization 2017). Vulnerable patient populations, such as older persons, those with limited health literacy, and those from culturally and linguistically diverse backgrounds (CALD), are at risk of experiencing medication problems for several reasons. Older persons taking anticoagulants are at risk of adverse events such as bleeding because they often have multiple comorbidities, severe chronic kidney disease, age-related functional and cognitive decline, or polypharmacy, all of which can increase their risk of clinically relevant drug–drug interactions (Bajorek 2011; Forbes & Polasek 2017).

Patients with limited health literacy are likely to have little understanding of the use of warfarin (Fang et al. 2006) and may struggle to understand written materials provided to them (Diamantouros, Bartle & Geerts 2013; Wilson et al. 2003). This can reduce their adherence and increase the risk of adverse events such as bleeding (Diug et al. 2011). In addition, patients from CALD backgrounds may have differing cultural perceptions or beliefs about prescribed treatment. Religious influences, language and communication barriers, inadequate use of interpreters, poor understanding of health-care services, and socio-economic barriers can limit their access to the health-care system (Alhomoud et al. 2013). The literature shows that patients from CALD backgrounds require information about medication to help them manage their use

of medications (Dilworth, Mott & Young 2009; El Samman et al. 2013; Mohammad, Saini & Chaar 2015). A patient-centered care approach is one way to support these vulnerable patient populations taking oral anticoagulants and to protect them from harm (Coleman et al. 2009; Coulter A et al 2013).

Several literature reviews have focused on educational, behavioral, and self-monitoring and self-management interventions for patients taking oral anticoagulant therapy (Clarkesmith et al. 2017; Clarkesmith, Pattison & Lane 2013; Heneghan et al. 2016; Nasser, Mullan & Bajorek 2012; Stacey et al. 2017; Wofford, Wells & Singh 2008). We chose to take a narrative review approach to gather different types of evidence from both qualitative and quantitative research (Mays, Pope & Popay 2005) and to synthesize this information to provide a comprehensive overview of this broad area of research. We used this narrative review approach to ensure the inclusion of full-text articles, published conference abstracts, and studies of populations with limited health literacy and CALD backgrounds. We reasoned that the information gathered from the diverse types of studies of warfarin could be applied to the design of future interventions involving direct-acting oral anticoagulants (DOACs) that are patient focused and cost effective.

The specific objectives of this review were:

1) to describe the range of interventions developed, implemented, and/or evaluated to support vulnerable patients using anticoagulant therapies (i.e., warfarin or one of the direct-acting oral anticoagulants (DOACs))
2) to report on the impact of these interventions on outcomes relevant to the use of anticoagulant therapy.

2.3. Definitions

2.3.1 Vulnerable populations

We defined a vulnerable population as those people who are at risk of medication-related problems (Alhomoud et al. 2013; Eassey et al. 2016; Forbes & Polasek 2017; Parekh et al. 2018). Studies that included the following people were included: older persons, those with limited health literacy and those from CALD backgrounds.

2.3.2 Older persons

We defined older persons as those aged 65 years or over (Orimo et al. 2006; World Health Organization 2018a).

2.3.3 Limited health literacy

The World Health Organization (WHO) defines health literacy as "the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health" (World Health Organization 2018c).

The articles identified in this review used different tools to measure the level of health literacy (Castelli et al. 2016; Collins, Barber & Sahm 2014; Machtinger et al. 2007; Schillinger et al. 2006). These included The Rapid Estimate of Adult Literacy in Medicine (REALM) tool (Davis et al. 1993) and the shortened version of the Test of Functional Health Literacy in Adults (S-

TOFHLA) (Baker et al. 1999). Newer tools such as the Health Literacy Questionnaire (Osborne et al. 2013) are available to access health literacy, however, were not identified in this review.

2.3.4 Culturally and linguistically diverse (CALD) patients

In Australia, CALD has been defined as those people born overseas in countries other than those classified by the Australian Bureau of Statistics as "main English-speaking countries". Others terms used to describe CALD include "ethnic minorities" (Alhomoud et al. 2013; Mohammad, Saini & Chaar 2015), "multicultural", "migrant", and "from a non-English speaking background" (Smith V and Schaffer E. 2014).

2.4. Method

A structured search of the literature was performed as described below.

2.5. Data sources

The following electronic databases were searched to retrieve original articles, review papers, and other publications published from 1 January 1995 to 30 June 2017: MEDLINE, Ovid, Embase, Scopus, the Cochrane Library, and the search platform Google Scholar. This time frame represents the period after which pivotal trials of anticoagulation therapy for stroke prevention in atrial fibrillation were conducted and published, which lead to an increase in the prescribing of these agents as well as exploration into the factors affecting their safe use (Clarkesmith, Pattison & Lane 2013). This time frame also incorporates the advent of alternative anticoagulants (i.e., the DOACs), which are a major focus of the current anticoagulation prescribing (Brieger et al. 2018; Steffel et al. 2018).

2.6. Search strategy and search terms

A three-tiered search strategy was used for each patient population: older persons (Tier 1); those with low literacy (Tier 2); and those from CALD backgrounds (Tier 3). The search was conducted by combining the US National Library of Medicine Medical Subject Heading terms and specific search terms related to oral anticoagulants and interventions. The following terms were used for each tier. Tier 1 included elderly, aged, older adult, and geriatrics. Tier 2 included health literacy, literacy, low health literacy, low English proficiency, patient literacy. Tier 3 included ethnicity, ethnic, ethnic groups, CALD, culturally and linguistically diverse, NESB, non-English-speaking background, race, racial groups, religion, religious groups, and minority groups. The terms used for each tier were combined with the following key words: anticoagulants, anticoagulation, warfarin, apixaban, dabigatran, rivaroxaban, new oral anticoagulants (or NOACs), novel oral anticoagulants, direct acting oral anticoagulant, DOACs, patient care, patient knowledge, comprehension, patient education, patient participation, and communication.

For the Scopus database, because of the number of articles, the term “older adult” was used from Tier 1, ethnicity from Tier 2, and all terms from Tier 3.

2.7. Selection criteria

One author performed the search to identify relevant articles. Duplicates were removed, and the articles based on titles and abstracts were screened. For all articles, (including published conference abstracts (Castelli et al. 2016; Davy et al. 2017)), the full-text version was retrieved and assessed according to the objectives of this review. The reference lists of the retrieved articles

and review articles were examined manually to identify further relevant studies not identified using the search strategy. The review procedure was verified by the co-researcher.

The studies were selected according to the following criteria: 1) involving a majority of people who were older persons (articles were limited to those including people aged 65 years and over identified using Medline and Embase), limited literacy, from a CALD background, and aged more than 18 years; 2) patient-focused interventions; 3) studies reporting the use of the oral anticoagulants warfarin and DOACs such as apixaban, rivaroxaban, and dabigatran; 4) studies reported in English; 5) original research articles; and 6) articles available in full text.

Case studies and articles without abstracts or full text were excluded. Articles that included programs supporting physicians and patients were excluded to ensure that the outcomes reported in this review reflected the impact of interventions that directly supported only patients. In addition, many studies have addressed the use of anticoagulants through the clinician's lens by focusing on interventions to optimize the use of these agents. Although this focus is important, it only partially considers the barriers to the use of anticoagulants. What is also needed is a comprehensive range of interventions to support patients' daily use of these agents and their long-term adherence. Although many resources are available in practice, few actually meet the needs of those patients who are most likely to need anticoagulation therapy but who are also more likely to experience difficulties (i.e., older persons, those with low literacy, and/or those from CALD backgrounds.

2.8. Data extraction

The following data were extracted from the included articles: author, publication year, setting, country, title of publication, trial design, type of intervention, subjects (number of patients, mean age in years, ethnicity/race, health literacy) and key findings (Table 2.1, Table 2.2 and Table 2.3).

2.9. Results

A total of 41 articles were included in the review (Figure 1). Most patient-focused interventions targeted older persons (*n*=37). For older persons, the most common intervention trialed involved monitoring of the international normalized ratio (INR) (*n*=20). Other interventions involved patient education and included written information (*n*=2), decision aids (DAs) (*n*=6), videos (*n*=3), pharmacist counselling (*n*=1), medication instructions (*n*=1), and programs with multiple components (*n*=4). Only two interventions for patients with limited health literacy and patients from CALD backgrounds were identified.

Studies about DAs included warfarin and the DOACs together, and one study incorporated a video and included the DOAC apixaban. These studies had limitations such as exclusion of non-English-speaking patients, difficulty recruiting warfarin-naïve participants, small sample size, and not being randomised controlled trials (RCTs).

2.9.1 Interventions for older persons

The main interventions to support older persons included INR monitoring (Table 2.1) and patient education through written and unwritten information (Table 2.2).

2.9.1.1. International normalised ratio (INR) monitoring for warfarin

The INR monitoring of the use of warfarin may occur through self-monitoring or patient self-management (PSM) and is important for minimizing the risk of hemorrhagic or thromboembolic complications. Self-monitoring is defined as the training of a patient to use point-of-care (POC) testing via a portable device to perform the INR test and inform their health-care provider of the result. The physician or another health-care provider uses the results obtained by the participant to adjust the anticoagulant dose as needed. PSM is defined as the patient obtaining INR values directly according to a predetermined dose–INR schedule and adjusting the warfarin dose independently (Grunau, Wiens & Harder 2011; Heneghan et al. 2016).

This review found that various INR monitoring models were beneficial in supporting older persons. These included POC testing (*n*=10) (Amruso 2004; Harrison, Shaw & Harrison 2015; Hodge et al. 2008; Jackson et al. 2004; Jackson et al. 2005; Khan et al. 2004; Matchar et al. 2010; Shaw & Harrison 2014; Stafford et al. 2011; Stafford et al. 2012) led by pharmacists in the community (Amruso 2004; Harrison, Shaw & Harrison 2015; Shaw & Harrison 2014) and in rural (Hodge et al. 2008) and home (Jackson et al. 2004; Stafford et al. 2011; Stafford et al. 2012) settings, along with home self-monitoring (*n*=2) (Khan et al. 2004; Matchar et al. 2010); telemonitoring using venipuncture testing (*n*=6) (Hassan et al. 2013; Levine, Shao & Klein 2012; Taylor et al. 1997; Waterman et al. 2001; Witt et al. 2005; Wittkowsky et al. 2006) led by a multidisciplinary team [45], pharmacists (Witt et al. 2005; Wittkowsky et al. 2006), and nurses (Hassan et al. 2013; Levine, Shao & Klein 2012; Taylor et al. 1997); and PSM using venipuncture

testing (*n*=3) through the use of nomograms (Grunau, Wiens & Harder 2011), a dosing algorithm (Jenner et al. 2015), or an online messaging system (Simmons et al. 2012).

However, some of these models of INR monitoring were beneficial only for certain patients. POC testing was suitable for patients who had limited access to an anticoagulant clinic (Matchar et al. 2010; Wittkowsky et al. 2006), for those with erratic INR control, and for frail people with a caregiver who could assist by performing the test at home (Khan et al. 2004; Matchar et al. 2010; Wittkowsky et al. 2006). PSM using venipuncture-acquired INR monitoring was shown to be feasible and suitable for those patients with stable INR control (Simmons et al. 2012), who had a preference for PSM over physician management (Grunau, Wiens & Harder 2011), and who were comfortable changing the warfarin dose on their own (Jenner et al. 2015).

Only two studies were RCTs that found benefits of education, home self-monitoring (Khan et al. 2004), and the role of a pharmacist follow-up service after discharge that included home monitoring (Jackson et al. 2004) in supporting older persons. Most of the other studies were prospective or observational.

2.9.1.2. Decision aids

The most commonly reported patient-focused intervention that included both warfarin and DOACs was the use of DAs (*n*=6) (Fatima et al. 2016; Holbrook et al. 2007; Hong et al. 2013; Man-Son-Hing et al. 1999; McAlister et al. 2005; Thomson et al. 2007). DAs can support patients by making their decisions explicit, providing information about options and associated benefits/harms, and helping to clarify congruence between decisions and personal values (Stacey et al. 2017). Three of the six articles identified were RCTs (Man-Son-Hing et al. 1999; McAlister et al. 2005; Thomson et al. 2007) (Table 2.2).

One prospective study (*n*=81) had the objective of validating a DA to assist patients in choosing between antithrombotic agents for AF (Fatima et al. 2016). This validated DA was unique because it presented and compared information between all antithrombotic treatment options for atrial fibrillation, such as warfarin and DOACs, was accessible for clinical use through a website, and was developed using the standard criteria of the International Patient Decision Aid Standards (Fatima et al. 2016). It also involved pretesting to refine the DA, which indicates that it was tailored to the needs of older persons (Fatima et al. 2016). The DA presented descriptions related to atrial fibrillation and charts depicting important outcomes for comparisons between: 1) no treatment, aspirin, and anticoagulants; 2) warfarin versus DOACs; and 3) dabigatran, rivaroxaban and apixaban (Fatima et al. 2016).

Overall, the DAs were available in a variety of formats such as paper booklets (Fatima et al. 2016; Hong et al. 2013), decision board (Holbrook et al. 2007), computerized DA (Thomson et al. 2007), and a combination of formats, such as a decision booklet with audiotape (Holbrook et al. 2007; Thomson et al. 2007), a 29-page paper booklet with a personal worksheet, and a 20-minute audiotape that guided the patient through the booklet and worksheet (Man-Son-Hing et al. 1999). One DA contained a graphic presentation of outcome probability data for the benefits and harms as a pie chart or pictogram (Holbrook et al. 2007).

2.9.1.3. Videos

Three studies trialed the use of videos as a format for educating older persons taking warfarin (Mazor et al. 2007; Moore et al. 2015) and the DOAC apixaban (Giuliano, Nofar & Edwin 2017). One study (*n*=40) showed that, compared with face-to-face counselling, informational videos coupled with teach-back questions significantly reduced pharmacist time spent on anticoagulation counselling on discharge without compromising short-term patient

comprehension, primarily in patients with prior warfarin use. However, this study found a nonsignificant reduction in patients using warfarin for the first time (Moore et al. 2015). Another study reported that the use of narrative evidence in the form of patient anecdotes was more effective than statistical evidence on certain outcomes, such as beliefs about the importance of laboratory testing, and on knowledge when baseline knowledge was included as a covariate (Mazor et al. 2007).

Educational videos that are indication-specific may improve short-term knowledge (less than 6 months) (Giuliano, Nofar & Edwin 2017). However, the studies involving videos did not specifically target older persons in their inclusion criteria and did not explain whether the target population was involved in the development of the videos. This suggests that the videos may not have acknowledged the needs of older persons and that the videos may not have been tailored to their needs.

2.9.1.4. Written information

Two studies in the United Kingdom (UK) (Fairbairn-Smith et al. 2011; Lane et al. 2006) showed that patient information booklets significantly improved older person's knowledge, such as the ability to name side effects of warfarin and to describe what would happen to their INR after omitting a dose of warfarin (Fairbairn-Smith et al. 2011), the target INR range, and factors that may affect INR level. The limitations of one study included a lack of patients' perceptions on the usefulness of the booklet and that only 33 (35.5%) of patients were able to complete the follow-up questionnaire (Lane et al. 2006).

The studies that described the use of booklets had several limitations. The development of the booklets was not explained, which suggests that the authors did not tailor the booklets according

to the needs of the participants. Although one booklet (Lane et al. 2006) significantly improved patients' knowledge of the target INR and factors that may affect INR levels, it had little effect on awareness of the bleeding risks associated with anticoagulants. In addition, patients' perceptions of the value of the booklets were not determined.

2.9.1.5. Pharmacist counselling

Before hospital discharge, pharmacists play an important role in educating patients about their medications through counselling. One study highlighted the importance of pharmacists educating patients about the critical information for warfarin counselling and the need for regular counselling sessions (Masnoon, Sorich & Alderman 2016). One limitation of this study was its small sample size (*n*=22).

2.9.1.6. Medication instructions

Another intervention involved giving patients instructions about medication use by either a physician or nurse, plus a pharmacist after the patient had filled the prescription for warfarin (Metlay et al. 2008). These patients had a reduced risk of experiencing hospitalization because of warfarin-related bleeding over the next 2 years. The instructions may have included statements such as things the patient should and should not do when taking the medication; written or spoken instructions; and instructions received from the doctor, nurse, or pharmacist (Metlay et al. 2008).

Overall, although most studies targeted older persons, only six studies specifically targeted this population in their inclusion criteria and rationale: two programs (Beyth, Quinn & Landefeld 2000; Mitchiner et al. 2012), one INR monitoring intervention (Khan et al. 2004), two DAs (Holbrook et al. 2007; Hong et al. 2013), and a medication instruction intervention (Metlay et al. 2008). Older persons were targeted because they are at increased risk of unstable control of

anticoagulation (Khan et al. 2004) and warfarin-related bleeding complications (Beyth, Quinn & Landefeld 2000) or because they are representative of the population with atrial fibrillation for whom anticoagulation is recommended to prevent strokes (Holbrook et al. 2007; Hong et al. 2013). Older persons are also at significantly greater risk of an adverse drug event compared with younger patients (Mitchiner et al. 2012). One study (Metlay et al. 2008) did not mention the reason for targeting older persons , although it highlighted the importance of patients taking warfarin receiving medication instructions from a physician or nurse and a pharmacist because those patients who could recall receiving instructions had a lower rate of warfarin-related hospitalization for bleeding (Metlay et al. 2008). These studies did not describe the development of the interventions and therefore may not have tailored the interventions to the needs of older persons.

2.9.1.7. Programs with multiple components

One RCT (Beyth, Quinn & Landefeld 2000) evaluated a program with multiple components, including patient education and training to self-monitor their INR levels. Another RCT (Clarkesmith et al. 2013) evaluated a complex educational-behavioral intervention to support older persons taking oral anticoagulants. Another program (n=97) was unique because it was theory driven and was based on the relevant current literature and clinical guidelines (Clarkesmith et al. 2016); it also involved the patients during the development of the intervention and had a multidisciplinary process involving patients, psychologists, and cardiologists (Clarkesmith et al. 2013). The program was compared with usual care, which comprised a standard yellow booklet and included an “expert patient”-focused DVD based on patient narratives, along with an educational booklet, self-monitoring diary, and worksheet. Critical elements in the development process included the use of clinical guidelines, appropriate theoretical models, patient input, and appropriate evaluation tools (Clarkesmith et al. 2016;

Clarkesmith et al. 2013). One result of this program was that 12 months after the initiation of warfarin, there was no significant difference in the time spent within the target INR range (TTR) between the intervention and control groups. This lack of difference suggested that the program needs to be repeated at regular intervals to refresh information and reinforce behavioural changes (Clarkesmith et al. 2016). The limitations of this study are its small sample size, noting that 234 (36.2%) eligible patients declined to participate because of the questionnaire burden and a large proportion of the sample failed to complete all questionnaires at every time point. The number of participants declining was higher than anticipated resulting in only 97 patients in total being recruited (Clarkesmith et al. 2013).

Other programs included a patient education campaign that involved toolkits with large print booklets, posters, bookmarks, pamphlets, and postcards (Mitchiner et al. 2012). Another program included personalized therapeutic information, including phone calls on days 15, 30, and 45, paper booklets offerings and websites suggestion (Davy et al. 2017).

2.9.2 Interventions for patients with limited health literacy

2.9.2.1. Hospital pharmacist counselling with a booklet

One study (n=34) trialled the use of hospital pharmacist counselling and a warfarin booklet (Collins, Barber & Sahm 2014); 39.5% of patients (n=17) in this study had limited health literacy (Table 2.3). The intervention significantly improved warfarin knowledge within 24 hours of verbal counselling (Collins, Barber & Sahm 2014). However, the knowledge score decreased significantly after 28 to 56 days of counselling (Collins, Barber & Sahm 2014).

2.9.2.2. Rivaroxaban patient assistance kit (R-PAK)

Another study, a prospective RCT (n=25), trialled the effect of a R-PAK with pharmacist counselling for patients discharged with rivaroxaban compared with the standard rivaroxaban group who were discharged with no kit. The aim was to determine whether the use of the kit increased proper dose transition and overall patient adherence. Proper transition to daily administration on day 22 did not differ between the groups, and adherence did not differ between the R-PAK patients and those patients taking rivaroxaban with no discharge kit (Castelli et al. 2016). However, in that study, health literacy was assessed based on a single-item health literacy screening tool. Most patients stated they rarely or never required help to read instructions, pamphlets, or other written materials from their doctor or pharmacy, meaning that their rate of health literacy was high (Castelli et al. 2016).

The authors of these two studies specifically targeted patients with limited health literacy because they are more likely to have little knowledge about warfarin, an increased risk of bleeding complications, and may not understand patient educational brochures about anticoagulants (Castelli et al. 2016; Collins, Barber & Sahm 2014). Furthermore, DOACs such as rivaroxaban have a short half-life, which requires a change in medication dosage and frequency on day 22 to prevent venous thromboembolism. This may increase the risk of patient error, especially for patients with limited health literacy (Castelli et al. 2016). The development of the visual aid, booklet, and R-PAK was not described, which suggests that these interventions may not have been tailored to the needs of those with limited health literacy despite the intentions of the authors.

A limitation of these health literacy studies was that they assessed health literacy using different tools and that most of the patients had an adequate (Machtinger et al. 2007; Schillinger et al. 2006) or high level of health literacy (Castelli et al. 2016).

2.9.3 Interventions for patients from CALD backgrounds

Two studies showed that the use of a visual aid (Machtinger et al. 2007; Schillinger et al. 2006) and a mobile health application (Lee et al. 2016) supported patients from a CALD background group by improving their anticoagulation control more rapidly than that observed in control subjects (Machtinger et al. 2007) and increased their knowledge of warfarin therapy (Lee et al. 2016) (Table 2.3).

2.9.4 Visual aids

Visual aids (Machtinger et al. 2007; Schillinger et al. 2006) have been used to specifically target patients from CALD backgrounds and those with limited health literacy. The visual aids were used to overcome potential communication and language barriers in this target group and to thereby reduce or prevent nonadherence and ensure clinician–patient concordance with the prescribed warfarin regimen.

In a prospective cohort study (n=220), English-speaking and Spanish-speaking patients from varied cultural backgrounds were asked to verbally indicate their weekly warfarin regimen and to identify this regimen from a digitized color menu of warfarin pills (Schillinger et al. 2006). Health literacy was assessed using the S-TOFHLA, the shortened form of a test of functional health literacy in adults (Baker et al. 1999).

Another RCT (*n*=147) (Machtinger et al. 2007) evaluated the use of a computer-generated visual medication schedule of digitized images of the patient's warfarin regimen printed on a 7-day calendar in combination with a brief 2-minute "teach-back" session (Machtinger et al. 2007). The visual schedule was translated into Spanish and Cantonese. The study found that CALD patients benefitted from the translated texts. Patients were categorized as having regimen concordance if there was no patient–clinician discrepancy in the total weekly dosage of warfarin (Machtinger et al. 2007).

2.9.5 Mobile health application

One study of the use of a mobile health application for patients from CALD backgrounds and older persons found that the mobile application may enhance self-management skills in terms of medication adherence and self-care with anticoagulation therapy (Lee et al. 2016). These patient groups were specifically targeted because they may struggle following a multicomponent treatment regimen that may affect their diet and activities. In addition, adherence of patients from CALD backgrounds, such as older Hispanic people, has been shown to be poor because of inadequate knowledge about warfarin therapy, especially about Latin foods containing a high amount of vitamin K (Lee et al. 2016). This intervention was tailored to the needs of older persons by having a simple layout, large navigation buttons and a component ("Message to tell doctors") to increase effective communication with their doctor on matters such as INR results, medication reminders, and symptom monitoring (Lee et al. 2016). It was also tailored to CALD participants by allowing them to invite family members, including grandchildren or daughters, to the training sessions and by providing a list of foods that Hispanic people commonly eat, along with data from the U.S. Department of Agriculture on the amounts of vitamin K in foods (Lee et al. 2016).

2.9.6 Interventions that included a combination of patient populations

Four studies included patient populations with several characteristics. One study that involved pharmacist counselling included older persons with limited health literacy (Collins, Barber & Sahm 2014). Two studies describing the use of visual aids included CALD populations with limited health literacy (Machtinger et al. 2007; Schillinger et al. 2006). One study that evaluated a mobile health application included older English-speaking and Spanish-speaking people (Lee et al. 2016).

2.10. Comparison of the impact of patient-focused interventions on outcomes

A variety of outcomes were assessed after the interventions. These included knowledge, anticoagulation control, adverse effects, decisional conflict, mortality, QOL, and patient satisfaction and persistence with warfarin therapy.

2.10.1 Impact on knowledge

Most interventions were effective in improving knowledge. These interventions included DAs (Fatima et al. 2016; Holbrook et al. 2007; Hong et al. 2013; Man-Son-Hing et al. 1999; McAlister et al. 2005; Thomson et al. 2007), written information (Fairbairn-Smith et al. 2011; Lane et al. 2006), a program (Clarkesmith et al. 2013), a video (Giuliano, Nofar & Edwin 2017), patient education by a pharmacist (Masnoon, Sorich & Alderman 2016; Stafford et al. 2012) and a mobile health application (Lee et al. 2016). Several DAs significantly improved knowledge about warfarin (Fatima et al. 2016; Holbrook et al. 2007; Hong et al. 2013; Man-Son-Hing et al. 1999; McAlister et al. 2005). One RCT (n=98) conducted in Canada reported significant improvements

in the mean knowledge score for atrial fibrillation, treatment options, and outcomes regardless of the format or graphic presentation of the DA (Holbrook et al. 2007). The intervention with the longest follow-up was conducted in an anticoagulation clinic (*n*=24) and showed that after 6 months of using a written booklet, patients' knowledge about the side effects of warfarin and the consequences of a missed dose of warfarin on the INR increased significantly (Fairbairn-Smith et al. 2011). In a RCT lasting 6 months (*n*=97), the educational intervention comprising a DVD with patient narratives, educational booklet, self-monitoring diary, worksheet, and a group discussion, knowledge scores significantly predicted TTR (Clarkesmith et al. 2013).

An intervention using a mobile health application showed a significant increase in anticoagulation knowledge from the baseline to the 3-month follow-up for participants taking warfarin (Lee et al. 2016). An intervention including a video about apixaban produced a significant improvement in knowledge about apixaban from before to immediately after the intervention; however, there was no significant change in knowledge at 1-month after the intervention or at the follow-up. The study also found that the scores were less likely to improve in patients who had previously received apixaban or another anticoagulant compared with new patients (Giuliano, Nofar & Edwin 2017).

Some of these studies had several limitations. The time frame for the decrease in knowledge retention varied from 28 days (Collins, Barber & Sahm 2014) to 6 weeks (Masnoon, Sorich & Alderman 2016) or 3 months (Stafford et al. 2012). The content of knowledge provided to educate patients and the instruments used to measure knowledge varied between studies, and this may have influenced the outcomes. The main topics for patient education included the indications and duration of warfarin use, dosing, administration time and actions in the event of missed doses, target INR range, side effects, interactions with other drugs and herbs, and lifestyle issues such as alcohol and diet. Knowledge improved in several areas, such as the purpose of the

medication and the identification of adverse effects (Fairbairn-Smith et al. 2011; Giuliano, Nofar & Edwin 2017; Masnoon, Sorich & Alderman 2016), patients' understanding of when to seek emergency attention (Giuliano, Nofar & Edwin 2017), management of missed doses (Fairbairn-Smith et al. 2011; Giuliano, Nofar & Edwin 2017), and target INR range (Fairbairn-Smith et al. 2011). The instruments used for some studies (Collins, Barber & Sahm 2014; Masnoon, Sorich & Alderman 2016; Moore et al. 2015; Stafford et al. 2012) included the Oral Anticoagulation Knowledge test (Zeolla et al. 2006), the Anticoagulation Knowledge Assessment tool (Briggs et al. 2005), and a tool described by Taylor et al. (Taylor et al. 1994).

2.10.2 Impact on anticoagulation control (INR Monitoring)

Most studies that showed a significant improvement in anticoagulation control, as indicated by the TTR, involved POC testing (Harrison, Shaw & Harrison 2015; Hodge et al. 2008; Jackson et al. 2004; Khan et al. 2004; Matchar et al. 2010). One unique finding from one RCT (n=125) (Khan et al. 2004), was the benefits of education alone in improving TTR. Other interventions that found a significant improvement in anticoagulation control included a written information booklet (Fairbairn-Smith et al. 2011), programs (Beyth, Quinn & Landefeld 2000; Clarkesmith et al. 2013), and a telemonitoring service led by pharmacists (Witt et al. 2005). Another RCT (n=147) showed that patients using a computer-generated visual medication schedule achieved anticoagulation control more rapidly than control subjects (Machtinger et al. 2007). The benefit of the intervention was significant for patients with baseline regimen discordance but not for those with baseline concordance (Machtinger et al. 2007).

2.10.3 Impact on adverse effects such as hemorrhagic or thromboembolic complications

Two studies involved a post-discharge home-based service by a pharmacist, which comprised point-of-care (POC) INR monitoring, warfarin education (Jackson et al. 2004; Stafford et al. 2011), and a home medicines review (Stafford et al. 2011). These interventions reduced the rate of adverse effects of warfarin. One of these studies was a randomised controlled cohort study (*n*=129) (Stafford et al. 2011), which found that the inclusion of a post-discharge service was associated with significantly lower rates of combined major and minor hemorrhagic events at 8 days post-discharge and up to 90 days post-discharge compared with usual care (*n*=139). In addition, the rate of combined hemorrhagic and thrombotic events to day 90 was also significantly lower, and persistence with warfarin therapy improved significantly. The second open-label RCT (*n*=128) showed a significantly lower rate of bleeding events 3 months after discharge in the intervention group compared with patients in usual care. Other studies included two PSM programs (Grunau, Wiens & Harder 2011; Simmons et al. 2012), POC testing (Khan et al. 2004; Matchar et al. 2010), telemonitoring (Witt et al. 2005; Wittkowsky et al. 2006), and a multicomponent program that included patient education about warfarin, training to increase patient participation in their care, self-monitoring of prothrombin time using a portable home monitor and guideline-based management of warfarin dosing (Beyth, Quinn & Landefeld 2000).

2.10.4 Impact on Decisional conflict

Most of the DAs assisted older persons with becoming more confident and comfortable with their treatment decision (Fatima et al. 2016; Holbrook et al. 2007; Hong et al. 2013; McAlister et al. 2005; Thomson et al. 2007). However, in a recent Cochrane review (Clarkesmith et al. 2017), data from two trials were pooled, and the random-effects analysis favored usual care in terms of reducing decisional conflict (Man-Son-Hing et al. 1999; McAlister et al. 2005).

Decisional conflict has been measured using a variety of tools, which makes it difficult to compare the outcomes. In one review (O'Neill et al. 2017), some of the studies reported decisional conflict outcome using the p-value (Man-Son-Hing et al. 1999; McAlister et al. 2005; Thomson et al. 2007), whereas other studies reported no p-value (Holbrook et al. 2007; Hong et al. 2013).

In contrast to other reviews (Clarkesmith et al. 2017; O'Neill et al. 2017), our review found one new study on a DA (Fatima et al. 2016). This study reported a low decisional conflict score of 7.2 [SD 10.8] on a scale of 1 to 100, which suggested that participants felt informed, clear about their values, supported and certain when making a decision (Fatima et al. 2016). Another finding of this study was that there was no significant correlation between the years of education and total Decision Conflict Scale score (Fatima et al. 2016). In addition, our review included one study (Thomson et al. 2007) that was excluded from a meta-analysis (Clarkesmith et al. 2017) because it did not have a usual care arm. This study found a significant decrease in decisional conflict in the computerized decision aid group immediately after a shared decision-making clinic compared to the evidence-based paper guidelines applied as direct advice.

2.10.5 Impact on mortality and quality of life (QOL)

Three studies measured mortality and showed no impact on mortality compared with the control group or comparison group (Beyth, Quinn & Landefeld 2000; Matchar et al. 2010; Stafford et al. 2011). Three studies (Clarkesmith et al. 2013; Khan et al. 2004; Matchar et al. 2010) measured QOL as an outcome. One program (Clarkesmith et al. 2013) showed that QOL increased in the intervention group at the 1-month follow-up but not at 12 months. The second study (Matchar et al. 2010) showed small but significant improvement in QOL at the 2-year follow-up only in the

patient group that undertook home monitoring with the self-testing. The third study (Khan et al. 2004) showed no change in QOL apart from the emotional role limitation (i.e. limitation in usual role activities because of emotional problems), however, the authors stated that this result was probably due to chance.

2.10.6 Impact on other outcomes

2.10.6.1. Patient satisfaction

Older persons expressed patient satisfaction with several interventions such as INR monitoring, DAs and videos. These included INR monitoring by pharmacists in an anticoagulation clinic (Amruso 2004), community pharmacy (Shaw & Harrison 2014), and rural pharmacy settings (Jackson et al. 2005),, and by a multidisciplinary telemonitoring service (Waterman et al. 2001). The patients in these studies were satisfied with the accessibility of the service (Shaw & Harrison 2014), convenience (Shaw & Harrison 2014), time saved, immediacy of the blood test results and dose (Shaw & Harrison 2014; Waterman et al. 2001), and monitoring service by a pharmacist (Amruso 2004; Jackson et al. 2005). Patients were also satisfied with the DAs (Fatima et al. 2016; Holbrook et al. 2007; Hong et al. 2013) and a video about apixaban (Giuliano, Nofar & Edwin 2017). Older participants and those from CALD backgrounds reported they were generally satisfied with the intervention using a mobile health application because of its ease of use and usefulness (Lee et al. 2016).

2.10.6.2. Beliefs about medication and persistence with warfarin therapy

In a study of older persons, the group given a theory-driven educational intervention group was significantly more likely to view medication as less harmful than the usual care group, and patients' perceptions of general harm predicted TTR at 6 and 12 months (Clarkesmith et al.

2013). In addition, persistence with warfarin therapy improved significantly in patients using a collaborative home-based, post-discharge warfarin management service (Stafford et al. 2011) (*n*=129).

2.10.6.3. Verbal and visual concordance, and patient provider concordance

CALD patients and patients with limited health literacy were categorized as having verbal concordance if there was no patient–clinician discrepancy in the total weekly dosage of warfarin when the patient verbalized the regimen. Patients were categorized as having visual concordance if there was no patient–clinician discrepancy in the total weekly warfarin dosage when the patient identified the regimen from the digitized pill menu or a visual aid (Schillinger et al. 2006). In this study that was conducted in an anticoagulation clinic at a San Francisco hospital, shifting from verbal to visual modes was associated with greater patient–provider concordance across all patient subgroups and especially for those with communication barriers such as Cantonese speakers. Clinician–patient discordance regarding the patients' warfarin regimen was common but occurred less frequently when patients used a visual aid (Schillinger et al. 2006). Another study conducted in the USA involved patients of various ethnicities ((*n*=147, Asian (40%), White (31%), Hispanic (17%), and Black (12%)) with poor anticoagulant control, most of whom had limited health literacy. Use of a visual medication schedule combined with brief counselling reduced the time to anticoagulation control (Machtinger et al. 2007).

Overall, most interventions did not specifically seek to include vulnerable patient groups as part of their recruitment process. Most of the interventions were not tailored to address the needs of each vulnerable patient group, and most of the authors failed to acknowledge the needs of each group or to describe the development of the interventions. Nonetheless, these studies were

included according to this review's search criteria because we felt that the lessons learned from their strategies could be applied to vulnerable patient groups in future studies.

Only a few interventions specifically targeted vulnerable patient populations based on the inclusion criteria and rationale of their studies. Of these studies, only one described how the intervention was developed and considered the participants' needs by tailoring the intervention to address them (Lee et al. 2016). The interventions that specifically targeted older persons included two programs (Beyth, Quinn & Landefeld 2000; Mitchiner et al. 2012); one INR monitoring intervention (Khan et al. 2004); decision aids (Holbrook et al. 2007; Hong et al. 2013) (one of which ensured that at least half the sample would be 65 years or older (Hong et al. 2013)); and a mobile health application that included participants who were 55 years and older (Lee et al. 2016). Other interventions specifically targeted patients with limited health literacy; these included pharmacist counselling with a booklet (Collins, Barber & Sahm 2014) and a rivaroxaban patient assistance kit (Castelli et al. 2016). Visual aids (Machtinger et al. 2007; Schillinger et al. 2006) specifically targeted patients with limited health literacy and those from a CALD background. In addition, the mobile health application (Lee et al. 2016) also specifically targeted both older persons and patients from CALD backgrounds.

2.11. Discussion

This review describes a range of interventions to support vulnerable patient groups taking anticoagulants such as warfarin or a DOAC and identifies the outcomes of these interventions when used with anticoagulant therapy. This review revealed several important findings.

We found that more interventions had been trialled to support older persons compared with those with limited literacy and from CALD backgrounds. Some of these interventions were

comprehensive multimodal programs that were successful. By contrast, a significant finding of this review was that fewer studies have focused on supporting patients with limited health literacy and patients from CALD backgrounds; such studies were also simpler and, in most cases, unidimensional. Moreover, it was difficult to determine which intervention was the best because of differences in methodology. Some of the interventions differed in their advantages and disadvantages and were suitable for certain patients only.

Another interesting finding was that few interventions specifically targeted vulnerable patient groups in their inclusion criteria and rationale. We identified only six studies (Beyth, Quinn & Landefeld 2000; Holbrook et al. 2007; Hong et al. 2013; Khan et al. 2004; Metlay et al. 2008; Mitchiner et al. 2012) describing interventions that specifically targeted older persons and two studies of interventions that specifically targeted those with limited health literacy (Castelli et al. 2016; Collins, Barber & Sahm 2014). The findings from one study (Collins, Barber & Sahm 2014) highlight the importance of assessing health literacy because of the positive correlation between health literacy and warfarin knowledge. This relationship between health literacy and knowledge was also highlighted in one study of patients with hypertension (Osborn et al. 2011). The authors concluded that it is important to ensure health education interventions are literacy sensitive because patient knowledge can link health literacy to self-efficacy, self-care and health outcomes for patients (Osborn et al. 2011).

Only three studies of interventions have specifically targeted several vulnerable patient populations at the same time, such as patients from CALD backgrounds and older persons with chronic diseases who were taking warfarin (Lee et al. 2016) or patients from CALD backgrounds and those with limited health literacy (Machtinger et al. 2007; Schillinger et al. 2006). These findings suggest that there is a need for more interventions that specifically target vulnerable patient populations.

This review also identified studies describing interventions that did not specifically target vulnerable patient populations groups; however, we included these according to our search criteria. The advantage of some of these reports was that they described how the interventions were developed according to patients' needs, meaning that they were tailored to address those needs. For example, a paper that describes a unique and successful multicomponent program (Clarkesmith et al. 2013) revealed how it was developed using critical elements such as patient input to tailor it to the needs of older persons. The beneficial impact of this program on outcomes such as knowledge and anticoagulation control suggest that future programs to support vulnerable patient groups should be developed based on a similar process, albeit with regular and long-term follow-up and repetition at regular intervals.

Another program provided personalized therapeutic information that supported older persons and found improved drug persistence with the DOAC rivaroxaban. This result may have occurred because the program prevented less compliant patients from stopping taking DOACs for futile reasons. The authors suggested that these patients should be the target of educational programs (Davy et al. 2017).

This review also identified a DA that was unique because it included all antithrombotic choices (i.e., warfarin and the DOACs) and was tailored to the needs of older persons (Fatima et al. 2016). The advantages of including all treatment choices are that the DA can assist patients who may have felt overwhelmed by having to decide on one treatment and it allows older persons to become engaged in shared decision-making with their doctor to help them select the most suitable anticoagulant in a systematic way, in alignment with their values and preferences (National Institute for Health and Care Excellence (NICE) 2018b). Similar to another review

(Stacey et al. 2017), we found that DAs improved older persons' knowledge about oral anticoagulants, helped participants feel informed and clear about their values and supported when making a decision. The implications of our findings suggest that future DAs should be developed in a similar way with the same features. However, although studies of DAs were beneficial in improving older persons' knowledge of the oral anticoagulants and confidence with their treatment decisions, one study reported a limitation: when the names of the treatment options were revealed, it was clear that some participants had chosen a less effective treatment (aspirin instead of warfarin) (Holbrook et al. 2007). The authors of this study suggested that, to optimize treatment, it is important for clinicians to allow patients time to express their preferences and rationale for treatment options at the time of prescribing (Holbrook et al. 2007).

Similar to the unique DA, this review also found a paper that described video that included the DOAC, apixaban, to support older persons (Giuliano, Nofar & Edwin 2017). The advantages of videos in supporting older persons are the ability to increase patients' knowledge about oral anticoagulants, to strengthen their beliefs in the importance of laboratory testing and the benefits of taking warfarin, to convey a large amount of complex information, to be watched several times at home with the family, and to be helpful to those patients who have difficulty reading written material, such as people with limited health literacy and from CALD backgrounds who cannot read English (Mazor et al. 2007). Considering similar findings noted in another review (Nasser, Mullan & Bajorek 2012), we suggest that videos should incorporate narrative evidence such as patient anecdotes into physician–patient dialogues or educational materials to increase the effectiveness of the message (Mazor et al. 2007). One of the potential problems of using a video is that knowledge may not be retained beyond 1 month, which is problematic because many patients, such as older persons with chronic atrial fibrillation, need to take oral anticoagulants

beyond 1 month. In addition, patients may not be motivated or empowered to watch the video again after discharge from the hospital (Giuliano, Nofar & Edwin 2017).

Several INR monitoring models were also identified to support older persons who take warfarin. The advantage of using POC INR measuring devices to support older persons in self-testing compared with venous plasma testing is that it allows for more frequent home monitoring of the INR through weekly self-testing (Khan et al. 2004). This in turn can lead to better anticoagulation control, better dosage advice, and improved concordance (Khan et al. 2004). POC INR monitoring promotes patient engagement in their own care and may improve clinical outcomes because out-of-range INR values can be identified and treated more quickly (Matchar et al. 2010). However, there are some disadvantages in using POC INR monitoring devices, including the resources required for extensive training of nurse clinicians or specialized physicians, cost of test strips, fear of self-testing or needles, and difficulty learning the technique to perform the test (Grunau, Wiens & Harder 2011; Khan et al. 2004).

Another model that used technology to support older persons with INR monitoring was telephone anticoagulation services. Studies using this model reported benefits such as accessibility, convenience, follow-up via the telephone for patients unable to present in person to an anticoagulation clinic, patient satisfaction, and improved clinical outcomes such as fewer anticoagulation complications (Wittkowsky et al. 2006). A telephone service also allows for a large number of patients to be managed by a few anticoagulation providers over a wide geographic area (Witt et al. 2005), in the home setting (Hassan et al. 2013), and in the anticoagulation clinic setting (Wittkowsky et al. 2006). However, some of these studies were limited because they were not RCTs and did not measure outcomes such as medical costs (Waterman et al. 2001; Wittkowsky et al. 2006).

In some PSM models using venipuncture, older persons were able to review their INR laboratory results on the same day the test was performed and communicate with health-care practitioners using a secure online messaging system, My Health Manager (Jenner et al. 2015; Simmons et al. 2012). These models have several advantages: the prompt receipt of INR results, unlike in other studies, in which INR results were communicated to patients in person or via mail (Grunau, Wiens & Harder 2011); no additional costs for finger-stick monitoring devices and testing strips; and no need to acquire the skill necessary to perform finger-stick INR tests (Simmons et al. 2012).

Another finding of our review was the beneficial role of multidisciplinary teams and allied health professionals in supporting older persons across different health-care settings and during the transition of care between settings. Examples include pharmacist-led INR monitoring in collaboration with general practitioners (Jackson et al. 2004; Stafford et al. 2011), post-discharge warfarin services, and pharmacist-led education (Masnoon, Castelli 2016) during the transition of care from the hospital to the home setting. The advantage of using pharmacists for INR monitoring and patient education is that they are conveniently located in a variety of health-care settings such as the community, hospital, and home, and during transitions of care, which can optimize patient safety. Providing support to vulnerable patients during transitions of care is important because as noted the WHO, patients are at increased risk of medication errors during this time (World Health Organization 2017).

Several authors have suggested that some INR monitoring models are suitable for certain older persons. POC testing and telephone-based management models can be considered for older persons who do not wish to travel or have difficulty traveling to an anticoagulation clinic,

particularly those with erratic INR control who require frequent monitoring, frail people with a caregiver who could perform the test at home (Khan et al. 2004), and those limited by physical disability and geographic distance (Matchar et al. 2010; Wittkowsky et al. 2006), such as people in rural or remote settings (Jackson et al. 2005) who are unable to wait for a face-to-face visit and INR blood withdrawal in an anticoagulation clinic (Wittkowsky et al. 2006). In the study of a venipuncture PSM model, patients needed to have access to online software such as My Health Manager (Jenner et al. 2015). Overall, these findings highlight the important role of a caregiver and the accessibility and convenience of managing INR monitoring using certain models such as those applicable to the home setting, which could be useful for older persons with limited mobility or transportation problems (Brieger et al. 2018).

Other interventions that supported older persons involved written information in the form of patient information booklets (Fairbairn-Smith et al. 2011; Lane et al. 2006). The lack of impact of one booklet on certain aspects of anticoagulants and of input from patients about their perceptions of the value of the booklets (Lane et al. 2006) suggests that written information alone is insufficient to increase patients' knowledge of anticoagulants and that, ideally, patients should have input into the development of a resource. A similar result was found in another study, in which patients and/or their caregivers viewed the supply of a booklet as inadequate and thought both verbal and written information were equally important (Bajorek et al. 2007). These findings are important because a lack of knowledge regarding warfarin can influence anticoagulation control and the rate of adverse outcomes (Nasser, Mullan & Bajorek 2012).

Another important finding of this review was that the beneficial impact of several interventions on outcomes, such as knowledge, anticoagulant control (TTR), and decisional conflict, were

short term and the length of follow-up was brief. These findings highlight the importance of regular and long-term follow-up and the need to repeat interventions at regular intervals.

Finally, only two interventions, a mobile health application (Lee et al. 2016) and a multicomponent program (Clarkesmith et al. 2016), were tailored to the needs of the vulnerable patient groups. These had a beneficial impact on outcomes such as improved knowledge, better anticoagulation control, and improved beliefs about medication. By contrast, several interventions were not tailored to the vulnerable patient groups and used a variety of INR monitoring models, DAs, videos, and booklets; however, they still had a positive impact on the same outcomes. These findings suggest that tailored and nontailored information can be used to support vulnerable patient populations to optimize patient outcomes. If tailored information is developed, health-care professionals should be trained in individualizing interventions and responding to patients' specific needs. Health-care professionals should also learn how to provide a suite of resources that are culturally relevant (Wilson et al. 2003) or adopt a culturally competence approach (Cantarero-Arévalo, Kassem & Traulsen 2014) and to consider each patient's health and computer literacy (Australian Commission on Safety and Quality in Health Care 2014; Lee et al. 2016).

2.11.1 Limitations

There are several limitations of this review. We excluded non-English language papers, selected only full-text articles, and set an age limit of 65 years for older persons and included only studies in which the majority of participants were over 65 years of age. Setting a lower age limit may have incorporated more articles. The articles were selected by one reviewer who could have introduced some bias towards the results.

This review shows that several studies used different tools to measure warfarin knowledge (Collins, Barber & Sahm 2014; Masnoon, Sorich & Alderman 2016; Moore et al. 2015; Stafford et al. 2012) and health literacy (Collins, Barber & Sahm 2014; Machtinger et al. 2007; Schillinger et al. 2006). Furthermore, the studies differed on a number of aspects: methodology, inclusion and exclusion criteria, sample size, setting, duration and type of study (i.e., only eight studies were RCTs) (Beyth, Quinn & Landefeld 2000; Clarkesmith et al. 2013; Jackson et al. 2004; Khan et al. 2004; Machtinger et al. 2007; Man-Son-Hing et al. 1999; McAlister et al. 2005; Thomson et al. 2007), follow-up, patient medical conditions, and inclusion of participants with a history of taking warfarin or a DOAC or those just starting medication. These differences made it difficult to compare the clinical outcomes across the trials and limited the generalizability of the results to other settings and countries. In addition, for two studies, it was difficult to determine the effectiveness of each component of the programs (Beyth, Quinn & Landefeld 2000; Mitchiner et al. 2012).

2.11.2 Future research

Future research is needed to develop patient-focused interventions that target patients from CALD backgrounds and those with limited health literacy who are taking oral anticoagulants, and to include caregivers and family members. To optimize the treatment of these patient groups, health-care professionals should be trained in developing interventions that are literacy sensitive and culturally appropriate. Other strategies that could be trialled for patients with limited health literacy taking oral anticoagulants may include the use of plain language and teach-back by providers (Koh & Rudd 2015), involvement of consumers when developing materials to ensure understanding of patient information (Aker et al. 2013), and clearly presented health educational materials and visual aids (Sudore & Schillinger 2009). For patients from CALD backgrounds taking oral anticoagulants, other strategies that could be explored include multilingual resources

and staff (Mohammad, Saini & Chaar 2015), encouraging patients to ask questions (Nadar et al. 2003), development of culturally appropriate information (Wilson et al. 2003), providing interpreters and bilingual-link workers, and using pictorial flashcards (Alhomoud et al. 2013).

More studies are also required to determine whether interventions that specifically target vulnerable patient populations by acknowledging their needs and being tailored lead to better patient outcomes compared with interventions that are not customized. Larger RCTs are needed of interventions that include all the antithrombotics, use technology such as mobile health applications, and involve multidisciplinary and multicomponent programs with critical elements such as patient input and regular postintervention follow-up to achieve a long-lasting impact on patient outcomes.

To enhance knowledge retention of information by vulnerable patients, who are often prone to recent memory loss, a repeated interactive session using text messaging and other smart phone applications such as FaceTime could be studied. Future studies should also ensure that health-care professionals are trained in individualizing interventions and responding accordingly. In addition, future interventions should consider exploring patient outcomes such as mortality, QOL, and adherence, and their cost-effectiveness. Finally, further research is required for standardizing information about oral anticoagulants and the tools used to measure health literacy and knowledge about anticoagulant use.

2.12. Conclusion

Although most of the interventions trialled supported older persons, only a few specifically targeted them. This review identified a major gap in the literature showing that limited

interventions have been trialled to support patients from CALD backgrounds and those with limited health literacy. Further research is needed to include patients with limited health literacy and those from CALD backgrounds as well as family members and caregivers of patients taking oral anticoagulants. It may be advantageous to determine whether patient outcomes differ between tailored and nontailored interventions. Future interventions should explore patient outcomes fully, such as mortality, quality of life and adherence, and the cost effectiveness of interventions.

Compliance with Ethical Standard

Funding This study did not receive funding from any source.
Conflict of interest AY and BB have no conflicts of interest to declare.

Table 2.1 INR monitoring interventions to support older persons

Authors, year, setting, country	Title	Trial design,	Patient Intervention	Number of patients Mean age (years)	Key finding(s)
Amruso et al.,2004, Two community pharmacies, USA	Ability of clinical pharmacists in a community pharmacy setting to manage anticoagulation therapy	Retrospective observational study	Clinical pharmacists monitored patients' INRs using point-of-care analyzers, made dosage adjustments as needed, and provided patient education	*n*=50, Age >65 years: N=42 (84%)	• During the 6 months of initial therapy with warfarin, majority of INRs were in desired therapeutic ranges • A total of 15 bleeding episodes were reported, of which 10 were minor and 5 were significant. Significant bleeding episodes required referral • The patient satisfaction rate with the service (*n*=11) was of above average to excellent
Harrison et al., 2015, 15 community pharmacies, New Zealand	Anticoagulation management by community pharmacists in New Zealand: An evaluation of a collaborative model in primary care	Prospective cohort study	Pharmacist-led anticoagulation care using point-of-care international normalized ratio testing and a computer decision support system for dose adjustments	*n*=671 Median age: 72 (age range from 13 to 97)	• A subgroup analysis (n = 221) of patients who completed 16 and 26 weeks in the pharmacist-led service showed a significant increase in mean TTR compared to under GP-led care ($p < 0.001$)
Shaw et al.,2014, 15 community pharmacies, New Zealand	A community pharmacist-led anticoagulation management service: Attitudes towards a new collaborative model of care in New Zealand	Observational descriptive study (qualitative study)	A collaborative community pharmacist-led anticoagulation management service (CPAMS)	*n*=412 patients completed the questionnaire Aged 65 years or over: (70.6%)	• The majority of patients reported: improved access of the service and convenience felt that it saved them time, a preference for capillary testing, found it helpful to receive a printed dose calendar and the immediacy of the test result and dose, found the pharmacist was able to help them with other aspects of their health care, had confidence that test results were reliable
Jackson et al., 2005, 16 rural, community pharmacies, Australia	Improving the outcomes of anticoagulation in rural Australia: An evaluation of pharmacist-assisted monitoring of warfarin therapy	prospective cohort study and patient satisfaction questionnaires	Rural Community Pharmacist training and INR monitoring of warfarin therapy, using POC testing via a portable CoaguChek S monitor compared to	*n*=137 Median age:72	• The pharmacy-based INR values (from a total of 120 tests) were significantly correlated with the laboratory INR values $p< 0.0001$) • Responses from satisfaction questionnaire revealed a majority of patients were satisfied with the monitoring by a pharmacist, rated the quality of the service as good or excellent , found that the monitoring service helped them to deal more effectively with warfarin, believed that the service

			conventional laboratory testing		should be available to all patients on warfarin and had a preference for the service to be provided in the pharmacy followed by the home and General practitioner's surgery
Hodge et al., 2008, Anticoagulation clinics, Australia	Coordinated anticoagulation management in a rural setting. Australian family physician	Prospective cohort and survey	A Victorian rural program that incorporated an anticoagulation clinic, point of care INR testing in remote centres, development of anticoagulation dosing protocols for GP use and, a comprehensive patient education program	*n*=227 Median age:72	• At one remote site, INRs were tested every 14 days resulting in a significantly higher median proportion of time in therapeutic range (78% of time, *p*=0.0004) compared to Horsham (main site) • Patients consistently praised the program, and felt more comfortable taking warfarin after undertaking the education
Jackson et al., 2004, Home-based follow-up of patients discharged from a 450-bed acute care teaching hospital, Australia	Improving the outcomes of anticoagulation: an evaluation of home follow- up of warfarin initiation.	Open-label randomised controlled trial	A Post-discharge home follow-up service by a pharmacist including home monitoring (HM), POC INR testing, telephone communication with the patient's GP about the INR results and dosage changes, and counselling with a warfarin educational booklet and a double-sided A4 warfarin document	*n*=128 Mean age for home monitoring:70 Mean age for usual care:72.5	• The percentage of patients with a therapeutic INR with HM at day 8 after discharge was significantly higher compared to usual care (*p*<0.002) • Bleeding events 3 months after discharge was significantly lower compared to usual care (*p*<0.01) • There was a significant decrease in total bleeding *(p*=0.009), major bleeding *(p*=0.05) and minor bleeding (*p*=0.01) events within 90 days of initial discharge in the HM group compared to usual care

Stafford et al., 2011, Home setting involving patients discharged from 8 hospitals across 5 metropolitan, rural and remote regions of Australia	Clinical Outcomes of a Collaborative, Home-Based Postdischarge Warfarin Management Service	Prospective, non-randomised controlled cohort study	A collaborative home-based post-discharge (PDS) warfarin management service that involved point-of-care international normalized ratio (INR) monitoring, warfarin education and a home medicines review (HMR) in the first 8 to 10 days post-discharge compared to usual care (UC)	*n*=129 Usual care mean age: 66.2 Intervention mean age:67.7	• The PDS (*n* = 129) was associated with statistically significantly decreased rates of combined major and minor hemorrhagic events to day 90 (5.3% vs 14.7%; *p*=0.03) and day 8 (0.9% vs 7.2%; *p*=0.01) compared with UC (*n* = 139) • The rate of combined hemorrhagic and thrombotic events to day 90 also decreased significantly (6.4% vs 19.0%; *p*=0.008) and persistence with warfarin therapy improved significantly (95.4% vs 83.6%; *p*= 0.004) • No significant differences in readmission and death rates or INR control were demonstrated
Stafford et al., 2012, Home setting, Australia	The benefits of pharmacist-delivered warfarin education in the home.	A prospective, non-randomised, controlled cohort trial	A home-based post-discharge warfarin management service, including warfarin education, a HMR and point-of-care INR monitoring by trained pharmacists, during two or three home visits, compared to usual care (community-based post-discharge care).	*n*=268 Intervention group, mean age: 67.7 Usual care group, mean age: 66.2	• There was a significant increase in mean warfarin knowledge scores (measured by OAK test) at day 8 compared to the intervention patients' baseline of 64.5% (95% CI=61.0-68.5%) and 78.0% (95% CI= 74.5-81.5%; *p*< 0.001), respectively • The intervention patients also scored significantly higher than the usual care patients at day 8 (65.0%, 95% CI= 61.5-68.0%; *p*< 0.001), but not at day 90
Khan et al., 2004, University based anticoagulation clinic, United Kingdom	The value of education and self- monitoring in the management of warfarin therapy in older patients with unstable control of anticoagulation	Single centre, randomised controlled trial	An anticoagulation programme consisting of education with weekly home self-monitoring of the INR vs education and anticoagulation clinic care vs control group (usual anticoagulation clinic)	*n*= 125 Mean age:73	• There was a significant increase in percentage time within the therapeutic range for the 6 months following education *(p*=0.054) and following education and self-monitoring (*p*=<0.001) compared to control • QOL measurements and health beliefs about warfarin were mostly unchanged with education or education and self-monitoring

Matchar et al., 2010, 28 Veteran Affairs medical centers with anticoagulation clinics, USA	Effect of home testing of international normalized ratio on clinical events	Prospective, randomised, nonblinded trial	Point-of-care INR devices with weekly self-testing at home compared to high quality testing in a clinic	*n*= 2922 Mean age: Self-testing group, 66.6 (9.7) Clinic-testing group, 67.4 (9.4)	• The difference in time to the first primary event (stroke, major bleeding episode, or death) between the self-testing group and clinic-testing group was not significant ($p = 0.14$) • The self-testing group had a small but significant improvement in TTR ($p<0.001$), QOL ($p<0.001$), and patient satisfaction with anticoagulation therapy ($p= 0.002$)

Waterman et al, 2001,
8 outpatient health centers,
USA
	Patient and physician satisfaction with a telephone-based anticoagulation service	Observational descriptive study (survey)	A multidisciplinary (physician, nurse, pharmacist, research associate, administrative assistant), telephone-based anticoagulation service (ACS) compared to physician management	*n*=215
				Mean age 73 years
					• Patients at ACS-available health centers were significantly:
					  • more satisfied with the timeliness of getting blood test results ($p=0.02$)
					  • more likely to know what a safe INR value was ($p=0.001$)
					  • felt safer taking warfarin ($p=0.04$)

Witt et al., 2005, Large non-profit, group-model health maintenance organization, USA	Effect of a centralized clinical pharmacy anticoagulation service on the outcomes of anticoagulation therapy	Retrospective, observational cohort study, 6 months in duration	Clinical Pharmacy Anticoagulation Service (CPAS) consisting of pharmacy technicians, clinical pharmacists and clinical pharmacy specialists	*n*=6,645 Intervention (CPAS) group, mean age:67.5 Control group, mean age: 68.1	• Patients in the CPAS group significantly spent more time within their target INR range compared to the control group ($p< 0.001$) • Patients in the CPAS group were 39% less likely to experience any anticoagulation therapy-related complication (hazard ratio=0.61; 95% CI= 0.42-0.88) • Differences in the occurrence rates of major bleeding and fatal adverse events between the study groups were not statistically significant after adjustment for age, gender, and indication for anticoagulation therapy • The CPAS had the greatest impact on reducing thromboembolic complications (hazard ratio, 0.82; 95% CI= 0.56 -1.20)
Wittkowsky et al., 2006, Two university-affiliated anticoagulation Clinics, USA	Outcomes of oral anticoagulant therapy managed by telephone vs in-office visits in an anticoagulation clinic setting	A retrospective, observational cohort study	Telephone based management of INR compared to office managed patients within an anticoagulation clinic	*n*=234 Intervention, Mean age: 65.28 Control (Office-Based), Mean age: 66.26	• Telephone follow-up can be successfully used to manage warfarin therapy in patients who are unable to present in person to an anticoagulation clinic • Monitoring outcomes (i.e. time in therapeutic range and clinic visits per patient-year) were similar between groups

Levine et al., 2012, 3 family medicine clinics in a primary care network, Canada	Monitoring of international normalized ratios: Comparison of community nurses with family physicians	A retrospective cohort analysis	A nurse-run, community-based anticoagulation program compared to a family physician monitoring the patient's INR	*n*=556 Mean age:74	• The percentage of INR values being out of range and the time between sequential INR readings did not differ significantly (p=0.115) before and after implementation of nurse monitoring • Nurse-led monitoring of INR is as effective as traditional physician monitoring
Taylor et al., 1997, An anticoagulant clinic, United Kingdom (UK)	Evaluation of a nurse specialist anticoagulant service	Prospective cohort study	A nurse specialist service (NSAS) compared to a consultant anticoagulant service (CAS)	Group A CAS *n*=110 >65, *n*=65, 59% Group A NSAS *n*=124 >65, *n*=72, 58% Group B CAS, *n*=122 >65, *n*= 79 75% NSAS, *n*=129 >65, *n*=66, 51%	• The NSAS was as good as the CAS in maintaining therapeutic control and better at documenting relevant clinical details, in reducing the number of drugs taken and in improving some aspects of patient knowledge for patients on long-term anticoagulation
Hassan et al., 2013, An anticoagulation clinic at Staten Island University Hospital, USA	Telephone-based anticoagulation management in the homebound setting: A retrospective observational study	Retrospective, observational study	Telephone-based dose-adjustments of warfarin in homebound patients	*n*= 406 Age: 65-75 (*n*=111,24.33%) Age:75-85 (*n*=190, 51.34%) Age:>85 (*n*=57, 14.51%)	• Telephone management of warfarin therapy in the homebound setting is feasible
Grunau et al., 2011, A Canadian primary care practice, Canada	Patient self-management of warfarin therapy: Pragmatic feasibility study in Canadian primary care	A pragmatic open-label randomised crossover trial	Patient self-management (PSM) of warfarin that included outpatient laboratory monitoring and training compared to physician management	*n*=11 Mean age:73	• No significant difference in proportion of INR values within therapeutic range (p=0.82), between PSM and physician-management groups. • The improvement in patient satisfaction was not significant • Ten of the 11 patients preferred PSM to physician management and elected to continue with strategy after study completion (p=0.001)
Jenner et al.,2015 The Clinical Pharmacy Anticoagulation and Anemia Service (CPAAS) at Kaiser	An Education Program for Patient Self-Management of Warfarin	Prospective, open-label pilot study	A Patient Self-Management (PSM) education program with a dosing algorithm that released venipuncture	*n*=44 Mean age:71	• The mean competency score significantly improved (p< 0.001) • The proportion achieving a passing score significantly increased (p< 0.001) • The warfarin PSM education program for patients with AF was feasible

Permanente Colorado (KPCO), USA			international normalized ratio results to patients via a secure, online Web site		• High levels of self-reported comfort with warfarin PSM was reported
Simmons et al., 2012, Kaiser Permanente Colorado, USA	Pilot study of a novel patient self-management program for warfarin therapy using venipuncture-acquired international normalized ratio monitoring	Prospective, open-label, 3-month, pilot study.	A Patient Self-Management Program consisting of patients receiving dosing decision support tools during a 2-hour live PSM training class to adjust their warfarin dosage	*n*= 44 Mean age:71 (*n*=39, that successfully completed the 90-day study)	• No significant difference in TTR occurred between the 90 days before PSM program participation and the 90 days of PSM (p=0.65) • The mean number of INR tests performed for each patient significantly increased after PSM program (p<0.01)

INR International normalized ratio, *QOL* Quality of life, *TTR* time in target INR range, *USA*- United States of America, *GP*- General Practitioner,

AF atrial fibrillation, *UC* usual care, *CI* confidence interval, *p* p-value, *vs* versus

Table 2.2 Patient education interventions to support older persons

Authors, year, setting, country	Title	Trial design	Patient Intervention	Number of patients Mean age (years)	Key finding(s)
Fatima et al., 2016, Cardiology and thrombosis clinics, inpatient hospital wards, Canada	Development and validation of a decision aid for choosing among antithrombotic agents for atrial fibrillation	Prospective cohort study	A patient decision aid booklet. Stroke prevention options: 1) no treatment, aspirin and anticoagulants, 2) warfarin vs DOACs, and 3) DOAC vs DOAC	*n*=81 Mean age: 75.2	• Mean decisional conflict score was low • Mean knowledge score improved (p<0.001) • Mean helpfulness score in making a treatment choice was high 6.2, standard deviation 0.9 on a scale from 1 to 7 • Information was rated as good or excellent in terms of clarity or comprehensiveness • The most preferred presentation format of the decision aid was verbal (74%), 51 (63%) participants found the pictograms to be helpful in addition to the pie charts
Holbrook et al., 2007, 4 family practices and one geriatric day clinic, Canada	Influence of decision aids on patient preferences for anticoagulation therapy: a randomized trial	Randomized trial (no control)	6 combinations of decision aid format (decision board vs decision booklet with audiotape vs interactive computer program) and graphic presentation of outcome probability data (pie chart or pictogram). Stroke prevention options: Aspirin vs warfarin vs no therapy	*n*=98 Mean Age:73.6	• Knowledge (maximum score 10) of AF and the treatment benefits and harms associated with anticoagulant therapy for AF increased (p<0.01) regardless of the format or graphic presentation • 96% of the participants felt that the decision aid helped them make their treatment choice • Number of patients choosing warfarin decreased after treatment names were revealed
Hong et al., 2013, An internal medicine and cardiology clinic, Canada	Validation of a patient decision aid for choosing between dabigatran and warfarin for atrial fibrillation	Prospective cohort study	A patient decision aid (a paper booklet) Stroke prevention options: warfarin vs dabigatran	*n*=35 Mean Age:62.7	• The mean total decisional conflict score was low 18.9 (SD:14.2) • The difference in mean knowledge score improved significantly 4.60 (SD 1.48) to 6.42 (SD 0.80) • The DA was understandable by the majority of participants (68.6%), and helpful in making a treatment decision by all of the participants

Man-Son-Hing et al., 1999, 14 medical centers that participated in the Stroke Prevention in Atrial Fibrillation (SPAF) III trial, United States and Canada	A patient decision aid regarding antithrombotic therapy for stroke prevention in atrial fibrillation: a randomized controlled trial	Randomized controlled trial	Audio booklet decision aid (paper booklet, personal worksheet, and audiotape) vs usual care. Stroke prevention options: Aspirin vs warfarin.	*n*=287 Mean Age intervention:65, Mean age usual care:67	• More patients in the AB group made a choice about antithrombotic therapy than in the control group (*p*= 0.02) • Patients in the AB group were more knowledgeable and had more realistic expectations about the risk of stroke and hemorrhage • Decisional conflict and satisfaction were similar for the 2 groups
McAlister et al. 2005, 102 community-based primary care practices, Canada	Impact of a patient decision aid on care among patients with nonvalvular atrial fibrillation: A cluster randomized trial	Prospective, multicentre, two-arm, cluster RCT	A home self-administered antithrombotic decision aid (Paper booklet and audiotape vs control (usual care) Stroke prevention options: No warfarin vs warfarin	*n*=434 Mean age:72	• There was a significant absolute improvement in the number of patients receiving appropriate care compared with the control group at 3 months (*p*=0.03) • Very-high-risk patients were significantly more knowledgeable about their personal biannual stroke risk without treatment (*p*=0.03) • Patients were significantly more knowledgeable in estimating the potential benefits and risks of warfarin such as their relative risk reduction with warfarin (*p*=0.001) and mean estimate of the biannual bleeding risk with warfarin (*p*=0.03) • Total Decisional Conflict Scale score was significantly lower in the intervention group • The beneficial effect of the decision aid did not significantly persist after 12 months between the intervention and control (*p*=0.44)
Thomson et al., 2007, 40 General Practices, England	A patient decision aid to support shared decision-making on anti-thrombotic treatment of patients with atrial fibrillation: randomised controlled trial	Two-armed open exploratory randomised controlled trial	Computerized decision aid Comprised of 2 components: 1) individualized risks and benefits, 2) Shared decision-making section compared to evidence-based paper guidelines applied as direct advice	*n*=109 Mean Age (SD) for the decision aid group:73.1 (6.7) Mean age for the guidelines group:73.7 (6.2)	• Decision conflict was lower in the computerized decision aid group immediately after the clinic; mean difference 20.18 (95% CI=20.34-20.01) • Participants not already on warfarin who were in the decision aid group were much less likely to start warfarin than participants not already on warfarin in the guidelines arm (OR=0.01 95% CI=0.001-0.16) • Knowledge about warfarin improved in the decision aid and guideline groups post-clinic, however, declined again in both groups by 3 months

			Stroke prevention options: warfarin vs aspirin therapy		
Giuliano et al., 2017, 772-bed community teaching hospital, USA	Can a Short Video Improve Apixaban Knowledge in an Inpatient Setting?	Prospective, quasi-experimental study	2 Apixaban videos; i) for the treatment and prevention of DVT/PE ii) for the prevention of stroke in AF	*n*= 33, Mean age:69.6	• Knowledge Scores significantly increased by 19.7% from the pre-test to the immediate post-test time point ($p< 0.001$) • Patients previously receiving apixaban or another anticoagulant were less likely to improve scores compared with new patients ($p< 0.05$) • For N=22, there was no significant difference of knowledge from pre-test to one-month post-test /follow-up ($p= 0.11$)
Moore et al., 2015, University of North Carolina Medical Center, USA	Impact of Video Technology on Efficiency of Pharmacist-Provided Anticoagulation Counseling and Patient Comprehension	Prospective, open, parallel-group study	Prerecorded informational videos provided on a tablet device coupled with "Teach-back" questions compared to a control group which received face-to-face counselling	*n*=40 Mean age:66	• The mean counselling time for a pharmacist was significantly reduced in the video group ($p<0.001$) • Following adjustment, mean total time was reduced 8.71 (95% CI = 5.15-12.26) minutes (adjusted $p<0.001$) in Restart participants (have taken warfarin therapy previously) and 2.31 (−2.19-6.81) minutes (adjusted $p=0.472$) in New Start (warfarin-naïve) participants receiving video counselling • Patient comprehension (measured by the Oral Anticoagulation Knowledge (OAK) test) post counselling did not differ between informational videos and traditional face-to-face (oral) counselling
Mazor et al., 2007, anticoagulation clinic located in an academic health center, USA	Patient education about anticoagulant medication: is narrative evidence or statistical evidence more effective?	Randomized clinical trial	• Three versions of videos incorporating narrative evidence, statistical evidence or both into patient education about warfarin	*n*=317 for those who completed baseline and post-intervention questionnaires, more than 50% of participants were over 65 years of age for each intervention arm	• Compared to patients in the control group, patients who watched any video showed significant gains on the knowledge test ($p<0.001$), greater positive shifts in their beliefs in the importance of laboratory testing ($p= 0.010$), and in their beliefs that taking warfarin is beneficial ($p= 0.012$) • Narrative evidence had a greater impact than statistical evidence on beliefs about the importance of lab testing ($p=0.05$) and on knowledge ($p=0.006$) when baseline knowledge was included as a covariate
Fairbairn-Smith et al., 2011, Anticoagulant monitoring clinic UK	Effect of provision of the NHS NPSA oral anticoagulant therapy patient information pack upon patients' knowledge and anticoagulation control	Prospective cohort study	The NHS National Patient Safety Agency (NPSA) patient information booklet	*n*=24, Mean age:68	• Knowledge improved significantly for the ability to name side effects of warfarin ($p<0.01$), ability to describe what would happen to their INR subsequent to omitting a dose of warfarin ($p<0.01$) • Anticoagulation control indicated by TTR, significantly improved ($p<0.05$)

Lane et al., 2006, AF outpatient clinic at the City Hospital, UK.	Patient knowledge and perceptions of atrial fibrillation and anticoagulant therapy: Effects of an educational intervention programme The West Birmingham Atrial Fibrillation Project	Prospective cohort study	• An information booklet.	*n*=33 patients out of 93 that completed the follow-up assessment 8 weeks later, Mean age:68.0	• Patient's knowledge of the target INR range and factors that may affect INR levels improved significantly (p=0.001 and p=0.014), respectively) for those who completed both questionnaires • Few patients were aware of the benefit of stroke prevention associated with anticoagulants at baseline (21%) or after the educational intervention (27%) • The intervention had little effect on increasing awareness of the bleeding risks associated with anticoagulants, although three in five people appeared to appreciate these risk
Masnoon et al., 2016, A General teaching hospital, Australia	A study of consumer retention of key information provided by clinical pharmacists during anticoagulant counselling	Prospective cohort study	Patient education about the anticoagulant warfarin through pharmacist counselling	*n*=22, Mean age: 69.0	• Immediately after counselling before discharge from hospital, participants were significantly able to recall the majority of key information elements than was observed 6 weeks after counselling, average (mean ± standard deviation) of 79.9 ±14.6%, (71.0 ±11.7%; p= 0.02) • From the three information elements that were considered critical (adverse effects, INR monitoring and drug interactions), recall of adverse effects was found to be the greatest • The two most poorly recalled information elements were mechanism of action of warfarin and diet interactions with warfarin therapy, both immediately after and 6 weeks after counselling • Indication for warfarin use was the most recalled element at immediately after and 6 weeks after counselling
Metlay et al., 2005, Hospital USA	Patient Reported Receipt of Medication Instructions for Warfarin is Associated with Reduced Risk of Serious Bleeding Events	Prospective cohort study	Patient report of receipt of medication instructions	*n*=2347 Majority of patients >75 years of age (65%)	• The rate of warfarin-related hospitalization for bleeding was substantially lower for patients who reported receiving medication instructions from a physician or nurse and a pharmacist
Beyth et al., 2000, University teaching hospital, USA	A multicomponent Intervention to Prevent Major Bleeding Complications in Older Patients	Randomized controlled trial	Multicomponent comprehensive program of management of warfarin therapy-patient education about warfarin, training to increase patient participation	*n*=325 Mean age:75	• Major bleeding at 6 months. Overt bleeding that led to the loss of at least 2.0 units of blood in 7 days or less or was otherwise life-threatening • Major bleeding was significantly more common at 6 months in the usual care group than in the intervention group (p=0.0498, log-rank test) • Death and recurrent venous thromboembolism occurred with similar frequency in both groups at 6 months in the intervention group vs usual care groups (p=0.2)

			in their care, self-monitoring of prothrombin time using a portable home monitor, guideline-based management of warfarin dosing Duration: 6 months		• Throughout 6 months, the proportion of total treatment time during which the international normalized ratio was within the therapeutic range was significantly higher in the intervention group than in the usual care group (56% vs. 32%; $p<0.001$) • The proportion of total treatment time during which the international normalized ratio was within the therapeutic range was significantly higher in the intervention group than in the usual care group ($p<0.001$)
Mitchiner et al. (2012) Community teaching hospital, USA	Evaluation of the B-SAFE Campaign to Reduce Clinically Significant Warfarin-Drug Interactions Among Fee-for-Service Medicare Beneficiaries	Prospective before and after study	B-SAFE Campaign to educate patients who take warfarin about the risk of serious drug-drug interactions and other adverse drug events that can occur while on these medications	*n*=65 Before intervention: Study hospital, Age>70, *n*=48 Control hospital, Age>70, *n*=11 After the intervention: Study hospital, Age >70, n=61, Control hospital, Age>70, n=33	• The authors observed a marginally significant decline in the rate of warfarin-related drug interactions (OR=0.66; 95% CI=0.33-1.29) among Fee-for-Service Medicare patients admitted for bleeding complications to the hospital targeted by the B-SAFE campaign • Patient exposure to the B-SAFE campaign may have resulted in a decrease in the rate of clinically significant warfarin-related drug interactions
Clarkesmith et al., 2013, Hospital outpatients clinic, UK	Educational Intervention Improves Anticoagulation Control in Atrial Fibrillation Patients: The TREAT Randomised Trial	Randomized controlled trial	A one-off group (1-6 patients) theory-driven educational intervention Content: DVD that included patient narratives, educational booklet, self-monitoring diary and worksheet and group discussion compared to usual care	*n*= 97 Mean age: 72.9	• Patients had significantly higher TTR than usual care at 6-months (76.2% vs. 71.3%; $p=0.035$); suggesting improved adherence, however, not at 12-months (76.0% vs. 70.0%; $p=0.44$) • At 6-months, knowledge scores significantly predicted TTR (r=0.245; $p=0.04$) • There was improved patient's understanding of the necessity of warfarin and perception of treatment harm. The intervention group significantly viewed medication as less harmful than the usual care group ($p<0.05$) • Patients' perception of the general harm and overuse of medication, as well as the perceived necessity of their AF specific medications predicted TTR at 6- and 12-months • QOL increased in the intervention group at the one-month follow-up. At all subsequent follow-ups there were no significant differences in QOL scores between groups

Davy et al. 2017, no setting mentioned, France	Higher persistence but lower compliance with direct oral anticoagulants treatment for atrial fibrillation following a personalized therapeutic information: paradoxical results of the MONACO study	Randomized, parallel, single blind, placebo control, usual care non-interventional study	Personalized therapeutic information for patients (group A active) recently prescribed rivaroxaban on days 15, 30, and 45 including 3 phone calls, paper booklets offerings and websites suggestion	*n*=196 Mean age:70	• At 1 year, persistence was higher in A group, 98% (90/92) vs 76% (76/92) ($p<0.001$) • However, compliance (primary outcome, measured per-protocol by design) was paradoxically slightly lower, at 7.4 ± 0.8 vs 7.6 ± 1.1 ($p=0.02$) • Knowledge results were mostly similar in the 2 groups

AF atrial fibrillation, *B-SAFE* Bring a list of all your medications with you, Standard dose, time and monitoring, Adverse effects, Fall and injury precautions, Evaluate and examine, *CI* confidence interval, *DOACs* direct-acting oral anticoagulant, *INR* International normalized ratio, *OR* odds ratio, *p* p-value, *QOL* quality of life, *RCT* randomised controlled trial, *r* correlation coefficient, *TTR* Time in therapeutic range, proportion of time spent within therapeutic INR range, *vs* versus

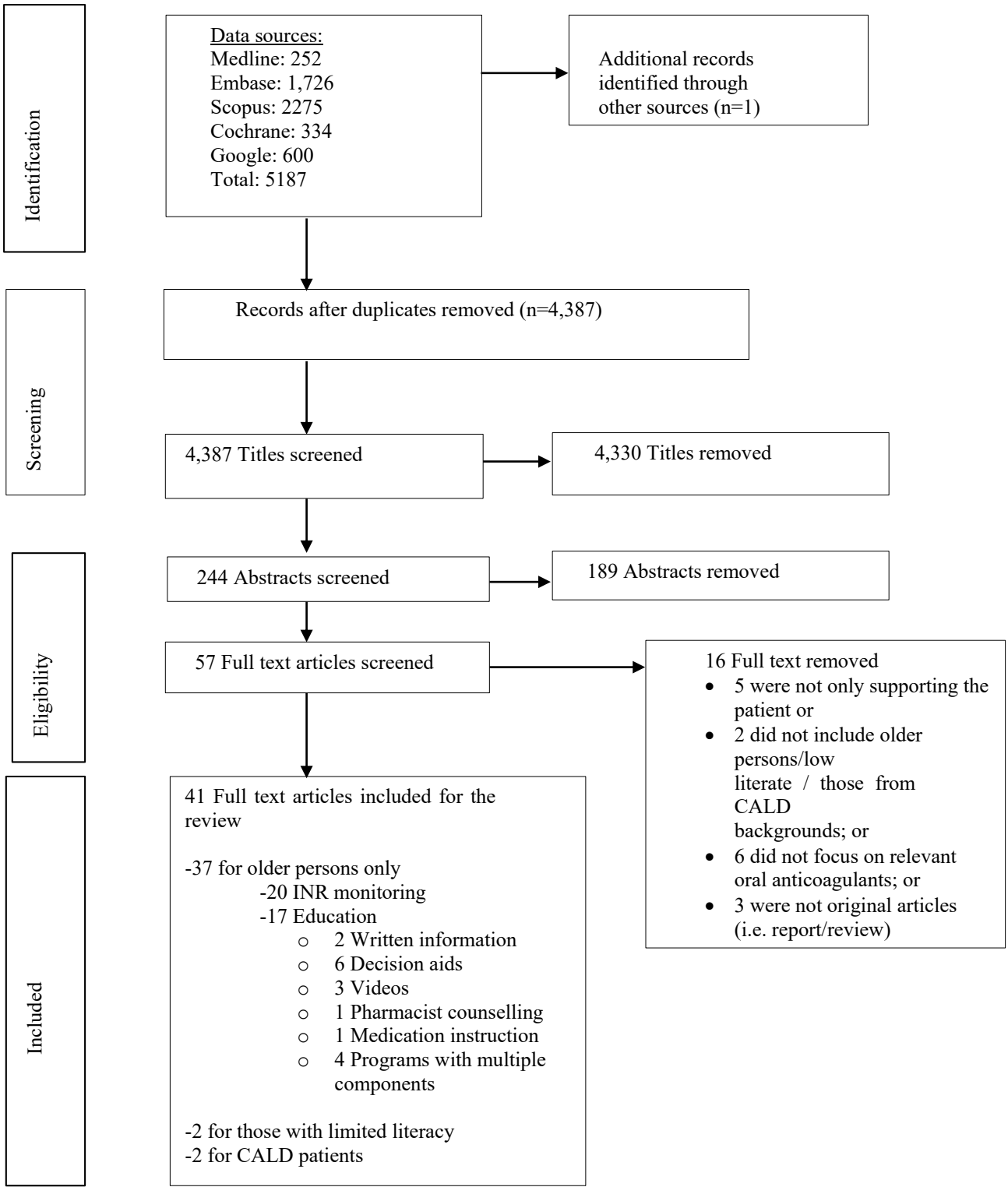
Table 2.3 Intervention to support those patients with limited literacy and from CALD background

Authors, year, setting, country	Title	Trial design	Patient Intervention	Number of patients Mean age (years)	Key finding(s)
Collins S et al.,2014, Public hospital, Ireland	Pharmacist's Counselling Improves Patient Knowledge Regarding Warfarin, Irrespective of Health Literacy Level	Prospective cohort study	Pharmacist counselling and a warfarin booklet	*n*=43 Mean age: 65.72 Health literacy (REALM): Adequate, *n*=26, 60.5% Limited, *n*=17, 39.5%	• Warfarin Knowledge at baseline improved significantly within 24 hours of verbal counselling ($p<0.05$) • Warfarin knowledge within 24 hours of counselling decreased significantly after 28 to 56 days of counselling ($p<0.05$) • Score improvement following verbal counselling was similar in those with adequate health literacy; and those with limited health literacy
Castelli et al., 2016 Academic medical centre, USA	Effect of a rivaroxaban patient assistance kit (R-PAK) for patients discharged with rivaroxaban: a randomized controlled trial	Prospective, randomised, controlled trial	R-PAK with counselling at discharge The R-PAK contained an individualized medication box with dividers to indicate twice daily or once daily dosing, a patient's guide to rivaroxaban, and a date of transition reminder card	*n*=25 Control, Mean age: 61 Intervention, Mean age:54 Health literacy score based on a single item screening tool for: - R-PAK: 12% not at risk - Control:13% not at risk	• No difference in baseline assessment of health literacy status • Proper transition to daily administration on day 22 was no different between the groups ($p<0.891$) • Adherence was reported in 99.8% of R-PAK patients and 97.65% of control patients ($p<0.074$)
Schillinger et al., 2006, Cardiologist-supervised, pharmacist-staffed anticoagulation clinic at San Francisco General Hospital (SFGH), USA	Language, literacy and communication regarding medication in an anticoagulation clinic: a comparison of verbal vs visual assessment	Prospective cohort study	A visual aid consisting of a digitized color menu of warfarin pills Bilingual research assistants asked patients to 1) verbalize their prescribed weekly warfarin regimen and 2) identify this regimen from a digitized color menu of warfarin pills and Coumadin pills	*n*=220 Median age=59 Age/ethnicity: Asian, *n*=87 (39%) Black, *n*=31 (14%) Latino, *n*=61 (28%) White, *n*=41 (19%) Health literacy (s-TOFHLA) of English and Spanish speaking patients: *n*=178	• There was a significant difference in concordance between verbal and visual modes with clinicians regarding the weekly warfarin regimen • Fifty percent of patients achieved verbal concordance and 66% achieved visual concordance with clinicians regarding the weekly warfarin regimen ($p<0.001$) • Verbal concordance was lower fo Cantonese than English speakers (38% vs 56%, OR=0.48, 95% CI=0.23–0.97, $p=0.04$) • Verbal concordance was lower for patients with inadequate vs adequate health literacy (42% vs 64%, OR=0.41, 95% CI=0.21–0.78, $p<0.01$)

				Inadequate, *n*=86, 39%, Marginal, *n*=23, 11%, Adequate, *n*=69, 31%	• When patients reported their regimen from verbal to visual modes, there was greater patient-provider concordance across all patient subgroups, especially for those patients with communication barriers such as Cantonese speakers compared to English speakers (45% vs 16% raw improvement, OR=4.38, 95% CI=2.02–9.48, $p<0.001$) • Neither language nor health literacy were associated with visual discordance
Machtinger et al., 2007, Cardiologist-supervised, pharmacist-staffed anticoagulation clinic at a general hospital and an affiliated public hospital USA	A visual medication schedule to improve anticoagulation control: A Randomized, Controlled Trial	Randomized controlled trial	A computer-generated visual medication schedule (VMS) of the updated warfarin dose from the clinic pharmacist	*n*=147, Mean age:61 Ethnicity: Asian, n=59 (40%), White, n=46 (31%), Hispanic, *n*=25 (17%), Black, *n*=17 (12%) Health literacy (s-TOFHLA): Inadequate, *n*=58, 63% Marginal, *n*=11, 12% Adequate, *n*=31, 33%	• Anticoagulation control was achieved more rapidly with intervention subjects than control subjects • The benefit of the intervention was significant among subjects with baseline regimen discordance but not among subjects with baseline concordance (median, 28 vs 49 days; HR=1.92; 95% CI=1.08-3.39) but not among subjects with baseline concordance (median, 28 vs 35 days; HR=1.14; 95% CI=0.71-1.83) •
Lee et al., 2016, Single university-affiliated medical center USA	Feasibility Study of a Mobile Health Intervention for Older Adults on Oral Anticoagulation Therapy	Prospective, quasi-experimental study with a single-arm pre-post design	Mobile health (mHealth) applications containing modules for warfarin therapy	*n*=18 Mean age: 67 Ethnicity: Caucasian, *n*=9 (50%), Hispanic, *n*=7 (39%), Other, *n*=2, (11%). Patients were English or Spanish speaking	• Anticoagulation knowledge significantly improved from baseline to follow-up (p=0.007) • Participants reported they were generally satisfied with the mobile health intervention, its ease of use and its usefulness •

CI confidence interval, *HL* Health literacy, HR hazard ratio, *OR* odds ratio, *p* p-value, *REALM* The Rapid Estimate of Adult Literacy in Medicine tool, *s-TOFHLA*, abbreviated version of the short-form test of functional health literacy in adults- English and Spanish versions, *TTR* Time spent in target range, *vs* versus

Figure 2.1 Flow Chart of search strategy and results



Chapter 3: Assessing knowledge and health literacy

Health literacy and knowledge in a cohort of Australian patients taking warfarin (Paper 2)

Angela Yiu and Beata V. Bajorek
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Abstract

Objectives: To: 1) characterise older patients taking warfarin, 2) assess these patients' level of warfarin knowledge, and 3) describe their strengths and limitations in health literacy, and 4) explore relationships between participants' characteristics, warfarin knowledge and health literacy.

Methods: A warfarin knowledge questionnaire and Health Literacy Questionnaire (HLQ) were administered to older patients (aged >65 years, N=34) taking warfarin in an Australian general practice setting.

Results: Key gaps in participant knowledge pertained to the consequences of an international normalized ratio (INR) being below the target INR range and safety issues such as when to seek medical attention. A limitation for participants with a lower level of health literacy was the ability to appraise health information. Patients who needed assistance in completing the HLQs had significantly lower warfarin knowledge scores (p=0.03). Overseas-born participants and those taking 5 or more long-term medications had lower HLQ scores for specific scales (p<0.05).

Conclusion: In this study warfarin knowledge gaps and a limitation of health literacy amongst a small sample of older patients were identified. The findings suggest that education and materials may need to be tailored to the needs of older patients taking warfarin and their carers to address these knowledge gaps and limitations in health literacy. Patients who may need greater support include those that need assistance in completing the HLQ, are overseas-born, or are taking 5 or more long-term medications.

Keywords:

Patient Medication Knowledge, Warfarin, Aged, Health Literacy, Patient Education as Topic, Surveys and Questionnaires, Australia.

3.1. Introduction

As the use of oral anticoagulants continues to rise, more attention is being paid to how well patients are being supported in their management of these treatment regimens. This is particularly the case in older persons who are high users of these medications for long-term indications, including stroke prevention in atrial fibrillation (Institute for Safe Medication Practices 2014; Lakshminarayan et al. 2006). Older people are vulnerable to experiencing harm from so-called 'high alert' medicines, such as warfarin (traditional anticoagulant) (Lavan, Gallagher & O'Mahony 2016).

Therefore, patient education regarding adverse effects (i.e., bleeding), dietary Vitamin K consumption, potential drug interactions, need for regular monitoring, and actions around missed doses, is paramount (Tideman et al. 2015) especially during transitions of care between hospital and primary care settings (Deitelzweig 2013).

Despite the advent of direct oral anticoagulants (NOACs), warfarin and warfarin education may still be needed in certain patient populations who are not good candidates for NOACs, such as those patients who have: mechanical heart valves (Wilson, Docherty & Gardner 2016); a creatinine clearance of <30mL/minute (calculated by the Cockcroft-Gault equation) ; haemodialysis (Diener et al. 2017); other specific contraindications; and/or who cannot afford the relatively higher costs of the newer agents (depending on the medication subsidies available in each country) (Gupta et al. 2017).

The education of older persons regarding warfarin has, however, been suboptimal, contributing to poor therapeutic outcomes, such as sub- or supra-therapeutic INRs, adverse events (e.g., bleeds), and/or an increase in hospitalisations (Nasser, Mullan & Bajorek 2012). Educational

challenges are more pronounced in older patients due to changing cognition, function, and psychological wellbeing, as well as lower health literacy (Kobayashi et al. 2016; Speros 2009).

Regarding the latter, the World Health Organization (WHO) defines health literacy as `the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health' and 'implies the achievement of a level of knowledge, personal skills and confidence to take action to improve personal and community health by changing personal lifestyles and living conditions' (Nutbeam 1998). In Australia, almost 60% of adults (15 to 74 years) have low health literacy (Australian Bureau of Statistics June 2009), and it has been shown that older age is associated with lower health literacy scores (Barber et al. 2009).

Health literacy has been recognized as a multi-dimensional concept and newer tools are now available to measure health literacy across several different domains (Beauchamp et al. 2015). In patients taking warfarin, low health literacy has been associated with deficits in warfarin knowledge (Fang et al. 2006). Recognition of this is critical to developing effective educational interventions or materials to better support patients taking oral anticoagulants. To our knowledge in Australia, there have been no studies that have assessed both warfarin knowledge and the health literacy of older persons who are taking oral anticoagulants in a primary care setting. This is important given the increasing use of anticoagulation, and that warfarin therapy remains a primary therapy, despite the increasing availability of alternative agents.

Therefore, the objectives of this descriptive pilot study were to: (1) report the characteristics of older patients taking warfarin in the local Australian primary care setting; 2) assess these patients' level of knowledge about warfarin; 3) describe their strengths and limitations in health

literacy, and 4) explore relationships between participants' characteristics, warfarin knowledge and health literacy.

3.2. Method

3.2.1 Study Design

A descriptive, questionnaire-based pilot study was conducted in an Australian general practice (primary care) setting between September 2015 and January 2016. Approval to conduct this study was granted by the Human Research Ethics Committee of the University of Technology of Sydney (Project number: 201 4000 863).

3.2.1.1. Setting

A general practice medical centre in The Hills Shire (Greater Western Sydney, New South Wales, Australia) was the primary location for this study due to its ageing population (.idcommunity) and therefore the high prevalence of warfarin users being treated for atrial fibrillation.

3.2.1.2. Participants and recruitment

The study participants comprised older patients who were:

- ≥ 65 years of age
- taking warfarin therapy for a long-term indication (regardless of when the medication was initiated)
- cognitively intact (based on the clinician's confirmed assessment and knowledge of the patient during the screening process)

- able to communicate in English and
- able to provide informed consent

For patients who were unable to fulfill the last three inclusion criteria, the primary carer who was responsible for managing their warfarin therapy was invited to participate instead. The carer was asked to complete the surveys based on their own knowledge and health literacy.

To recruit participants, the medical centre staff (5 general practitioners, and one on-site cardiologist screened their electronic patient records to identify 87 potential participants (80 patients and 7 carers) that met study criteria. 36 participants agreed to participate in the study, however, 2 participants dropped out during the study due to a lack of time to complete the questionnaires and provide feedback. Fifty-one participants declined to participate in the study. The target sample size was based on an estimate of the proportion of participants likely to attain correct answers to the brief warfarin knowledge questionnaire. Using a point- estimate of effect of 65% (proportion of patients likely to get at least half the answers correct (Ching et al. 2016), with 90% confidence and 10% precision, the target sample size was 34 participants).

A medical receptionist then sent (via postal mail) each patient a generic letter informing them about the study and inviting them to contact the main researcher (AY). Non-responders received a once-only telephone call from the medical centre to follow up on the invitation (one week post first mail out). On contacting the researcher, the person's eligibility (per inclusion criteria) was confirmed and consent to participate in the study was obtained (Appendix 7.2, 7.3).

3.2.1.3. Data collection

Data collection occurred during scheduled face-to-face appointments with the researcher at the medical centre, or via the telephone. A set of questionnaires was used:

- purpose-designed questionnaire to record participants' medical history, medication history, history of warfarin use, previous education received about warfarin (Appendix 7.4)
- customized brief Warfarin Knowledge Questionnaire (Appendix 7.5)
- Health Literacy Questionnaire (HLQ) (Osborne et al. 2013)

3.2.1.4. Warfarin Knowledge Questionnaire

To assess participants' knowledge about basic aspects of warfarin therapy, a brief customised 10-item questionnaire was developed. The questionnaire comprised a selection of open-ended and closed-ended questions (e.g., multiple choice answer-style questions), comprising nine questions used in previous studies (Estrada et al. 2004; Tuiskula et al. 2011; Zeolla et al.2006) and one additional question (question 8) designed by the authors (Appendix 7.5). This shorter customised questionnaire was used instead of others (e.g., Oral Anticoagulation Knowledge test (OAK), Anticoagulation Knowledge Assessment (AKA), Anticoagulation Knowledge Test (AKT)) to enable time-efficient knowledge assessment via a researcher- administered questionnaire, and to allow open-ended responses in this target older patient population (Briggs et al. 2005; Obamiro, Chalmers & Bereznicki 2016; Zeolla et al. 2006).

The responses provided to the open-ended questions were categorised thematically and coded, (transformed into numbers) (Bryman A 2016) to enable quantitative analysis of the data and determine a warfarin knowledge score. Responses to all questions were given a score of 1 for a

correct answer, and each question had equal weighting. For the open-ended questions, if the participant wrote 1 word that was similar to any of the words in the pre-determined answer, that answer was considered correct and given a score of 1. If the participant wrote no words that matched the pre-determined answers, a score of 0 was given. The participant's overall level of basic warfarin knowledge was reported as a total score out of 10, and a score ≥5 was considered to indicate high or good knowledge. A score <5 was considered to indicate low or poor knowledge, as adapted from a previous study (Tang et al. 2003)

Within this descriptive study, no further validation of the shortened questionnaire was undertaken beyond checking of face validity and pilot-testing among the researchers.

3.2.1.5. Health Literacy Questionnaire (HLQ)

The HLQ was chosen to determine health literacy after consideration of other studied health literacy measures such as the Newest Vital Sign (Weiss et al. 2005), shortened version of the Test of Functional Health Literacy in Adults (S-TOFHLA) (Weiss et al. 2005), shortened version of the Test of Functional Health Literacy in Adults (S-TOFHLA) (Baker et al. 1999), Rapid Estimate of Adult Literacy in Medicine- Short Form (REALM-SF) (Arozullah et al. 2007) and the Short Assessment of Health Literacy-English (SAHL-E) (Lee et al. 2010). The latter tools only focus on reading ability, comprehension and numeracy, and some also have substantive psychometric weaknesses, drawing different conclusions when applied concurrently, and providing limited guidance on how to improve health literacy (Barber et al. 2009; Osborne et al. 2013).

The HLQ uses a multidimensional health literacy profile which provides better insight into the health literacy strengths and limitations of both individuals and populations (Osborne et al. 2013). This tool may better reflect the overall health literacy of an individual, as it captures the

broad components that contribute to it (Australian Commission on Safety and Quality in Health Care. Sydney 2014) and key elements from the perspective of the general population, practitioners and policymakers (Osborne et al. 2013). The HLQ scales have strong to very strong psychometric properties and provide unique insights across nine independent indicators of health literacy (Osborne et al. 2013). The HLQ comprises of 44 questions which can be administered quickly (reported average of 7 to 30 minutes) in 14 different languages (Dodson S 2014).

The validated HLQ measures health literacy and comprises 44 items spread across 9 scales (Beauchamp et al. 2015). For each item, participants were asked to respond as follows:

- for scales 1 to 5 (Table 3): Strongly Disagree=1, Disagree =2, Agree=3, Strongly agree=4.
- for scales 6 to 9 (Table 3): Cannot do =1, Very Difficult =2, Quite Difficult =3, Quite Easy =4, Very easy =5.

To determine the overall scale scores, item scores were added, and the sum divided by the number of items in that specific scale (Beauchamp et al. 2015). Using these scale scores, participants with a lower level of health literacy for a particular scale were defined as those having a:

- mean scale score of <3 for scales 1 to 5. That is, they on average "strongly disagree" or "disagree" with the item statement

OR

- mean scale score of < 4 for scales 6 to 9. That is, they on average "cannot do" or find it "very difficult" or "quite difficult" to do those tasks listed in the item statements.

Conversely, participants with a higher level of health literacy for a particular scale were defined as having a:

- mean scale score of ≥3 for scales 1 to 5. That is, they on average "strongly agree" or "agree" with the item statements

OR

- mean scale score of ≥4 for scales 6 to 9. That is, they on average found it "quite easy" or "very easy" to do the tasks listed in the item statements.

3.2.1.6. Data Analysis

Quantitative data were analysed using the software program IBM SPSS™ version 23.0 (SPSS Incorporation, Chicago, II, USA), and Microsoft Excel™. Descriptive statistics, such as measures of central tendency (e.g., means, medians), were used to summarise the characteristics of the participants and responses to survey questions. Categorical variables were expressed as frequencies and percentages, and continuous variables were presented as medians (interquartile range). Inferential statistics (non-parametric tests, e.g. chi-square test, Mann-Whitney U test, Spearman correlation test) were used to explore differences in characteristics and responses between patient sub-groups, and to explore the relationship between warfarin knowledge and health literacy. A significant difference was defined as $p<0.05$. The categorisation of HLQ scores into lower and higher literacy does not rely on an assumption of normality in the data, and hence mean cut-off scores were used to categorise data.

3.3. Results

3.3.1 Participant characteristics

Among the study's 34 participants, 30 were patients taking warfarin and 4 were carers of patients taking warfarin (Table 3.1). The median age for patients was 81.0 years, 80.0% were male, and 30.0% were born overseas. The highest level of education attained by the majority of patients was: University (26.7%), Technical and Further Education or Trade (26.7%) and partial high schooling (26.7%). The median age of carers was 61.0 years (range 43 to 85 years), with three being overseas-born females. Two carers completed partial schooling and the other two carers were university educated.

Approximately 94.1% of patients (n=32) had multimorbidity (i.e., co-occurrence of ≥3 chronic conditions (Harrison et al. 2014)) and 88.2% (n=30) used polypharmacy (i.e. ≥ 5 medications (Gnjidic et al. 2012)) (Table 3.2). Aside from cardiovascular issues, the most common chronic medical conditions were: respiratory (47.1%) and rheumatological (47.1%) (Table 2). The most common number of long-term medications used were: antithrombotics (100%) cardiovascular (88.2%) and complementary and alternative medicines (CAMS) including herbs or vitamins (64.7%) (Table 3.2).

The prevailing indication for warfarin was stroke prevention in AF (61.8%). Most patients had been taking warfarin for between 6 to 10 years (32.4%) and recalled receiving warfarin education from their general practitioner or specialist doctor (76.5%). The location of their warfarin education was most commonly a primary care setting (44.1%). The time since the participant last recalled receiving information about warfarin was 1 to 5 years (35.3%) for most patients. One carer reported never receiving any formal warfarin education.

3.3.2 Assessment of Warfarin Knowledge

Across the 34 participants, the mean warfarin score out of 10 was 8.3, indicating a good level of knowledge about the basic aspects of warfarin use. The questions that received the highest proportion of correct responses (**Error! Reference source not found.**) were:

- question 1 (97.1%): “Reason for taking warfarin”
- question 8 (97.1%): “Informing other health care providers”
- question 3 (88.2%): “What to do if you miss a dose of warfarin”

The questions that received the lowest proportion of correct responses were:

- question 6: “The importance of a consistent diet” (58.8%)
- question 10: “When to seek urgent medical attention” (67.6%) and
- question 5: “What happens if an INR value is below the target INR range” (73.5%)

The mean warfarin knowledge score was the same for face-to-face and telephone interviews.

3.3.2.1. Assessment of Health Literacy

Table 3.3 summarises the median scores for each HLQ scale. The strengths and limitations for the sample population can be explained in terms of the number of participants with a lower or higher level of health literacy for each scale. The scale with the largest number of participants demonstrating a lower level of health literacy (N=17) was scale 5 (“Appraisal of health information”), i.e., many more participants indicated that they did not consistently appraise the quality and reliability of health information.

The scales with the most participants with a higher level of literacy was scale 1 (“Feeling understood and supported by healthcare providers”) (N=32) and scale 6 (“Ability to actively engage with healthcare providers”) (N=30).

3.3.3 Relationship between patient characteristics, warfarin knowledge and health literacy

There were no significant differences between the participants’ warfarin knowledge scores and gender, country of birth, Aboriginal or Torres Strait Islander status, whether English spoken at home, number of chronic medical conditions, number of long-term medications, age, private health insurance status, duration of warfarin therapy, and the time since they last were educated about warfarin.

Patients who needed assistance in completing the HLQ had significantly lower warfarin knowledge scores compared to those patients who did not need assistance (p= 0.03). Participants born overseas had significantly lower HLQ scores for scale 1 (Feeling understood and supported by healthcare providers) compared to those born in Australia (p=0.01).

Participants who took 5 or more long-term medications had lower HLQ scores for scale 9, (Understand health information enough to know what to do) compared to those who took less than 5 medications (p=0.04). There was no significant association between other characteristics, warfarin knowledge scores and HLQ scores.

3.4. Discussion

This study has described the level of warfarin knowledge and assessed the health literacy amongst an older population taking warfarin and a few carers in the local Australian primary care setting.

The majority of participants in our study had several characteristics that highlighted why the management of this older population can be complex. Older age has been associated with a lack of warfarin knowledge, low literacy (Fang et al. 2006) comorbidities (Australian Institute of Health and Welfare 2014), polypharmacy and drug interactions (Focks et al.2016). Polypharmacy has been also associated with increased mortality, stroke and major bleeding for patients with AF (Focks et al. 2016). Consequently, the need for carer assistance in the management of warfarin for older patients may be required.

The gaps in warfarin knowledge encountered in this study primarily related to medication safety issues and self-management strategies with respect to a consistent diet, recognising when to seek medical attention and actions to take when the international normalised ratio (INR) readings are outside the desired target range.

A particularly significant finding here is the gap in knowledge regarding knowing when to seek help; in the context of high-risk anticoagulant therapy, patients and their carers must be acutely aware of the signs and symptoms of potentially life-threatening adverse effects from warfarin (e.g., haemorrhage) which require urgent medical attention. Increasing patient's knowledge about these will help to reduce their risk of major complications and poor treatment outcomes (including death) (Khudair & Hanssens 2010; Wysowski, Nourjah & Swartz 2007).

These findings are similar to those reported by other studies in the literature and highlight ongoing problems with respect to patient's understanding of these key points (Nasser, Mullan & Bajorek 2012; Vormfelde et al. 2014). In addition to gaps in warfarin knowledge, the majority of our study participants had not received updated warfarin counselling in more than 1 to 5 years. These results highlighted a need for effective and ongoing education with regular follow-up to address the knowledge gaps.

To overcome these knowledge gaps warfarin patient education needs to be standardised (Wofford, Wells & Singh 2008) and more targeted to topics relating to patient safety and actions required. In this study, most participants were educated by their general practitioners or physicians in the primary care setting, at the time of warfarin commencement. In our study, despite being long-term users of warfarin, the majority of participants had not had a warfarin 'refresher' in the previous one to five-year period, nor had they received warfarin education by pharmacists. This is important as knowledge retention on some aspects of warfarin is as short as 28 to 56 days (Collins, Barber & Sahm 2014). General practitioners or specialists may not have sufficient time to educate and follow-up on the patients about warfarin (Tang et al. 2003).

To address this barrier, a multidisciplinary approach, involving doctors, pharmacists, nurses and nutritionists (Khudair & Hanssens 2010), is suggested to facilitate patient follow-up and re-education. The beneficial role of pharmacists in supporting patients receiving anticoagulants in the hospital, community and general practice settings, has been particularly highlighted in the literature (Collins, Barber & Sahm 2014; Jordan, Frew, Stewart & Mullan 2015, Stafford, Peterson, Bereznicki, Jackson, van Tienen, Angley, Bajorek, McLachlan, Mullan & Misan 2011).

In considering approaches to patient education (Table 3.4), it is important to note that around half of the study participants had a lower level of health literacy for scale 5 ("Appraisal of information"). These participants could not understand most health information and could become confused when there is conflicting information (Osborne et al. 2013). A unique finding was that patients who needed assistance in completing the health literacy questionnaire had significantly lower warfarin knowledge scores, suggesting they may also need specific assistance with understanding information about warfarin. Health care providers may need to communicate information about warfarin in appropriate formats so that these patients can understand the key messages and improve their knowledge.

Although the literature identifies that health literacy must be assessed and addressed for effective patient education, there is limited research specifically reporting on successful interventions in the context of anticoagulation management. More broadly, one method of educating patients with limited health literacy includes pharmacist counselling about warfarin supported by a written information booklet (Collins, Barber & Sahm 2014).

In addition, the literature has suggested specific communication techniques to support patients with limited health literacy in understanding their medications, including: the Indian Health Service model (i.e., 3 key questions are asked to assess a patient's baseline knowledge: *What were you told this medication is for?, How were you told to use it?, and What were you told to expect?*) (Johnson, Moser & Garwood 2013; Lam, Muravez & Boyce 2015); 'Teach-back' (Paasche-Orlow 2011); 'Ask-tell-ask' methods to confirm understanding (Australian Commission on Safety and Quality in Health Care. Sydney: ACSQHC 2014); "Ask Me 3" method (i.e., patients ask themselves: *1) What is my main problem?, 2) What do I need to do?, and 3) Why is it important for me to do this?*) (National Patient Safety Foundation); or use of a

digitised colour menus of warfarin tablets to confirm regimen dosage concordance (Schillinger et al. 2006).

Other techniques include using slow speech, limiting the number of key points discussed to three or less (Sudore & Schillinger 2009), reinforcing messages using pictures or graphs (Sudore & Schillinger 2009), using plain language, assessing health information, and involving consumers in the process of developing information through focus groups, online surveys and telephone interviews, and using shared-decision making tools to communicate risk information about treatment options (Australian Commission on Safety and Quality in Health Care. Sydney 2014).

Regardless of the techniques that may be used, there is a need to implement specific policies in practice to guide the assessment of health literacy in patients and ensure it is appropriately addressed. In our local setting, these study findings have prompted the development of a warfarin action plan (written information leaflet) that considers the principles espoused in many of the communication techniques listed above. This warfarin action plan will be subsequently evaluated as a resource in the education of patients with limited health literacy, particularly older persons and their carers.

Other notable study findings included the lower level of health literacy identified in participants who were born overseas or who took five or more long-term medications. In our study, participants who were born overseas found it difficult to feel understood and supported by healthcare providers. Participants who took 5 or more long-term medications had difficulty in understanding health information to enable them to know what actions to take.

Previous studies have reported similar findings (Beauchamp et al. 2015), including that patients using polypharmacy and who have inadequate health literacy also have low understanding of pre-admission medications such as the frequency and dosing of their medications (Marvanova et al. 2011).

Polypharmacy has been associated with increased mortality, stroke and major bleeding for patients with AF (Focks et al. 2016). Consequently, vulnerable patients who are at risk of poor medication understanding (due to factors such as polypharmacy and low literacy) may need more intensive medication reconciliation, educational counselling and follow-up to prevent post-discharge adverse drug events (Marvanova et al. 2011).

Culturally and linguistically diverse (CALD) patients may not be able to fully engage with doctors and other healthcare providers about anticoagulant therapy due to language barriers and cultural beliefs (Lip et al. 2002; Nadar et al. 2003). To address this, education about warfarin may need to involve the patient's family, friends or carers, accredited interpreters and/or a health care provider that can speak the same language. Further research is required to evaluate the use and impact of medical interpreters on improving knowledge in CALD patients.

To date, there has been limited research focusing on supporting older patients taking oral anticoagulants through the use of carers. For this reason, we included a small number of carers in our study. The role of the carer in shared decision-making has been noted in a previous qualitative study (Manias 2015). However, whilst we know the challenges around managing older patients, we also need to consider the challenges of supporting the carers of older persons, who are often older persons themselves (e.g., spouses, partners, adult children). In our study, the mean age of carers was 61 years; this signals a need to assess the warfarin knowledge and health literacy of carers as well as the patients themselves

Whilst this study provides insights into the medication management challenges of high-risk patients in the local setting, this study has several limitations. First, the generalisability of the findings may be limited by: the relatively small sample size as this was a pilot study, the number of general practitioners agreeing to recruit patients, the number of participants agreeing to do the study, and by the specific characteristics of our study sample, i.e., 27% were university-educated with a median age of 80, were not culturally diverse nor warfarin- naïve, which may have influenced the level of warfarin knowledge. Furthermore, our patients were recruited from one specific setting (one medical centre). The patients in this study may not represent the preferences and perspectives of the thousands of patients encountered in other practice settings, whether in Australia or more globally.

Second, the medical staff were involved in identifying potential participants so this may have introduced some selection bias. Third, having the participants answer the questionnaire via the telephone may have adversely influenced their experience, compared to those who answered in person. Fourth, the shortened questionnaire was not specifically validated for use in this setting. Fifth, due to the small sample size, the data from both patients and carer was combined and precludes an exploration of whether any patient characteristics may have affected patient preferences. Nevertheless, the study provides some useful insights into the local Australian practice setting, identifying gaps that need to be filled.

Future research should focus on involving a greater number of participants and their carers from different cultural backgrounds, using the multi-dimensional HLQ tool to assess health literacy and a validated questionnaire to assess knowledge about oral anticoagulants (warfarin and the NOACs) in the community and hospital settings. In addition, health outcomes of health literacy, knowledge and health impact of self-managed patients versus carer-managed patients taking oral anticoagulants could be explored.

Furthermore, although there have been some studies involving pharmacist education to older persons (Collins, Barber & Sahm 2014; Masnoon, Sorich & Alderman 2016; Stafford, Peterson, Bereznicki, Jackson, van Tienen, Angley, Bajorek, McLachlan, Mullan & Misan 2011) and those with limited literacy (Collins, Barber & Sahm 2014), there is a need for pharmacists to develop interventions to support CALD patients about warfarin. Several studies in the literature have highlighted the need for medicines information among CALD patients (Dilworth, Mott & Young 2009; El Samman et al. 2013; Mohammad, Saini & Chaar 2015).

3.5. Conclusion

This study provides insights regarding the challenges of managing warfarin in older persons due to their characteristics, and highlights the ongoing knowledge gaps about warfarin, the limitations of health literacy, and the importance of involving carers of the older persons during education. Participants born overseas and those using polypharmacy may require more support with tailored education and follow-up to improve their health literacy and warfarin knowledge.

3.5.1 Key Points

- Among older patients and their carers, knowledge gaps about warfarin therapy remain.
- There is a need for warfarin education to include medication safety and self- management strategies, for both patients and carers.
- It is important to assess warfarin knowledge and the health literacy of older patients using warfarin therapy and their carers.

- Participants born overseas and those using polypharmacy may require more support with tailored education and follow-up to improve their health literacy and warfarin knowledge

3.6. Acknowledgement

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Table 3.1 Characteristics of Participants (N=34)

Participant characteristics	Patients (n=30) (Percentage in subgroup)	Carers (n=4) (Percentage in subgroup)	Warfarin knowledge score (N=34) Mean (SD) Median (IQR)	P-value*
Median age (years), IQR	81.0, 11.0	61.0, 35.5	N/A	N/A
Age range (years)	67.0 to 99.0	43.0 to 85.0	N/A	N/A
Age Group (years)				*p* =0.37
<80 years	12 (40.0)	3 (75.0)	8.3 (1.8) 9.0 (0.8)	
≥80 years	18 (60.0)	1 (25.0)	8.1 (1.4) 8.0 (2.3)	
Gender				*p*=0.76
Male	24 (80.0)	1 (25.0)	8.1 (1.7) 8.0 (1.5)	
Country of birth				*p*=0.47
Born in Australia	21 (70.0)	1 (25.0)	8.2 (1.1) 8.0 (2.0)	
Born from overseas †	9 (30.0)	3 (75.0)	8.0 (2.2) 9.0 (3.3)	
English spoken at home	30 (100.0)	3 (75.0)	8.1 (1.6) 9.0 (2.0)	*p*=0.71
Aboriginal	1 (3.3)	0	N/A	*p*=0.77
Education and schooling				*p*=0.25
Primary school or less	1 (3.3)	0	N/A	
High school-partial completion	8 (26.7)	2 (50.0)	8.3 (1.2) 8.0 (2.3)	
High school (completed)	5 (16.7)	0	8.4 (1.9) 9.0 (2.5)	
TAFE or Trade	8 (26.7)	0	7.8 (1.2) 8.0 (2.3)	
University	8 (26.7)	2 (50.0)	8.4 (2.1) 9.0 (0.8)	
Private health insurance	25 (83.3)	3 (75.0)	8.2 (1.5) 8.5 (1.8)	*p*=0.95
Assistance required†† for the completion of the HLQ questionnaire	9 (30.0)	0	7.4 (1.1) 7.0 (2.0)	*p*=0.03
Lives alone	10 (33.3)	0	8.5 (1.5) 9.0 (2.5)	*p*=0.38

* Comparison of warfarin knowledge scores across subgroups using Mann-Whitney test.

† Born in countries including Germany, Taiwan, Philippines, New Zealand, United Kingdom and Malaysia.

†† Assistance refers to explaining questions, statements and responses to the participant.

Abbreviations: SD=standard deviation; IQR =Interquartile range; N/A: not applicable; TAFE: Technical and Further Educatio

Table 3.2 Patients' history of warfarin use, medical conditions and medications

Warfarin use and information provision Number of participants (% in subgroup)	Patients who self- manage their warfarin (N=30)	Patients whose warfarin is managed by carers (N=4)	All participants (N=34)
Duration of warfarin use			
< 1 years	2 (6.7)	0	2 (5.9)
1 to 5 years	7 (23.3)	3 (75.0)	10 (29.4)
6 to 10 years	10 (33.3)	1 (25.0)	11 (32.4)
11 to 15 years	5 (16.7)	0	5 (14.7)
16 to 20 years	3 (10.0)	0	3 (8.8)
>20 years	3 (10.0)	0	3 (8.8)
Indication for warfarin			
Atrial Fibrillation (AF)	19 (63.3)	2 (50.0)	21(61.8)
Stroke or transient ischaemic attack	2 (6.7)	1 (25.0)	3 (8.8)
AF and stroke or transient ischaemic attack	2 (6.7)	0	2 (5.9)
Deep vein thrombosis or Pulmonary	5 (16.7)	0	5 (14.7)
Valve replacement	2 (6.7)	1 (25.0)	3 (8.8)
Chronic medical conditions (≥3)	28 (93.3)	4 (100.0)	32 (94.1)
Types of medical conditions			
Cardiovascular	30 (100.0)	4 (100.0)	34 (100)
Respiratory	15 (50.0)	1 (25.0)	16 (47.1)
Rheumatology	13 (43.3)	3 (75.0)	16 (47.1)
Endocrine	12 (40.0)	2 (50.0)	14 (41.2)
Other ‡	17 (56.7)	4 (100.0))	21 (61.8)
Gastrointestinal	13 (43.3)	1 (25.0)	14 (41.2)
Neurology	8 (26.7)	2 (50.0)	10 (29.4)
Liver or kidney	8 (26.7)	1 (25.0)	9 (26.5)
Psychotropic	4 (13.3)	4 (100.0)	8 (23.5)
Cancer	5 (16.7)	2 (50.0)	7 (20.6)
Stroke or transient ischaemic attack	4 (13.3)	1 (25.0)	5 (14.7)

‡ Other conditions include; ophthalmology, dermatology, ear, genitourinary, peripheral neuropathy, restless legs syndrome, obesity, bone marrow disorder and shingles.

‡‡ Patient's records may have reported more than one long term medication.

‡‡‡ Other long-term medications include; ear ointment, antifungal, iron chelator, non-cytotoxic antineoplastic, intranasal corticosteroid spray and somatostatin analogue.

‡‡‡‡ Primary care settings include; General Practice Medical Centre, Community Pharmacy and Specialist's office

Abbreviations: AF = atrial fibrillation; NA= Not Applicable.

Table 3.2 (cont.)

Warfarin use and information provision Number of participants (% in subgroup)	Patients who self-manage their warfarin (N=30)	Patients whose warfarin is managed by carers (N=4)	All participants (N=34)
Polypharmacy (≥5 long term medications)	26 (86.7)	4 (100)	30 (88.2)
Number of patients taking long term medications in the following categories ‡‡			
Antithrombotic	30	4 (100)	34 (100)
Cardiovascular	26	4 (100)	30 (88.2)
Herbs/vitamins	18	4 (100)	22 (64.7)
Gastrointestinal	15	4 (100)	19 (55.9)
Analgesics	13	1 (25)	14 (41.2)
Dermatological	12	1 (25)	13 (38.2)
Respiratory	12	0	12 (35.3)
Psychotropic	9	3 (75)	12 (35.3)
Endocrine	8	2 (50)	10 (29.4)
Rheumatology	8	0	8 (23.5)
Genitourinary	8	0	8 (23.5)
Ophthalmic	6	1 (25)	7 (20.6)
Neurological	4	1 (25)	5 (14.7)
Antimicrobial	3	0	3 (8.8)
Other‡‡‡	11	1 (25)	12 (35.3)

‡ Other conditions include; ophthalmology, dermatology, ear, genitourinary, peripheral neuropathy, restless legs syndrome, obesity, bone marrow disorder and shingles.

‡‡ Patient's records may have reported more than one long term medication.

‡‡‡ Other long-term medications include; ear ointment, antifungal, iron chelator, non-cytotoxic antineoplastic, intranasal corticosteroid spray and somatostatin analogue.

‡‡‡‡ Primary care settings include; General Practice Medical Centre, Community Pharmacy and Specialist's office.

Abbreviations: AF = atrial fibrillation; NA= Not Applicable.

Table 3.2. (cont.)

Warfarin use and Information provision Number of participants (% in subgroup)	Patients who self-manage their warfarin (N=30)	Patients whose warfarin is managed by carers (N=4)	All participants (N=34)
Time since information about warfarin was last received			
0 to 1 years	4 (13.3)	0	4 (11.8)
1 to 5 years	9 (30)	3 (75.0)	12 (35.3)
6 to 10 years	9 (30)	0	9 (26.5)
11 to 15 years	2 (6.7)	0	2 (5.9)
16 to 20 years	2 (6.7)	0	2 (5.9)
>20 years	3 (10.0)	0	3 (8.8)
Not sure	1 (3.3)	1 (25.0)	2 (5.9)
Main provider or warfarin education / information when warfarin was initiated			
General Practitioner/Specialist	23 (76.7)	3 (75)	26 (76.5)
Pharmacist	2 (6.7)	0	2 (5.9)
General Practitioner/Specialist and Nurse	4 (13.3)	0	4 (11.8)
Not sure	1 (3.3)	0	1 (2.9)
No one	0	1 (25)	1 (2.9)
Location of education:			
Primary care setting‡‡‡‡	15 (50.0)	0	15 (44.1)
Hospital setting	12 (40.0)	2 (50)	14 (41.2)
Primary care and hospital settings	3 (10.0)	0	3 (8.8)
Not sure	0	1 (25)	1 (2.9)
Patient self-reported nil counselling received	0	1 (25)	1 (2.9)

‡ Other conditions include; ophthalmology, dermatology, ear, genitourinary, peripheral neuropathy, restless legs syndrome, obesity, bone marrow disorder and shingles.

‡‡ Patient's records may have reported more than one long term medication.

‡‡‡ Other long-term medications include; ear ointment, antifungal, iron chelator, non-cytotoxic antineoplastic, intranasal corticosteroid spray and somatostatin analogue.

‡‡‡‡ Primary care settings include; General Practice Medical Centre, Community Pharmacy and Specialist's office.

Abbreviations: AF = atrial fibrillation; NA= Not Applicable

Table 3.3 Health Literacy Questionnaire (HLQ) scores for all participants (N=34)

	Median score (IQR) for all participants	Number of participants with a lower level of health literacy[§] within individual scale
HLQ Scale	Range 1 (lowest score) - 4 (highest score) [§§]	
1. Feeling understood and supported by healthcare providers (N= 4 items)	3.5 (0.8)	2 (5.9%)
2. Having sufficient information to manage my health (N= 4 items)	3.0 (0.3)	7 (20.6 %)
3. Actively managing my health (N= 5 items)	3.0 (0.7)	12 (35.3%)
4. Social support for health (N= 5 items)	3.1 (0.7)	8 (23.5%)
5. Appraisal of health information (N= 5 items)	2.9 (0.7)	17 (50.0%)
	Range 1 (lowest score) - 5 (highest score) [§§§]	
6. Ability to actively engage with healthcare professionals (N= 5 items)	4.2 (0.6)	4 (11.8)
7. Navigating the healthcare system (N= 6 items)	4.1 (0.5)	7 (20.6)
8. Ability to find good health information (N= 5 items)	4.0 (0.5)	12 (35.3)
9. Understand health information enough to know what to do (N= 5 items)	4.1 (0.8)	10 (29.4)

§ Lower level of health literacy was defined as a mean scale score of less than 3 for scales 1 to 5 and a mean scale score of less than 4 for scales 6 to 9.

§ § Mean Scale scores range between 1 and 4 for the first 5 scales. Items asked from how strongly the participant disagrees (lowest score of 1) to strongly agrees (highest score of 4).

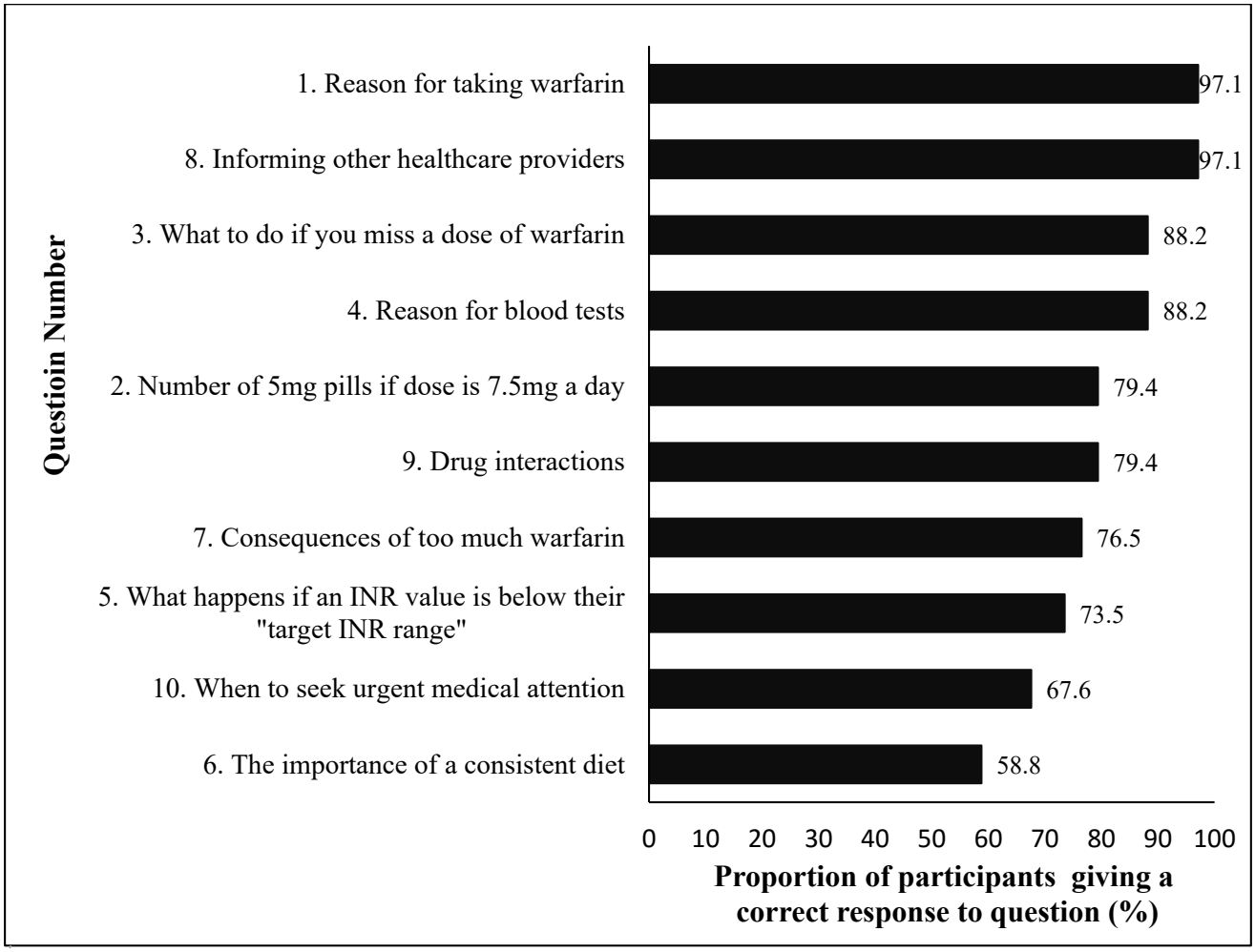
§ § § Mean Scale scores range between 1 and 5 for scales 6 to 9. Items asked how difficult or easy the following tasks are for you now from cannot do (lowest score of 1) to very easy (highest score of 5).

Abbreviations: HLQ, Health Literacy Questionnaire; IQR, interquartile range.

Table 3.4 Communication Strategies for healthcare providers

- Prioritise the educational domains, standardise the educational content and deliver the content efficiently (Wofford, Wells & Singh 2008).
- For leaflets use simple, clear statements in lay terminology that are easy to follow. Use simple and familiar icons and simple list formatting. Ensure patients are able to find information and take the appropriate actions (Aker & Beck 2013).
- Work with consumers for the development of simple and clear drug information (Aker & Beck 2013).
- Supplement written information with other modes of delivery such as verbal information, multidisciplinary programs involving doctors, nurses, dieticians and pharmacists, DVD, booklets, audiovisual resources depicting real-life scenarios, brown bag medication reviews, and visual aids (Koh & Rudd 2015).
- Involve the carer and family members when doing patient education to older patients (Nasser, Mullan & Bajorek 2012; Vormfelde et al. 2014).
- Use the teach back method for patients with low literacy to confirm comprehension (Koh & Rudd 2015).
- Help patients to ask questions. For example, ask, “What are your questions?” (Koh & Rudd 2015).
- Help patients make decisions about their care. Communicate risks and benefits of information in a balanced and transparent way (McDowell et al. 2016

Figure 3.1 Proportion of participants correctly answering warfarin questions



Chapter 4: Warfarin Action Plan (WAP)

Patient Feedback on a Warfarin Action Plan (WAP) used in a local Australian setting (Paper 3)

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(Submitted to *Therapeutic Innovation and*

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Abstract

Background

Warfarin is a high-risk medicine, and older persons who take this therapy need education about it that is at a level which is both understandable and comprehensive to improve their knowledge (Diamantouros, Bartle & Geerts 2013; Nasser, Mullan & Bajorek 2012). Therefore, the primary objective of this study was to report patient feedback on a Warfarin Action Plan (WAP) (leaflet) and identify patients' preferences regarding its content and format. The secondary objective was to canvass in-depth feedback regarding the participants' information needs and current information-seeking practices with respect to warfarin therapy.

Method

In an Australian General Practice medical centre setting, a qualitative study comprising 34 individual interviews was conducted. Emergent themes were elicited via a qualitative analysis using manual inductive coding.

Results

The majority of participants gave very positive feedback on the WAP leaflet stating that it was a useful and concise resource. In canvasing this feedback four themes emerged: 1) the need for information about warfarin therapy, 2) reliance on doctors and/or pharmacists for information, 3) need for information to normalise their daily life and 4) patients and carers acting on the new information.

Conclusion

The WAP is a simple and well received tool that meets the knowledge and education needs about warfarin therapy for older people and their carers.

Key words:

written medicine information, patient engagement, patient education, older person, warfarin.

4.1. Introduction

Given their potential for causing significant patient harm such as life-threatening haemorrhagic complications (Di Fusco et al. 2018; Sennesael et al. 2018), oral anticoagulants are considered to be 'high risk'(Clinical Excellence Commission (CEC) 2015).To ensure the safe and effective use of warfarin, patient education is paramount (Tideman et al. 2015).

Patient education about warfarin in the form of written information must be provided in an understandable format (Diamantouros, Bartle & Geerts 2013), particularly for older persons (Bajorek et al. 2007; Bajorek et al. 2009; Tang et al. 2003). Studies have reported problems with their use, including that they do not contain essential advice for the safe use of the medicine, may not be comprehensible (Diamantouros, Bartle & Geerts 2013) or contain excessive information (Tong et al. 2016). Both patients and caregivers have expressed a need for more information about warfarin (Bajorek et al. 2007). Therefore, the aim of this study was to gauge patients' perspectives on a Warfarin Action Plan (WAP). The primary objective was to report patient feedback on the WAP leaflet and identify patient's preferences regarding its content (specific information and detail) and format (presentation and appearance) (Part A). The secondary objective was to canvass in-depth feedback regarding the participants information needs and current information-seeking practices with respect to warfarin therapy (Part B).

4.2. Methods

4.2.1 Study design and setting

A qualitative research design was chosen so as to elicit more detailed, in-depth feedback than would have been possible through a quantitative data approach (Bradshaw, Atkinson & Doody 2017). A pragmatic (i.e., qualitative description) approach was chosen as it seeks to discover and understand a phenomenon, a process, or the perspectives and world views of the people involved (Bradshaw, Atkinson & Doody 2017). This approach is an inductive process, involving an emic stance (i.e., focused on the participant's perspective), and is conducted in the natural setting (Bradshaw, Atkinson & Doody 2017). The consolidated criteria for reporting qualitative studies (COREQ 32-item checklist) were used to guide the structure of the study (Tong, Sainsbury & Craig 2007).

This study comprised individual face-to-face or telephone-based semi-structured interviews, conducted between September 2015 and January 2016, in an Australian general practice medical centre located in Greater Western Sydney, New South Wales, Australia. The site was chosen as it was a relatively large medical centre (i.e., employed numerous doctors (n=21)), where the majority of anticoagulated patients were taking warfarin (per feedback from the medical centre).

4.2.2 Ethics approval

Approval to conduct this study was granted by the Human Research Ethics Committee of the University of Technology of Sydney (Project number: 201 4000 863).

4.2.3 The Warfarin Action Plan (WAP)

WARFARIN ACTION PLAN

 Shutterstock	**Learn about why you are taking warfarin.** Warfarin helps to stop clots forming in your blood vessels. Blood clots can block the blood supply in your legs, lungs, heart, or brain and can cause strokes. **Find very good information** at: • National Prescribing Service (NPS) www.nps.org/warfarin (see videos) • NPS Medicines Line Phone: 1300 633 424
 iStock	**If you forget to take a dose**: • Tell your doctor • Take the next dose at your usual time. • Do not take an extra dose to make up for the missed dose. **Have a routine to remember your dose. Take warfarin ONCE a day.**
 Shutterstock	**Have regular blood tests** as advised by your doctor. The blood test is called INR (International Normalised Ratio). It helps your doctor check that your dose is right. If your dose is too low you can get a clot. If your dose is too high you can bleed. After the test your doctor may change your dose. **Keep a record of your blood (INR) test results and doses** using: • Page 2 of this leaflet • www.nps.org.au/warfarin-dose-tracker or phone (02) 8217 8700
 Shutterstock	**Eat the same amount of vitamin K rich foods each day** to keep your INR stable. Vitamin K is mostly found in green, leafy vegetables such as kale, spinach, broccoli and cabbage. Talk to your doctor or an accredited dietician for advice.
 Shutterstock	**Tell all of your health providers** that you are taking warfarin. This includes your doctor, surgeon, pharmacist, dentist and physiotherapist. **Carry:** • **Identification:** - A MedicAlert bracelet or a warfarin card, in case of an emergency - See www.medicalert.org.au or Phone: 1800 88 22 22 • **An up-to-date medicine list**
 Shutterstock	**Ask your doctor or pharmacist questions** such as: • What products can affect how my warfarin works? • Can I start or stop or change any of my medicines, herbs, vitamins and products from the pharmacy or supermarket? • How much alcohol can I drink safely? • What advice can you give me about preventing falls and injuries?
 iStock	**Call your doctor** if you notice any unwanted side effects such as bruising and bleeding (such as nose bleeds) **Call your doctor or hospital urgently** if you have: Bleeding that will not stop, a headache, fever or diarrhoea that does not go away, red or brown urine, red or black stools, coughing up or vomiting blood, difficulty in breathing, unusual pain, purplish toes, a serious fall or injury.

Warfarin Action Plan Version 2 (27th August 2015).
Patient Feedback on a Warfarin Action Plan to be used in the local Australian setting
Investigators: Angela Yiu, A/Prof Beata Bajorek. Email: Angela.W.Yiu@student.uts.edu.au
Disclaimer: This leaflet may not contain all the information you need to know about warfarin. Please consult your doctor and the consumer medicine information leaflet for further information. Copyright 2015.

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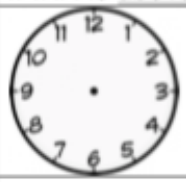
WARFARIN ACTION PLAN **Date plan prepared: ___/____/____**

My name:		**Telephone:**
Doctor:	**Name:**	**Telephone:**
Pharmacy:	**Name:**	**Telephone:**
Pathology:	**Name:**	**Telephone:**
My warfarin is for:		
I am taking warfarin for:	❑ Ongoing treatment ❑ _____ months	Date warfarin started: ____/ ____ / _____
My target INR range is:	Between _____ and _____	If INR is below range: clot more likely If INR is above range: bleed more likely
I will take warfarin at:	_____:_____ ❑ AM ❑ PM	 Take warfarin at the same time each day with food or no food.
My brand of warfarin is (tick):	❑ COUMADIN™	❑ MAREVAN™
The colour and strength of my tablets are (tick):	Light tan 1mg ❑ Lavender 2mg ❑ Green 5mg ❑	Brown 1mg ❑ Blue 3mg ❑ Pink 5mg ❑

DOSING RECORD

Date of blood (INR) test	Blood (INR) test result	Dose of warfarin to be taken each day (as advised by doctor)							Date for the next blood (INR) test	Doctor signature
		Mon	Tues	Wed	Thurs	Fri	Sat	Sun		

Investigators: Angela Yiu, A/Prof Beata Bajorek. Email: Angela.W.Yiu@student.uts.edu.au

The WAP is a double-sided, A4-size sheet summarising the main actions to be taken by patients in managing their warfarin therapy with pictorial reinforcement. It also includes a definitive dosing record alongside the blood test results. The leaflet uses simplified language and pictorial reinforcement, referring patients to relevant resources and services/health professionals for further information or assistance. The leaflet was designed to provide: practical and key information regarding warfarin therapy; advice on what actions to take to manage situations such as missed doses; and encouragement of patient engagement with their health care providers on common issues affecting adherence to therapy.

The WAP leaflet was developed by two pharmacists and one general practitioner, guided by a guideline, policy, framework and resources in the literature (Aker et al. 2013; Australian Commission on Safety and Quality in Health Care 2010, 2014; Clarkesmith et al. 2016; Clinical Excellence Commission (CEC) 2015; Kirchhof et al. 2016; Nasser, Mullan & Bajorek 2012; National Institute for Health and Care Excellence (NICE) 2018a; Raynor & Dickinson 2009; Wofford, Wells & Singh 2008). The leaflet covered the following key topics: action and indication of warfarin (Barcellona, Contu & Marongiu 2002; Masnoon, Sorich & Alderman 2016; Nasser, Mullan & Bajorek 2012), brand name (Callahan et al. 2013), directions including missing a dose (Barcellona, Contu & Marongiu 2002; Callahan et al. 2013; Khudair & Hanssens 2010; Maikranz et al. 2017), blood tests (Amara et al. 2015; Masnoon, Sorich & Alderman 2016; Nasser, Mullan & Bajorek 2012), diet (Barcellona, Contu & Marongiu 2002; Lane et al. 2006; Maikranz et al. 2017; Tideman et al. 2015), the effect of other medications and alcohol on anticoagulation (Callahan et al. 2013; Lane et al. 2006; Masnoon, Sorich & Alderman 2016; National Institute for Health and Care Excellence (NICE) 2012; Tideman et al. 2015), interaction with health providers (Maikranz et al. 2017; National Institute for Health and Care Excellence (NICE) 2012), carrying identification (Maikranz et al. 2017; National Institute for Health and

Care Excellence (NICE) 2012), when and how to seek medical help if you notice unwanted side effects (Maikranz et al. 2017; Masnoon, Sorich & Alderman 2016; Nasser, Mullan & Bajorek 2012; National Institute for Health and Care Excellence (NICE) 2018a; Tideman et al. 2015), duration of treatment (National Institute for Health and Care Excellence (NICE) 2018a), target INR range (Maikranz et al. 2017; Nasser, Mullan & Bajorek 2012) , timing of dose (Barcellona, Contu & Marongiu 2002) and dosing record with INR results/ monitoring (Callahan et al. 2013; National Institute for Health and Care Excellence (NICE) 2018a).

4.2.3.1. Participants

Study participants were patients and their carers of the medical centre as recruited via purposive sampling. The inclusion criteria comprised older patients who were:

- ≥ 65 years of age
    - This age criterion was chosen based on definitions in the literature (Orimo et al. 2006; World Health Organization 2018a) and due to the association of a higher prevalence of atrial fibrillation in older persons; anticoagulant therapy is an important treatment in this population to prevent the risk of a stroke (Go et al. 2001).
- taking warfarin therapy for a long-term indication (regardless of when initiated)
- cognitively intact (based on the clinician's knowledge of the patient)
- able to communicate in English
- able to provide informed consent.

For patients who were unable to fulfil the last three inclusion criteria, the primary carer who was responsible for managing their warfarin therapy was invited to participate instead.

To recruit participants, the medical centre staff (5 general practitioners, one on-site cardiologist) screened their electronic patient records to identify potential participants. A receptionist then sent (via postal mail) to each patient a generic letter informing them about the study and inviting them to contact the student researcher (AY). Non-responders received a once-only follow up telephone call (1-week post first mailout). On response, the person's eligibility (per inclusion criteria) was verified. All participants received a participant information sheet and then consent to participate in the study was obtained.

4.2.4 Data collection and analysis

After data were collected during scheduled face-to-face appointments at the medical centre, or via the telephone, participants were given a paper-copy of the WAP leaflet (either in person or via mail) for their review. De-identified background information about each participant was extracted from the electronic medical records at the medical centre or via interview. Patients' perspectives were elicited using a semi-structured interview schedule comprising several open-ended questions (Appendix 7.6).

Due to the straightforward nature of the questions, the interview guide was not pilot-tested, and repeat interviews were not required. None of the researchers had any pre-existing relationships with the study participants.

Participants were interviewed one-on-one within one week of receiving the leaflet. The student researcher conducted all interviews for consistency. The interviews were audio (digitally) recorded, de-identified and transcribed verbatim. Thematic analysis of the transcribed interviews was performed using manual inductive coding, involving: becoming familiar with the data; generating initial codes; then searching, reviewing and defining themes (Braun & Clarke 2006;

Maguire & Delahunt 2017). Investigator triangulation was undertaken whereby two researchers (BB and one pharmacist unrelated to the study) each read and independently coded a random selection of transcripts for theme verification. The emergent themes were discussed among the researchers to ensure that consensus was attained. The transcripts were not returned to participants for comment and/or correction.

4.3. Results

Of the 87 patients invited to the study, 36 participants agreed to participate, with 2 subsequently withdrawing due to a lack of time. The mean duration of each interview was 26 minutes and theme saturation was attained.

4.3.1 Participant characteristics

Among the 34 participants, 30 were patients taking warfarin and 4 were carers of patients taking warfarin. The median patient age was 81 years (range 67 to 99 years) and the majority of patients (n=21; 70%) were born in Australia. The median age of carers was 61 years (range 43 to 85 years) and the majority (n=3) born from overseas. Approximately 94.1% of patients (n=32) had multimorbidity (i.e. co-occurrence of ≥3 chronic conditions (Harrison et al. 2014) and 88.2% (n=30) used polypharmacy (i.e. ≥ 5 medications) (Gnjidic et al. 2012).

The most common indication for warfarin was stroke prevention in atrial fibrillation (61.8%). Although most patients had been taking warfarin for between 6 to 10 years (32.4%), only one-third (35.3%) of patients recalled receiving any information within the last 1 to 5 years. The

location of their warfarin education was most commonly a primary care setting (44.1%) and the main provider for the warfarin education was a general practitioner or specialist doctor (76.5%).

4.3.2 Part A: Patient feedback on a Warfarin Action Plan

The majority of participants gave very positive feedback on the WAP leaflet and liked its format (see Table 4.1). In relation to content, most participants felt that all of the information was very important, highlighting specific aspects such as information on: what to do about missed doses; and different brand names of warfarin (including pictures of the tablets). Additionally, most participants liked that the leaflet was interactive. It was interactive because the patients could interact directly with the content by completing the blank sections and could be prompted to take practice action such as to carry a MedicAlert bracelet or warfarin card. One carer stated that information in the leaflet would be helpful to share with her sisters when they cared for her mother (see Table 4.1).

A few participants expressed the potential limitations of such a concise leaflet. Some participants suggested clearer instructions with regards to taking the same brand of warfarin, and that the dosing record table might not be long enough, or that information regarding drug interactions and Vitamin K-containing foods might be too brief. One participant particularly felt that the choice of images (i.e., people with happy faces) needed to be reconsidered (see Table 4.1)

4.3.3 Part B: In-depth feedback on information needs

Four key themes emerged from the data (see Figure 4.1). These included: the need for information about warfarin therapy, reliance on doctors and/or pharmacists for information, the need for information to ‘normalise’ their life, and patients and carers acting on new information.

4.3.3.1. Theme: Need for information about warfarin therapy

The interviews identified that 15 participants, even those participants (n=13) who had experience with warfarin for five years or more, demonstrated gaps in their knowledge of warfarin therapy (see Table 4.2). For one participant, this elicited a strong sense of annoyance that she had not been made aware of the information about the different brands of warfarin previously as she realised that her mother kept both brands of warfarin in the cupboard.

> "…. it shouldn't have happened in the first place" (P36 carer, Participant 36).

Two long-term warfarin users (minimum 10 years) lacked knowledge about the importance of recording the dose of warfarin and were unaware of factors that can affect the international normalised ratio (INR) levels, leading to dose changes.

> "Well it's not necessary… if you are taking the same dose every day which you should be and …if you're having your INR taken once a month which you should be. so why do you want to write it down for?..... my dose doesn't change" (P5)

Although there was an expressed need for more information, there was not much desire for information to be provided using technology as a few participants were not computer literate. However, as suggested by one participant, a range of formats might cater for different preferences, needs and concerns.

> "if you are dealing with the younger people, a video or an app would be quite good, but a leaflet better for older people" (P19).

"You might need all these options …" (P22).

4.3.3.2. Theme: Reliance on doctors and/ or pharmacists for information

Knowledge gaps existed for some participants as they relied on doctors and /or pharmacists for all the information about warfarin- they were passive recipients of information, not active information seekers (see Table 4.3). One carer felt that this over-reliance may also increase the potential for mistakes to be made when managing the therapy.

"We utterly rely on the doctor and the pharmacist….you know their knowledge, their professionalism in regard to their role you know" (P36 carer, Participant 36).

Overall, there was a sense of complete trust in their health care professional as the main source of information about warfarin, with no real impetus to seek further information.

4.3.3.3. Theme: Need for information to 'normalise' their life

The participants were not keen to receive information that was simply instructional or about warnings. They were looking for practical information about how to integrate warfarin into their everyday lives such as establishing routines for INR monitoring and useful dietary advice aside from a need for more information in general, several participants expressed a need for information that 'normalised' warfarin therapy for them (see Table 4.4). They were looking for the information to be more reassuring by conveying warfarin therapy as being less complicated,

describing the potential risks as being less ‘urgent’ or ‘severe’, and diminishing the potential implications of missed doses/dietary interactions.

4.3.3.4. Theme: Patients and carers acting on new information

Many patients already acted on the information or indicated their intentions to act on the information, e.g. the recording of their doses and INR results and obtaining a Medic-Alert™ bracelet (see Table 4.5).

4.4. Discussion

The findings from the results suggest that there is a need for information about warfarin by patients and their carers and these needs can be addressed on a relatively simple scale with resources such as the WAP leaflet. In addition, the WAP leaflet is a simple tool which can have a meaningful impact by improving patient’s knowledge about warfarin and has the potential to enable patients to act on the information provided so they can self-manage their warfarin therapy.

The beneficial impact of written medicines information on clinical outcomes such as the improvement in knowledge about warfarin is consistent with other findings in the literature for a one page leaflet (Aker et al. 2013), booklets (Fairbairn-Smith et al. 2011; Fatima et al. 2016; Lane et al. 2006) and a multicomponent educational intervention (Clarkesmith et al. 2013). However, there was limited research which showed the impact of improved knowledge from written information about warfarin on patient actions or behaviour (Lee et al. 2016).

The findings suggest that the WAP leaflet may be used to engage and motivate patients to act with the information presented to them. In addition, the WAP leaflet is an inexpensive resource which can be customised for a range of vulnerable, at-risk patient groups across a range of health care settings.

4.4.1 Strengths, limitations and future research

Among the strengths of this study is the inclusion of carers in the feedback process, and the use of qualitative feedback as an alternative to quantitative readability assessments of information resources (Diamantouros, Bartle & Geerts 2013; Estrada et al. 2000; Schwartz, Woloshin & Welch 2009; Wilson et al. 2003). However, there were some potential limitations. Our results may not be generalisable as data collection pertained to a single primary care-based medical centre, and that participants were not new warfarin users and were mostly older persons. A validated and standardised tool was not used to assess cognition to formally characterise the participants. Further research is required to evaluate the resource in other languages and settings such as the hospital.

4.5. Conclusion

This study has highlighted the potential role of a WAP leaflet as a tool for older people and their carers to improve patient's knowledge about warfarin. It also has the potential for harm reduction, as well as assisting patients to self-manage their warfarin therapy and integrate the therapy in their normal daily life.

Acknowledgements

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This study has received no funding and the authors declare that they have no conflict of interest.

Photo credits

An image of a lady with a computer (from Image Point Fr/Shutterstock.com), an image of a man with a question mark (from iStock.com/yelet), an image of a blood test (from IvanRiver/Shutterstock.com), an image of vegetables (from Serge64/Shutterstock.com), an image of a doctor in a green uniform (from wavebreakmedia/Shutterstock.com), an image of a doctor behind a computer (from kurhan/Shutterstock.com) and an image of a lady with a telephone (from iStock.com/Feverpitched).

Figure 4.1 Thematic Schema

Three themes were related to the drivers for the WAP leaflet and one theme reflected patients and carers acting on new information.

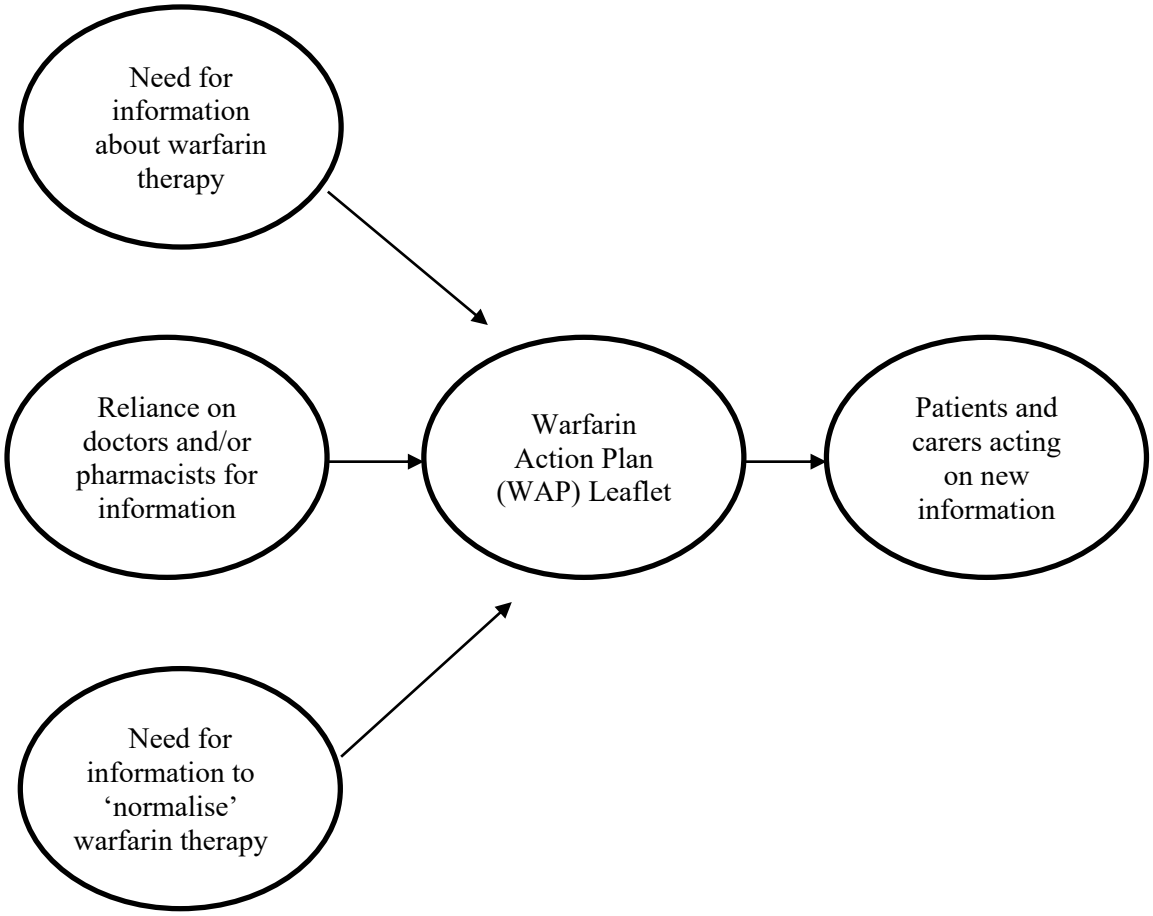

Table 4.1 Participants' comments about the WAP leaflet

WAP Feature	Positive feedback	Negative feedback	Suggested improvements
Format	"A one-page leaflet is good for first timers. Long term users could use a booklet "(P8) "As it is its fine as it is because they can quickly read through it" (P6) "People are more likely to read this than they are a lengthy routine in a book (p7) "Everything on here is very good" (P28)	"A booklet is more convenient to carry" (P28) "A little booklet …may be easier to store" (P11)	Make the black lines thicker on page 2 (P32) Have the same concise information in a quarter size (P28) or two thirds of (P29) or half the size (P3, P12) or one quarter of a size of an A4 sheet of paper (P12) Make the leaflet into a pocket size leaflet (P24) Laminate the leaflet (P23, P24), attach a magnet so the leaflet can be put on the fridge (P16) Consider an app or a video (P23.P22) or DVD and leaflet (P36) To have an app or video for younger people (P19, P22) but a leaflet for older people (P19)
Inclusion of pictures	"For those for whom English is a second language would be a benefit" (P5) "I like the pictorial aspects because some people are visual learners" (P12) With regards to the pictures of the warfarin tablets: I'm a colour-blind person..it's good that you've got the brown, blue, and pink… explanations underneath (P18)	"Just the front one … they look a little bit squashed up "(P3) "I don't know if I'd be showing the hypodermic needle" (P7) "I can't imagine that woman would be standing there with a big grin on her face while she's calling the doctor urgently" (P7)	Increase the size of the leaflet (P3) Format the pictures so the pictures do not appear squashed (P19) With regards to the pictures of the warfarin tablets: "add a dotted line (P1). Add," Use only the brand your doctor prescribes. Stop! Do not use... do not change brand". Add "I use one brand only" (P20) …or "it is dangerous to switch brands with something much stronger if that's the case" (P14)

			Write in red, "You should only be on either the Coumadin™ or Marevan™ brand and continue to stay with one brand" (P36). To have a warning, "It is dangerous to switch brands "(P14) To have health care professionals such as pharmacists be accountable for patient education by signing their name after educating a patient about warfarin, so the doctor is aware that the patient has been educated (P36)
Font size	"I thought it was pretty clear and the writing is pretty big" (P1) "The font size is sufficient for me to able to read it clearly" (P22)	"The font should be bigger for elderly people" (P35)	Increase the font size to 14 (P35)
Content	"You have captured in one document advice which is comprehensive, but at the same time simple and easy to follow. I really like that you made it interactive "(P12) "It is short, it is concise" (P17) "my sisters may look after mum, so I could just give them that…" "(P36, carer)	"Too wordy, some sentences are repetitive" (P8) "summarise the headings in point form" (P35)	Have an action plan with only the bold statements (P24) Reiterate the points that are in bold at the end of the leaflet with a numbering system, so the patient can go refer back to the points in more depth (P35) Summarise the key points in font on the back of the page with numbers (P35)
Information about forget to take a dose	Liked if you if forget to take a dose (P12) A common occurrence and patients need to know what to do (P8)	No comments	No suggestions

Information about the dosing record	"Liked the dosing record to assist with potentially losing memory" (P22) "That's what I like because I follow it as a very strict regime" (P20) The left chart is very good particularly with the INR test results and the dates (P28)	"I can't imagine any doctor having the time or taking the time to sign it" (P17) "Found the dosing record table a bit limiting "(P19)	Remove the doctor's signature in the dosing record table (P7) Make the dosing record table longer by using a booklet or another sheet of A4 paper (P19) Add 2 punch holes to the side of the leaflet so it can be put into a folder (P1) To put information on the back of page one onto a new page as people may not see the back of the page and to reword the brand section as "I use one brand only" (P20)
Information about the Vitamin K content food	"I thought the eating the same amount of vitamin K was a good warning" (p14) "I like the piece about you know what you need, the greens" (P21)	"There could have been a little bit more about the greens and things to keep away from..… Like spinach at the top of the list" (P16) "The only thing I can see missing is the thing about the fruit and also it could be mentioned that antibiotics or other medications could affect it" (P31) "most people haven't got a bloody clue what they mean by a daily serving" (P12)	To include a list of more vegetables such as kale, spinach and broccoli (P2, P28, P10) in terms of what is high, moderate and low in Vitamin K (P23) To list a website link for people to read the topic about food in more detail (P19) Use an analogy like a fist size daily serving so then people can understand the concept of having a consistent Vitamin K diet (P12)

Table 4.2 Illustrative quotes on WAP feedback, focusing on specific information points

	Illustrative Quotes
About carrying warfarin identification	"I didn't realise that I should carry a card …" (P10)
About missed doses	"Well, I didn't know that... if you miss taking a dose not to double up on it or anything" (P6)
About the need to record INR results and doses of warfarin and know the target INR range	"I don't get it checked often... because... I normally remain stable" (P6) "I don't and are unlikely to record my Warfarin results. I've never thought about it" (P10) "I don't know my target range" (P1)
About falls	"What advice can you give me about preventing falls and injuries? "(P17)
About interactions with alcohol or other drugs	"I don't know exactly what effect does alcohol have on the warfarin anyway" (P28) "I was just wondering to know if some of them (drugs) are particularly bad to take" (P28)
About the different brand names of warfarin	"I didn't realise ...that the two brands, Coumadin™ and Marevan™ ...have different effects" (P12)
About foods containing Vitamin K content food	"I didn't know anything about the kale with Vitamin K" (P23)
About informing health care professionals	"Well I don't know about the physiotherapists" (P18)
About the National Prescribing Service (NPS) website	"I didn't know about that first box, find very good information" (P22)

Table 4.3 Theme: Reliance on doctors and/or pharmacists for information

Theme	Illustrative Quotes
Reliance on doctors	"Would you believe I haven't had any other information about Warfarin?..No, brochures just information from the doctor.… I just do as I'm instructed by the doctor, I don't really read through the other information" (P20) "When I first started on warfarin my doctor explained everything to me" (P31)
Reliance on pharmacists	"I always consult my pharmacist and saying, "Look I've heard about this stuff, will it interfere with warfarin?" They say, "Oh, yeah." Well that's the end of it" (P5)

Table 4.4 Theme: Desire for information to 'normalise' their life

Information which is less 'alarmist' and less 'worrisome'	"The bruising without trauma is not to be worried about….". Once you learn to manage it, it's not a problem at all" (P2)
Reflection the 'reality' of being on warfarin	"You might just want to think about putting some sensible statement about the daily serving for the people that don't stop eating vitamin K rich foods because a daily serve of green vegetables is a good thing" (P12) "To indicate the amount of Vitamin K rich foods, refer participants to "a daily dollop, a fist size dollop of spinach or similar vitamin K rich food on their dinner plate each night…" (P12)

Table 4.5 Theme: Patients and carers acting on new information

Information-seeking behaviours	"I'm going to use the back page...in the next few years my memory won't be so good. It will help me ensure that I'm taking the medication each day" (P22) With regards to a warfarin card or Medic-Alert™ bracelet, "I haven't had anything like that but I'm going to do something about that (P10) With regards to the NPS MedicineWise website, "I would be interested to look at the video" (P22) "Oh, I will have a look at it for sure" (P31)
Engaging with health care providers	"Some people might think they're being rude if they ask those sort of questions" (P36)
Initiating self-management behaviours	"And above on the second page, …I've written my mobile number, and Dr BE. his number, the health information pharmacy and their number and [pathology service] who handle the INR (P3) With regards to the recording of INR results, "I've started writing on the leaflet… I'll make copies of yours…. I'll keep doing it ...I'll punch holes in it. I'll put it in a folder" (P1)

Chapter 5: Evaluating NOAC web- based material

Chapter 5

Evaluating the understandability and actionability of web-based education materials for patients taking non-vitamin K oral anticoagulants (NOACs) (Paper 4)

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(submitted to Therapeutic Innovation and Regulatory Science Journal, February 2019)

Abstract

Background

More patients are now taking high-risk medicines such as Non-Vitamin K oral anticoagulants (NOACs). Patient education materials need to be in an understandable format so that they can be empowered to act on their knowledge. Factors such as health literacy and the design of the medicine information material may influence the patient's ability to understand and act on key information.

Method

The PRISMA checklist was used to inform the study design. A structured search was conducted to obtain all freely accessible online educational resources designed for patients about the non-vitamin K antagonists (NOACs) during August 2018. Three search engines were used: Google, Yahoo! and Bing, using the search terms," NOAC or anticoagulant" combined with "patient/consumer information and patient/consumer resources". We applied the Patient Education Materials Assessment Tool (PEMAT) to evaluate web-based patient education materials in terms of understandability and actionability for patients taking NOACs.

Results

Of the 35 materials included, the majority of the materials (n=32, 91%) were rated as highly understandable (PEMAT score ≥70%) and more than three quarters of all the materials (n=29, 83%) were rated as poorly actionable (PEMAT score <70%). Regarding understandability, the majority of materials neither provided a summary of the key points nor used visual aids for several items such as simple tables, illustrations and photographs. For actionability, few materials provided a tangible tool, such as a checklist, to prompt the user into action (n=4). Few used visual aids such as non-verbal cues to the written instructions (n=4).

Conclusion

To improve the understandability and actionability of most of the NOAC patient education materials, there is a need to include more summaries of information, visual aids and tangible tools such as checklists. Further research is warranted where patients are involved in providing feedback on the design of medicine information materials for NOACs.

Key words:
Patient education, internet, health communication, search engines, websites.

5.1. Introduction

Anticoagulants are among the most commonly used high-risk medicines, often used by older persons as long-term therapy for indications such as atrial fibrillation (AF). Most recently Non-vitamin K antagonist oral anticoagulants (NOACs) are now recommended in preference to warfarin to prevent stroke in patients with AF, particularly in patients newly started on anticoagulation (Brieger et al. 2018; Steffel et al. 2018). Although they are devoid of some of the complexities of warfarin, they are not without risk and require attention to several factors such as dosing, administration and drug-drug interactions, risk of bleeding and thromboembolism, monitoring (e.g., renal / liver function) and patient preferences (Brieger et al. 2018; Steffel et al. 2018).

The benefit and safety of anticoagulants is in large part dependent on patient's understanding of the therapy, and therefore education is critical. To date, little attention has been paid to the nature of patient education materials available to patients to support their use of NOACs. Furthermore, there has been relatively limited evaluation of such materials to ensure their usefulness among those patients who are most likely to need extra support, e.g., older persons, those with limited health literacy and those from Cultural and linguistically diverse (CALD) backgrounds (Diamantouros, Bartle & Geerts 2013; Wilson et al. 2003).

The literature highlights the need for carefully and well-designed patient educational materials as most materials are too complex for patients with low health literacy (Diamantouros, Bartle & Geerts 2013; Shoemaker, Wolf & Brach 2014; Wilson et al. 2003). Patient information materials need to be both easy to understand by a wide audience and facilitate consumers of diverse backgrounds and varying levels of health literacy about knowing what actions to take (Morony et al. 2017; Shoemaker, Wolf & Brach 2014). These needs are important as it has been shown

that patient-related factors such as a lack of understanding about the risks and benefits and knowledge about anticoagulant therapy may underpin non-adherence (Pandya & Bajorek 2017). In addition, patients with limited health literacy are one and half to three times more likely to experience a given poor outcome (DeWalt et al. 2004).

Furthermore, providing medicines information which is understandable to patients, including those with limited health literacy, is critical to ensuring the safety and the quality of their health care. Recognising this, in 2010, the U.S. Department of Health and Human Services implemented the 'National Action Plan to Improve Health Literacy' (U.S. Department of Health and Human Services 2010), advocating the need to develop and disseminate health and safety information that is accurate, accessible and actionable. In 2014, the Australian Commission on Safety and Quality in Health Care proposed strategies to ensure effective communication (Australian Commission on Safety and Quality in Health Care 2014), including: 1) the provision of clear, focused and useable information about health care via content and formats that are easy to understand for those with limited health literacy, and 2) effective interpersonal communication through the use of plain language and following up about actions to be taken by consumers (Australian Commission on Safety and Quality in Health Care 2014). These recommendations necessarily extend to health information accessed from digital sources, e.g., the internet (Hesse et al. 2005).

A consumer medicine information (CMI) document is written by the sponsor responsible for the medicine and can be hosted on government regulator's websites such as the Therapeutic Goods Administration (TGA in Australia), European Medicines Agency (EMA in Europe), Food and Drug Administration (FDA in the United States of America (USA)) and Medicines and Healthcare products Regulatory Agency (MHRA in the United Kingdom). CMI documents

written for Australian consumers must meet the guidelines for the provision of CMI as outlined in Schedules 12 and 13 of the Therapeutic Goods Regulations. Schedule 12 lists all the information that must be contained in CMIs for prescription medicines (S4 and S8) (Sless & Shrensky 2006). Schedule 13 lists all the information that must be contained in CMIs for pharmacist only medicines (S3). In Australia, The Therapeutic Goods Administration (TGA) also strongly encourages CMI documents to follow the principles in a publication called, "Writing About Medicines for People: Usability Guidelines" as it provides the optimal way of designing CMIs so that they can be most useful to consumers (Sless & Shrensky 2006). A limitation of this publication is that it was written in 2006 and is in need of updating due to the digital age.

Following from above, it is important to properly assess the understandability and actionability of written health information resources, whether accessed in hard copy, online, or downloaded printed from websites (e.g., PDF brochures) (Shoemaker, Wolf & Brach 2014). Therefore, the primary objectives of this study were to evaluate the understandability and actionability of web-based education resources for patients taking non-vitamin K oral anticoagulants (NOACs).

5.2. Method

This study comprised a critical assessment of medicines information that was accessible via websites.

5.2.1 Data search and selection

A structured search was conducted to obtain all freely accessible online educational resources designed for patients about the non-vitamin K antagonists (NOACs) during August 2018 (see

Figure 5.1). The search was limited to a time span of 8 years (2011–2018), representing the time period following the inclusion of the first marketed NOAC (dabigatran) as a treatment option for stroke prevention in AF within USA clinical guidelines (Wann et al. 2011). Three search engines were used: Google, Yahoo! and Bing, using the search terms," NOAC or anticoagulant" combined with "patient/consumer information and patient/consumer resources". Only the first three pages of each engine (10 websites per page) were searched because it has been shown that Internet users rarely go beyond the 30th result when choosing which website to view (Demetriades, Alg & Hardwidge 2014; Morahan- Martin 2004).

The websites were screened to identify resources that:

- presented information focusing on the use of NOACs
- contained information designed for patients
- were available in the English language
- did not have access/subscription charges
- were not duplicates
- were last updated or reviewed date after August 2011

5.2.2 Ethics Approval

There were no participants in this study and the data were based on publicly available websites, so institutional ethics approval was not required. However, the PRISMA checklist was used to inform the study design, where relevant, to maximise the robustness of the research process (Moher et al. 2010).

5.2.3 Analysis of websites

The content was rated by the student researcher (AY) using a validated tool, the Patient Education Materials Assessment Tool for Printable materials (PEMAT-P) (Agency for Healthcare Research and Quality 2013; Shoemaker, Wolf & Brach 2014).

5.2.4 Patient Education Materials Assessment Tool (PEMAT)

The PEMAT tool provides two scores for each patient education material: understandability and actionability. Understandability refers to the extent to which patient education materials are understandable to consumers of diverse backgrounds and varying levels of health literacy, that is, patients can process and explain key messages. Actionability refers to the extent to which consumers of diverse backgrounds and varying levels of health literacy can identify what they can do based on the information presented (Shoemaker, Wolf & Brach 2014). The PEMAT was purposefully chosen to assess these education materials for two reasons. First, for practical reasons, as it can be applied by untrained lay and health professionals (Shoemaker, Wolf & Brach 2014). Second, although several tools have been used to assess health information materials, such as the Health Literacy INDEX (Kaphingst et al. 2012) and the Centers for Disease Control and Prevention (CDC) Clear Communication Index (Centers for Disease Control and Prevention 2014), they do not measure whether the material is actionable (Shoemaker, Wolf & Brach 2014).

5.3. Results

Of the 189 websites initially identified in the search (Figure 5.1), 110 websites remained after duplicates were removed. From these, 7 websites were further excluded from the analyses because of broken web links or because they could not be freely accessed. Some websites had links to several relevant resources within them, and 113 resources were reviewed. Of the

remainder, 78 resources were excluded because they did not contain information for patients (*n*=37), were not printable or downloadable material (*n*=8) therefore excluding materials from sites such as the National Prescribing Service (NPS), did not contain information specific to NOACs (*n*=14), were journal articles (*n*=15), and/or did not state when they were last updated (*n*=4). From a total of 21 websites that were included in the analyses, 35 downloadable or printable materials were identified.

To determine what web-based educational materials were understandable and actionable, a PEMAT score of 70% or less was considered as being poorly understandable or poorly actionable (Shoemaker, Wolf & Brach 2014). A PEMAT score of 70% or more was considered to be highly understandable or highly actionable. The majority of the materials (n=32, 91%) were rated as highly understandable (PEMAT score ≥70%) and more than three quarters of all the materials (n=29, 83%) were rated as poorly actionable (PEMAT score <70%).

Regarding understandability, the majority of materials did not provide a summary of the key points or review the key points at the end of the material and use visual aids such as graphs, tables, charts, diagrams and pictures (see Table 5.1). Only 3 materials used simple tables with short and clear row and column headings, and only 6 materials used visual aids whenever they could make the content more easily understood. For actionability, only a small number of materials provided a tangible tool such as checklists whenever it could help the user take action (n=4) and used visual aids whenever they could make it easier to act on the instructions (n=4) (see Table 5.1).

Interestingly, those materials that are written by the product sponsor, hosted on government regulator websites, and are commonly distributed to patients with their medication supply, e.g.,

consumer medicines information (CMI) leaflets in Australia and the FDA medication guides in USA, had lower understandability and actionability scores compared to other materials such as those obtained from Clinical Excellence Commission and the Western Australian Government websites. A summary of the understandability and actionability scores for each of the patient education materials are shown in Table 5.1.

5.4. Discussion

Our primary aim was to evaluate the understandability and actionability of web-based education resources for patients taking non-vitamin K oral anticoagulants (NOACs). Overall, this study showed that the majority of material was understandable, however, few of the reviewed materials were actionable.

Our findings suggest that there is a need for patient education materials about NOACs to contain visual aids and provide a summary of the key points to assist with understandability. In one qualitative study (n=45), it has been reported that for patients with limited health literacy, visuals in written medicine information may be beneficial by: increasing the leaflet's appeal; helping patients to ask questions; providing an overview; helping with understanding of textual information; aiding information recall; providing reassurance, and even leading to increased confidence, empowerment and feelings of safety (van Beusekom et al. 2016). In another study, pictures/icons helped consumers taking an oral anticoagulant find important information more easily (Aker et al. 2013).

With regard to actionability, our findings suggest that there is also a need to include visual aids such as checklists to make it easier for patients to act on instructions. Simple list formatting has been shown to improve understanding, recall and speed of accessing information compared to

paragraph format (Aker et al. 2013; G. Morrow Von O. Leirer Jill M. Andrassy Catherine M. Hier William E. Menard 1998).

We also found that there is a need for the product sponsor to consider improving the standard of Consumer Medicines Information (CMI) leaflets and Food and Drug Administration "Medication Guides" by including more visual aids, checklists, and summaries of the main points. Regulators, such as the Therapeutic Goods Administration (TGA) in Australia, Food and Drug Administration (FDA) in the USA, and Medicines and Healthcare products Regulatory Agency (MHRA) in the UK, should consider revising their regulations and guidelines for CMIs so that they will encourage sponsors to write these documents with high levels of actionability and understandability. In one Australian study it was shown that participants found CMIs too long, unattractive and too technical (Koo, Krass & Aslani 2002). Written medicines information needs to have appropriate design features as technical jargon and lengthy content can decrease the likelihood of a consumer reading a CMI and can influence the patient's ability to understand the information about their medicines (Koo, Krass & Aslani 2002).

In the USA, alternative formats to the Food and Drug Administration (FDA) medication guide have been evaluated, revealing that format strongly influences consumer's propensity to read the medicine information leaflet (Aker et al. 2013). It has been reported that consumers prefer the characteristics of patient medicine information leaflets to have desirable features such as a design layout using white space, formatting (the use of bolding and font size), ordering (being able to find the most important information easily) and ease of navigation (being able to find information you are looking for quickly and easily) that is easily understood by consumers (Aker et al. 2013).

Another study from USA evaluated 3 prototypes of the FDA medication guide (Wolf et al. 2014). The first prototype used 2 columns to organise content (Column), the second was similar to the over-the-counter "Drug Facts" labeling (Drug Facts) and the third was a simple table format with actionable column headings to easily locate content, following health literacy best practices (The Health Literacy prototype) (Wolf et al. 2014). Comprehension was significantly greater for all three prototypes compared with the current standard FDA medication guide (Wolf et al. 2014). The Health Literacy prototype, which had a major feature including a left side column with actionable headings to easily find content, consistently demonstrated the highest comprehension scores compared to the other prototypes.

To address the limitations of the standard FDA "Medication guides", a new framework has been developed by the FDA to implement a "One-Document Solution" that contains easy-to-understand information that highlights the most important medicine information (Yuan, Raynor & Aslani 2018). Another suggestion in the literature is the use of a computerized system that could automatically tailor leaflets to patient's characteristics and medical conditions in an easy-to-read and understandable format (Young, Tordoff & Smith 2017). Patients need direct and clear instructions so patients know when action is required and what action should be taken (Young, Tordoff & Smith 2018).

Overall, the findings in this study suggest that those patient education materials that are currently available on the internet need to incorporate features such as visual aids to promote understandability and actionability of the information contained within them. Historically, materials such as CMI leaflets were developed for print distribution, hence, the inclusion of features such as diagrams and tables would have had an impact on their production cost. However, the move to distribution via digital formats as e-CMI/patients leaflets provides the

opportunity to improve the understandability and actionability of these documents to the benefit of patients, thereby helping to improve patient use and adherence and ultimately the quality use of these medicines. Furthermore, although this study focused on education materials for NOACs, the findings in particular with regard to CMI could also be relevant to other medicines.

5.4.1 Strengths and Limitations of this study

Although this study had strengths, such as including the review of websites and materials that patients taking NOACs would likely have access to, there were also a few limitations. This study focused only on accessible and printed website information or downloaded pdf files about NOACs, which excluded audiovisual, non-printable website and app-based material. However, material from reliable government websites, such as the Clinical Excellence Commission and Therapeutic Goods Administration, were included. Furthermore, the assessment of understandability and actionability was done by only one reviewer (AY).

Another potential limitation is that the website information may be suitable only for some older people who are computer literate or who are keen to use the internet. Therefore, it is important to consider whether an elderly patient would actually use a web-based tool or other digital resources. A Pew Research Center survey found that internet adoption among seniors has risen steadily over the last decade and a half with roughly two-thirds of those aged 65 years and older go online (Anderson & Perrin 2017). However, one-third of adults aged 65 years and over say they never would use the internet (Anderson & Perrin 2017). With the growing trend of older people using technology over the past decade, one may expect the next generation of older people to become more tech savvy in the future.

Additionally, some limitations of the PEMAT tool are that it does not assess if the factual content of the information is accurate and up-to-date with a strong evidence base (Clerehan, Buchbinder & Moodie 2004; Shoemaker, Wolf & Brach 2014). We attempted to minimise the limitations by including materials dated 2011 onwards. Other tools such as the Evaluative Linguistic Framework (ELF) addresses some of the limitations of the PEMAT tool and readability formulas (Clerehan, Buchbinder & Moodie 2004). Accordingly, future research is warranted with tools such as the ELF to evaluate NOAC information materials.

5.5. Conclusion

To improve the understandability and actionability of most of the NOAC patient education materials, there is a need to include more visual aids and tangible tools such as checklists.

Further research is warranted where patients are involved in providing feedback on the design of medicine information materials for NOACs.

Compliance with Ethical Standards

Funding

This study did not receive funding from any source

Conflict of interest

No potential conflict of interest was reported by the authors (AY, BB, KN and VL).

Figure 5.1 Outline of Search strategy

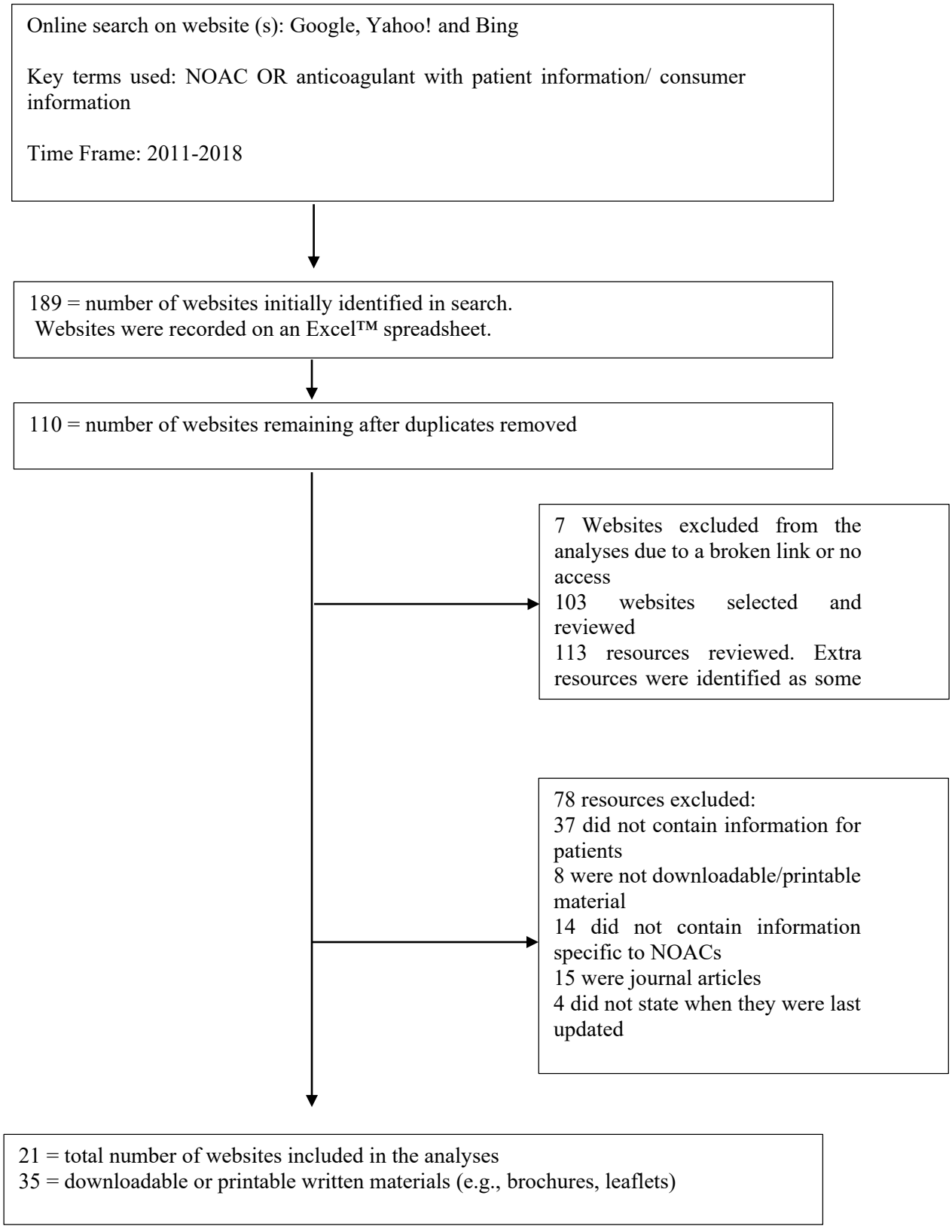

Table 5.1 Understandability and Actionability scores

	Title	Website links (Last accessed 25th August 2018)	Associated institution, (Country)	Understandability score (%)	Actionability score (%)
1	Apixaban (Eliquis) Information for patients, families and carers	http://www.cec.health.nsw.gov.au/patient-safety-programs/medication-safety/high-risk-medicines/anticoagulants	Clinical Excellence Commission, Government (Australia)	94%	67%
2	Rivaroxaban (Xarelto) Information for patients, families and carers	http://www.cec.health.nsw.gov.au/patient-safety-programs/medication-safety/high-risk-medicines/anticoagulants	Clinical Excellence Commission, Government (Australia)	94%	67%
3	Dabigatran (Pradaxa) Information for patients, families and carers	http://www.cec.health.nsw.gov.au/patient-safety-programs/medication-safety/high-risk-medicines/anticoagulants	Clinical Excellence Commission, Government (Australia)	94%	67%
4	Apixaban CMI	https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-CMI-03085-3&d=201808311016933	Therapeutic Goods Administration, Government (Australia)	77%	60%
5	Dabigatran CMI	https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2009-CMI-01176-3	Therapeutic Goods Administration, Government (Australia)	81%	60%
6	Rivaroxaban CMI	https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-CMI-03447-3	Therapeutic Goods Administration, Government (Australia)	77%	60%
7	Living with a Non-Vitamin K Antagonist Oral Anticoagulant (NOAC)	http://www.watag.org.au/wamsg/docs/Living_with_a_NOAC_2015.pdf	Government of Western Australia, Department of Health, Government (Australia)	94%	100%
8	Novel Oral Anticoagulant (NOAC) Patient Information Booklet	http://www.derbyshiremedicinesmanagement.nhs.uk/assets/Clinical_Guidelines/Formulary_by_BNF_chapter_prescribing_guidelines/BNF_chapter_2/NOAC_Patient_Booklet.pdf	Southern Derbyshire, Erewash, North Derbyshire, Hardwick Clinical Commissioning Groups, Government (UK)	77%	60%
9	Direct oral anticoagulants (DOACs) for use in atrial fibrillation	https://www.guysandstthomas.nhs.uk/resources/patient-information/pharmacy/NOACs.pdf	Guy's and St Thomas' NHS, Government (UK)	75%	60%
10	Apixaban in adults	https://www.lmsg.nhs.uk/guidelines/health-community/new-oral-anticoagulants/	Leicestershire Medicines, Government (UK)	92%	60%
11	Rivaroxaban in adults	https://www.lmsg.nhs.uk/guidelines/health-community/new-oral-anticoagulants/	Leicestershire Medicines, Government (UK)	92%	80%

Table 5.1 Continued…. Scores for understandability and actionability of patient education materials for NOACs

	Title	Website links (Last accessed 25th August 2018)	Associated institution, Type of resource /Country	Understandability score (%)	Actionability score (%)
12	Dabigatran in adults	https://www.lmsg.nhs.uk/guidelines/health-community/new-oral- anticoagulants/	Leicestershire Medicines, Government (UK)	92%	60%
13	FDA Rivaroxaban Medication guide	**https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022406s024lbl.pdf#page=45**	FDA, Government (USA)	75%	60%
14	FDA Apixaban Medication guide	**https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/202155s020lbl.pdf#page=40**	FDA, Government (USA)	75%	60%
15	FDA Dabigatran Medication guide	**https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/022512s014mg.pdf**	FDA, Government, (USA)	75%	60%
16	Anticoagulants	https://patient.info/health/anticoagulants	A team of GPs, Commercial (UK)	75%	60%
17	Atrial fibrillation and Stroke Prevention	https://patient.info/health/anticoagulants	Patient.info, Professional (UK)	69%	60%
18	Apixaban	https://www.drugs.com	Drugsite Trust, Commercial (USA)	77%	60%
19	Rivaroxaban	https://www.drugs.com	Drugsite Trust, Commercial (USA)	85%	60%
20	Dabigatran	https://www.drugs.com	Drugsite Trust, Commercial (USA)	85%	60%
21	Direct oral anticoagulant therapy (DOAC) (formally known as NOACs)	http://www.icid.salisbury.nhs.uk/diagnostics/pathology/laboratoryeaflets/documents/doac%20pi1322.medicine/patientinformationlpdf	Salisbury NHS Foundation Trust, Government (UK)	85%	80%
22	Rivaroxaban (Xarelto) for the treatment of deep vein thrombosis and pulmonary embolism	http://www.kingsthrombosiscentre.org.uk/index.php/anticoagulation n/anticoagulation-guidelines	King's College Hospital NHS Foundation Trust, Government (UK)	88%	80%
23	Dabigatran (Pradaxa) for stroke prevention in atrial fibrillation	http://www.kingsthrombosiscentre.org.uk/index.php/anticoagulation n/anticoagulation-guidelines	King's College Hospital NHS Foundation Trust, Government (UK)	85%	60%

Table 5.1 Continued…. Scores for understandability and actionability of patient education materials for NOACs

	Title	Website links (Last accessed 25th August 2018)	Associated institution, Type of resource /Country	Understandability score (%)	Actionability score (%)
24	Apixaban (Eliquis) Information for patients	http://www.kingsthrombosiscentre.org.uk/index.php/anticoagulation/anticoagulation-guidelines	King's College Hospital NHS Foundation Trust, Government (UK)	85%	60%
25	Patient information-Anticoagulants in Non-valvular atrial fibrillation (NVAF)	http://www.eastcheshire.nhs.uk/Patient%20Information%20Leaflets/On%20the%20A-Z/NVAF%20-%20anticoagulants%20-%2015044.pdf	East Cheshire, Government (UK)	62%	20%
26	New Oral Anti-Coagulant or NOAC Medicines Important information for patients	http://wessexahsn.org.uk/img/programmes/NOAC%20Patient%20information%20September%202016.pdf	Portsmouth Hospitals NHS Trust, Government (UK)	94%	100%
27	Apixaban for the treatment of non-valvular atrial fibrillation	http://mm.wirral.nhs.uk/document_uploads/guidelines/af_apixaban_leaflet_20160902.pdf	Wirral Clinical Commissioning Group NHS, Government (UK)	75%	33%
28	Atrial Fibrillation and Stroke Prevention: Anticoagulants	https://www.hrsonline.org/Patient-Resources/Patient- Information-Sheets	Heart Rhythm Society (Commercial) (USA)	77%	40%
29	Medicines for my heart	https://www.bhf.org.uk/informationsupport/publications/heart-conditions/medicines-for-your-heart	British Heart Foundation, Non- profit (UK)	83%	80%
30	Atrial fibrillation	https://www.bhf.org.uk/informationsupport/publications/heart-conditions/atrial-fibrillation	British Heart Foundation, Non- profit (UK)	77%	40%
31	Atrial fibrillation: Know your Risks	http://www.stroke.org/sites/default/files/resources/A Fib-and-Bleeding%20Risk-Fact-Sheet.pdf	National Stroke Association, Non-profit (USA)	77%	60%
32	Oral anticoagulant therapy to reduce the risk of stroke	https://www.ekhuft.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=405632	East Kent Hospitals University NHS Foundation Trust, Government (UK)	83%	60%
33	Should I take blood thinners to control my atrial fibrillation?	https://utswmed.org/medblog/blood-thinners-afib/	UT Southwestern Medical Center, Commercial (USA)	62%	40%
34	Direct Oral Anticoagulant (DOAC) Therapy	http://www.ggcprescribing.org.uk/media/uploads/patient_information/doac_booklet_-_1808.pdf	Greater Glasgow and Clyde NHS, Government (UK)	77%	60%
35	Anticoagulant medicines	https://www.nhs.uk/conditions/anticoagulants/	National Health Services (NHS) (UK)	85%	60%
			Average	81%	62%

Chapter 6: Discussion and Conclusion

6.1. Discussion

This thesis focused on promoting medication safety through the 'Provision of medicines information' stage of the Medicines Management Pathway (MMP) to ensure safe, effective and efficient use of high-risk medications such as oral anticoagulants by patients and their carers. The findings of this thesis highlight the importance of patient education and information using a person-centred care approach.

Patients need medicine information to help them understand the proper use of their medications, especially in high-risk situations such as polypharmacy and during transition of care between different health settings. Particular groups of interest include older persons, those with limited health literacy and people from culturally and linguistically diverse (CALD) backgrounds. This chapter discusses the main findings in the context of the literature, makes recommendations and suggests future directions for research.

6.1.1 Limited research about those with limited health literacy and CALD patients (Paper1)

A significant finding in this thesis was that there is limited research on interventions to support patients with limited health literacy and CALD patients when they take high-risk medications such as oral anticoagulants. This is an important finding because these patients are at risk of medication-related problems (Alhomoud et al. 2013; Eassey et al. 2016), such as an increased risk of bleeding complications (Diug et al. 2011) and may struggle to understand the written materials about anticoagulants provided to them (Estrada et al. 2000; Wilson et al. 2003). Their

lack of knowledge (Collins, Barber & Sahm 2014) may increase their risk of adverse effects and non-adherence (Nasser, Mullan & Bajorek 2012; Pandya & Bajorek 2017).

6.1.2 Supporting patients with limited health literacy and CALD patients (Paper 1)

The interventions identified in the literature to support CALD patients have included the use of visual aids, such as a digitised colour menu of warfarin tablets (Machtinger et al. 2007; Schillinger et al. 2006) and, for those with limited health literacy, pharmacist counselling using a warfarin booklet (Collins, Barber & Sahm 2014). These interventions have led to improved knowledge about warfarin (Collins, Barber & Sahm 2014), improved concordance with clinicians regarding the weekly warfarin regiment (Schillinger 2006) and better anticoagulation control (Machtinger et al. 2007).

6.1.3 Interventions to support older persons (Paper 1)

The literature review in this thesis identified several interventions to support older persons taking oral anticoagulants. Written information in the form of booklets is effective in supporting older persons in terms of knowledge (Fairbairn-Smith et al. 2011; Lane et al. 2006) and anticoagulation control (Fairbairn-Smith et al. 2011). These studies identified knowledge gaps about warfarin therapy, such as the side effects, target international normalised ratio (INR) range and factors that may affect the INR. A theory-driven educational intervention with a one-off group of patients (1–6) was shown to support older persons by significantly improving their knowledge and adherence, as indicated by a higher time within therapeutic range (TTR) than in usual care (Clarkesmith et al. 2013). This study included a variety of interventions, such as a standard yellow booklet, and included an ‘expert–patient’ focused DVD based on patient narratives, an educational booklet, a self- monitoring diary and a worksheet. That study also involved a

multidisciplinary approach and used critical elements in the development process such as clinical guidelines, appropriate theoretical models, patient input and appropriate evaluation tools (Clarkesmith et al. 2016; Clarkesmith et al. 2013).

6.1.4 Importance of improving knowledge (Papers 1 and 2)

The findings from the literature review emphasised the importance of improving anticoagulation knowledge. Providing understandable information about oral anticoagulants such as warfarin is critical to helping vulnerable patients to acquire the knowledge they need to make decisions about their treatment with their health care providers (Diamantouros, Bartle & Geerts 2013). Understandable information is also needed to manage key challenges such as the need for regular INR monitoring, frequent dose changes and dietary considerations (Pandya & Bajorek 2017). A lack of knowledge about anticoagulants may result in poor outcomes such as non-adherence (Di Minno et al. 2014) and increased risk of clotting and stroke (Wittkowsky & Devine 2004). To ensure medication safety, as explained in the MMP framework, patient education and the provision of medicine information are important ways to improve knowledge, adherence and health outcomes (Bellamy, Rosencher & Eriksson 2009; Nasser, Mullan & Bajorek 2012; Osborn et al. 2011).

6.1.5 Importance of health literacy (Papers 1 and 2)

One interesting finding from the literature review was that one study of patients with limited health literacy found a positive correlation between health literacy and warfarin knowledge based on information in a warfarin booklet (Collins, Barber & Sahm 2014). This highlights the need to consider health literacy when providing patients with warfarin counselling (Collins, Barber & Sahm 2014).

6.1.6 Assessing warfarin knowledge and health literacy (Paper 2)

The findings from the literature review suggest that, when providing education and medicine information, it is important to consider the patient's and their carer's knowledge about warfarin and health literacy (Osborn et al. 2011) so that information can be tailored to the knowledge gaps and limitations in health literacy.

The model proposed by Osborn et al. can explain the mechanisms linking health literacy, knowledge and health outcomes (Osborn et al. 2011). The model shows an indirect pathway from health literacy to health status via determinants of self-care (knowledge and self- efficacy) and actual self-care behaviour (physical activity). This model includes significant paths from health literacy to knowledge, knowledge to self-efficacy, self-efficacy to physical activity and physical activity to health status (Osborn et al. 2011). This model also reveals the role patient knowledge plays in linking health literacy to health outcomes and highlights the impact of patient education on improving health outcomes (Osborn et al. 2011).

Paper 2 in this thesis highlights the importance of considering the patient's health literacy and knowledge gaps about anticoagulant therapy. Using the Health Literacy Questionnaire (HLQ) tool, Osborne et al found a lower level of health literacy for the scale relating to appraisal of health information; that is, more participants indicated that they did not consistently appraise the quality and reliability of health information (Osborne et al. 2013). This study also showed that, despite their long-term use of warfarin, participants and their carers exhibited knowledge gaps about warfarin therapy, in particular how to respond in an emergency situation and the importance of a consistent diet. These findings highlight the need to assess patients' health literacy and knowledge gaps so that patient education materials can be tailored to the limitations of their health literacy and their information needs.

Osborne et al also found that participants born overseas may not be able to engage with doctors and their healthcare providers, and that those using polypharmacy may have problems understanding written health information or instructions about treatments or medications (Osborne et al. 2013).

6.1.7 The role of the Warfarin Action Plan leaflet (Paper 3)

Based on the findings from the literature review (Paper1) and Paper 2, a Warfarin Action Plan (WAP) leaflet was developed, as outlined in Chapter 4, and feedback was obtained from a group of older persons in a general practice setting (Paper 3).

By encouraging communication between the patient and their healthcare provider, the information in the leaflet addressed knowledge gaps and encouraged shared decision making. The leaflet also encouraged patient empowerment; some participants commented that they had already acted on the information in the leaflet (in the period up to the interview) by recording their INR results and doses in the WAP leaflet.

6.1.8 Patient and carer involvement and the role of the WAP leaflet (Paper 3)

Based on the findings from the literature review (Paper 1), knowledge gaps and information needs (Paper 2), a WAP leaflet was developed using a person-centred care approach by involving patients in feedback (Paper 3). When developing materials, the information needs of patients and carers (i.e. knowledge gaps and health literacy needs) must be considered to allow information to be tailored to their preferences and needs (Papers 2 and 3). Feedback from patients were used

to identify the patients' preference and need for warfarin information. The simple WAP leaflet intervention can be effective for patients and their carers in the following ways:

- By conveying key information that has been identified in the literature as gaps in knowledge. Key topics included medication safety issues, such as what to do in an emergency situation, and self-management strategies such as maintaining a consistent diet.
- By providing a link to an independent, not-for-profit and evidence-based Australian organisation such as the National Prescribing Service (NPS) Medicine Wise. There is a need for healthcare professionals to refer patients to reliable websites, as found in Paper 2, because some patients with limited health literacy may struggle with appraising health information.
- By presenting information in a clear manner with visual pictures in one column and information next to the pictures, this desirable format and use of visual aids caters for those with limited health literacy. Their use is consistent with findings in the literature (Aker et al. 2013; Gibson Smith et al. 2017; Wolf et al. 2014).
- By promoting patient engagement and empowering patients to take action because the WAP is an interactive leaflet with features such as a chart for recording the dose.
- By facilitating shared decision-making and discussion between patients/carers, family members and their healthcare provider about topics, such as the choice and brand of anticoagulant agent, time of administration and frequency of monitoring requirements.
- By reinforcing knowledge retention. The leaflet can be referred to by the patient at a later date.
- By using simple and plain language to make the leaflet understandable.

In the future, the WAP leaflet may be able to be used as standardised content during transition of care by allowing the resource to be available in a variety of healthcare settings such as the community and hospitals. This would prevent patients from receiving too much information from a variety of materials and feeling overwhelmed. One study showed that older persons and carers need more information about warfarin in the hospital and community settings (Bajorek et al. 2007). Having standardised information in all settings would help to resolve this issue and could be explored using an information portal such as the My Health Record (Australian Government Australian Digital Health Agency 2018).

In addition, the WAP leaflet may be part of multicomponent programs to empower patients to self- manage their medications. A variety of modes of patient education is needed because patients have different needs and preferences. Furthermore, the WAP leaflet may be converted into a mobile application to cater for those patients who are technologically literate. As shown in the literature review in Paper 1, a mobile health application containing modules for warfarin therapy significantly improved anticoagulation knowledge (Lee et al.2016). Finally, the feedback from the WAP leaflet may be used to develop a similar leaflet for the NOACs in a future study.

6.1.9 Knowledge gaps concerning both warfarin and the non-vitamin K anticoagulants NOACs (Paper 1)

Overall, the literature has shown that there are knowledge gaps relating to both old and new therapies (warfarin and the NOACs) (Fairbairn-Smith et al. 2011; Giuliano, Nofar & Edwin 2017; Lane et al. 2006). This explains why both types of medicines need proper patient education and useful information materials to address the knowledge gaps. Important factors to consider

when developing these materials are the health literacy of patients and ethnocultural needs or factors. Due to the gaps in knowledge about warfarin, a few authors have suggested that information about warfarin needs to be standardised (Diamantouros, Bartle & Geerts 2013; Wofford, Wells & Singh 2008). This suggestion could also be applied to the NOACs.

6.1.10 NOAC materials that are actionable and understandable (Papers 1, 4)

The previous findings of the feedback obtained in Paper 2, which showed the WAP leaflet to be understandable and actionable, and the literature review (Paper 1), which found that only limited research has been done on NOACs, prompted a further study (Paper 4) to evaluate whether web-based education materials for patients taking NOACs were also understandable and actionable.

An unexpected finding from this study (Paper 4) was that when the Patient Education Materials (PEMAT) tool was used, most of the NOAC information materials were not actionable. This finding indicates that more attention should be paid to the design and content of these materials and less to the mode of delivery (hard copy versus online). The findings of this study are consistent with others that have assessed the understandability and actionability of patient education materials (Brütting et al. 2018; Morony et al. 2017).

6.1.11 The needs and role of the carer (Papers 1–3)

Another finding of this thesis was the important role of the carer in supporting older persons in self-testing and in training for use of a coagulometer for warfarin INR monitoring (Matchar et al. 2010). Given the ageing population, the role of a carer in supporting older persons, some of whom are unable to self-monitor their INR independently using point-of- care (POC) devices and who require oral anticoagulants for their chronic conditions such asatrial fibrillation to prevent a stroke, will become more important. In addition, older age is associated with a lack of warfarin knowledge, limited health literacy ((Fang et al. 2006), comorbidities (Australian Institute of Health and Welfare 2014), polypharmacy and drug interactions (Focks et al. 2016). Polypharmacy, involving warfarin or NOACs, is associated with increased mortality, stroke and major bleeding in patients with AF (Focks et al. 2016). Consequently, carer assistance may be required in the management of warfarin for older persons.

This thesis also found knowledge gaps about warfarin in carers (Paper 3) and that this group need information about oral anticoagulants. Practical materials targeting carers are needed, especially given carers that are instrumental in managing therapy, such as recording INRs in the WAP leaflet. Carers also play an essential role in advocacy, family-centred care and shared decision-making, which may influence thromboprophylaxis treatment choices and, potentially, adherence (Ferguson et al. 2015). A previous study revealed that older persons and their carers found that the provision of information was inadequate and that verbal and written information are equally important but need to be provided in a way that checks patients' understanding at a later time (Bajorek et al. 2007). These findings suggest that, ideally, patient medicine information and education about oral anticoagulants should be made available to carers. In addition, the carer's health literacy and knowledge about oral anticoagulants should also be assessed so that

information can be tailored to their needs and limitations in health literacy. This thesis devoted attention to carers in Papers 2 and 3.

6.1.12 Tailoring interventions for patients and their carers (Paper 1 and 3)

Feedback on the WAP leaflet indicated that a few participants and their carers suggested alternative formats such as booklets, videos and mobile applications (Paper 3). This finding suggests that a range of options for patient education and information should be offered to patients and their carers, and should be tailored to their needs and preferences.

In addition to written interventions, the literature review also identified a range of alternative educational interventions to support older persons. These included decision aids, counselling by the pharmacist such as in the hospital and home settings, programs, provision of certain medication instructions and a mobile application.

6.2. Strengths and limitations

The strength of this research was a combination of quantitative and qualitative methods were used to gain insight into the information needs of patients taking oral anticoagulants and their carers. The research also identified major gaps in the literature regarding the limited research being done to support patients with limited health literacy and CALD patients. A simple, inexpensive, tool, the WAP leaflet, was developed. This resource could be used in a variety of

clinical settings and for a variety of patients such as older persons and those with limited health literacy.

The thesis research had several limitations. The literature review (Paper 1) excluded non- English language papers and selected only full-text articles that included older persons who were 65 years and over or if the mean age was 65 years and over. A lower age limit may have led to inclusion of more articles. The articles were selected by one reviewer, who could have introduced bias towards the results.

The review also showed that several studies used different tools to measure warfarin knowledge, such as the Oral Anticoagulation Test (Masnoon, Sorich & Alderman 2016; Stafford et al. 2012), the Anticoagulation Knowledge Assessment tool (Collins, Barber & Sahm 2014), and health literacy tools such as the Rapid Estimate of Adult Literacy in Medicine tool (Collins) and an abbreviated version of the short-form Test of Functional Health Literacy in Adults (Schillinger 2006, language, literacy and communication). This made it difficult to compare clinical outcomes between studies. Differences in methodology, such as the inclusion and exclusion criteria, and sample size, also made it difficult to compare the clinical outcomes across the trials and limited the generalisability of the results to other settings.

The tool used in this thesis to measure warfarin knowledge comprised a selection of six open-ended and five closed-ended questions. The responses provided to the open-ended questions were categorised thematically and coded (transformed into numbers) (Bryman A 2016) to enable quantitative analysis of the data and calculation of a warfarin knowledge score. Responses to all questions were given a score of one for a correct answer, and each question had equal weighting. For the open-ended questions, if the participant wrote one word that was similar to any of the

words in the pre-determined answer, that answer was considered correct and given a score of one. If the participant wrote no words that matched the pre-determined answers, a score of 0 was given. The participant's overall level of basic warfarin knowledge was reported as a total score out of 10, and a score ≥5 was considered to indicate good knowledge. A score <5 was considered to indicate poor knowledge, as adapted from a previous study (Tang et al. 2003).

Another limitation was that, when recruiting patients to assess their health literacy and warfarin knowledge (Paper 2), medical staff were involved in identifying potential participants, and this may have introduced some selection bias. In addition, because of the small sample size, the data from both patients and carers were combined, which precluded an exploration of whether any patient characteristics may have affected patient preferences. Furthermore, in Paper 2, the participants included 30 older adults (aged 65 years and over) and 4 carers (aged >60 years). The sample cohort was 80% male with an average age of 81 years, and 30% were born overseas. In addition, the literature has shown that there are higher percentages of women 75 years or older alive than men (Australian Institute of Health and Welfare 2018a). According to these data, more women should be taking warfarin; therefore, women were underrepresented in this cohort. Therefore, the sample cohort was not representative of the general older adult population in Australia or New Zealand. As a result, the mean warfarin score of 8.3/10 across the 34 participants that indicated a good level of warfarin knowledge could be biased.

In addition, some of the findings in this thesis may not generalisable given that, for some studies (Papers 2 and 3), data collection Whe to a single primary care-based medical centre with a relatively small sample of 30 patients (plus 4 carers). This thesis focused only on the local Australian setting and issues may be different in other settings such as rural Australia or overseas. For example, in the review paper (Paper 1), the patients included in the study of a visual

medication schedule in San Francisco, USA, may not be easily compared with an Australian urban, inner city population such as that studied in Chapter 4. Furthermore, the thesis focused on the provision of written information but did not explore verbal information provided to patients and carers.

Finally, the PEMAT tool has some limitations. It does not assess whether the factual content of the information is accurate and up-to-date, and has a strong evidence base (Clerehan, Buchbinder & Moodie 2004; Shoemaker, Wolf & Brach 2014). We attempted to minimise these limitations by including materials dated from 2011 onwards (Paper 4). In addition, one researcher (AY) performed the assessment for understandability and actionability for the web-based materials, which may have contributed to some bias.

6.3. Recommendations and future directions for research

Overall, the findings in this thesis suggest that there is a need to address more closely the needs of vulnerable patients, who comprise a large proportion of those using anticoagulants in Australia, and that this can be done through low-cost interventions such as the WAP. The positive feedback on the WAP leaflet suggest that it could be used in a number of settings:

- by pharmacists in high-risk situations such as the hospital setting
- by community pharmacists
- by general practitioners in medical centres

- by patients with polypharmacy in their home setting and those who receive a home medicines review

- during transition of care.

The introduction of new therapies such as NOACs must be equally supported with good- quality, relevant information and this information should not be limited only to older therapies such as warfarin. Collectively, this should facilitate better medication adherence, therapeutic control and clinical outcomes.

A leaflet similar to the WAP leaflet could be developed for other high-risk medicines such as NOACs and could be evaluated for actionability and understandability provided that it has appropriate design features and high-quality content. More studies that include warfarin and the NOACs are needed. These should target carers, patients from CALD backgrounds and patients with limited health literacy.

Further research is required about standardising the content of information about anticoagulants (both warfarin and NOACs) and about the tools used to measure anticoagulation knowledge and health literacy. This will help to minimise patient knowledge gaps and allow outcomes to be compared.

In addition, to ensure that interventions are patient tailored, it is worth exploring alternative interventions to a written WAP leaflet, such as verbal interventions in which the 'teach-back' technique is used to confirm comprehension, technology including mobile health applications

and telehealth. Other interventions may include multicomponent programs based on frameworks and guidelines (Clarkesmith et al. 2016), with regular post-intervention follow- up and home setting trials to achieve a long-lasting impact on patient outcomes and knowledge retention. Future research is warranted in translating the WAP into other languages and evaluating its use among CALD patients while assessing their health literacy. More research about effective ways to design interventions, such as patient education materials for those with limited health literacy and CALD patients, to ensure that these materials are understandable, actionable and tailored to the needs of patients. One way to advance research in this area is to utilise pharmacists as they are easily accessible and have a unique skill set that is able to deliver the interventions in a timely manner across various healthcare settings, such as hospitals, primary care, General Practice clinics and home-based or residential care facilities.

6.4. Conclusion

This thesis showed that a simple, inexpensive tool such as the double-sided A4 size WAP leaflet, which contains simple language, visual images and references to reliable websites, was considered useful by older persons taking warfarin and their carers. The feedback and study of this leaflet also indicate that an inexpensive intervention can be effective in supporting patients and that high-technology interventions/materials may not always be needed.

When developing patient information materials for use of oral anticoagulants, input and feedback should be obtained from patients and their carers. Leaflets such as the WAP can be incorporated with other interventions such as verbal communication by pharmacists and be part of

multidisciplinary programs with regular follow-up or ‘refresher education’ so that patient outcomes, such as knowledge retention, can be optimised.

In addition, to ensure medication safety with high-risk medicines using a person-centred approach, several factors should be considered when providing patient education and medicine information. These include the patient and carer’s health literacy, knowledge gaps about oral anticoagulants and patient needs and preferences. The provision of information should be of high quality in terms of understandability and actionability.

Chapter 7: Appendices

7.1. Ethics approval for the conduct of the study

From: <Research.Ethics@uts.edu.au>

Subject: UTS HREC Approval - 2015000665 Date: 7 October 2015 at 4:27:37 pm AEDT

Dear Applicant

UTS HREC REF NO. 2015000665

The UTS Human Research Ethics Expedited Review Committee reviewed your amendment application for your project titled, "Patient Feedback on a Warfarin Action Plan for use in the local Australian setting" and agreed that the amendments meet the requirements of the NHMRC National Statement on Ethical Conduct In Human Research (2007). I am pleased to inform you that the Committee has approved your request to amend the protocol as follows:

1. Amendment to Dr Lee's title;
2. Letter to participants from the doctor;
3. Additional information has been provided on the Participant Consent Form and

Participant Information sheet;

4. Contacting participants;
5. Footers updated; and
6. Email to ethics stating support for the study.

You should consider this your official letter of approval. If you require a hardcopy, please contact the Research Ethics Officer (Research.Ethics@uts.edu.au). In the meantime, I take this opportunity to wish you well with the remainder of your research.

Yours sincerely,

Professor

Marion Haas

Chairperson

UTS Human Research Ethics Committee

7.2. Participant information sheet

UNIVERSITY OF TECHNOLOGY SYDNEY

PARTICIPANT INFORMATION SHEET

Evaluation of a Warfarin Action Plan for the use in the local Australian setting

Dear ……..

The purpose of this study is to obtain your opinions on an educational pamphlet about warfarin therapy, and to see how this resource influences your understanding of this therapy.

We have asked you to participate in this research because you are taking warfarin or care for someone who is taking warfarin.

The research will involve completing questionnaires and providing feedback about a warfarin pamphlet.

The meetings will take place in a room at the Castle Hill Medical Centre for up to around one hour with a follow up interview of half an hour two weeks later. Each appointment should take no more than one hour of your time.

We will be happy to answer any questions with regards to your warfarin after the study.

A Research Pharmacist named, Angela Yiu, at the University of Technology, Sydney will conduct the research in our medical centre. This research is for her studies in a Masters of Pharmacy.

If you are interested in participating, we would be glad if you would contact her on [redacted] or email Angela.W.Yiu@student.uts.edu.au.

You are under no obligation to participate in this

research. Thank you for your time.

Yours sincerely,

[Dr's name]
[Title]
[Address]
[Phone number]

NOTE:
This study has been approved by the University of Technology, Sydney Human Research Ethics Committee. If you have any complaints or reservations about any aspect of your participation in this research, which you cannot resolve with the researcher, you may contact the Ethics Committee through the Research Ethics Officer (ph: +61 2 9514 9772 Research.Ethics@uts.edu.au), and quote the UTS HREC reference number. Any complaint you make will be treated in confidence and investigated fully and you will be informed of the outcome.

7.3. Participant consent form

UNIVERSITY OF TECHNOLOGY SYDNEY

CONSENT FORM for patients

Evaluation of a Warfarin Action Plan for use in the local Australian setting

I_____*(participant's name)* agree to participate in the study, Evaluation of a Warfarin Action Plan for use in the local Australian setting (UTS HREC approval reference number___) being conducted by Angela Yiu, (Email: Angela.W.Yiu@student.uts.edu.au and phone:) under the supervision of Associate Professor Beata Bajorek of the University of Technology, Sydney, for her Masters of Pharmacy degree.

I understand that the purpose of this study is to obtain your opinions on an educational pamphlet about warfarin therapy, and to see how this resource influences your understanding of this therapy.

I understand that I have been asked to participate in this research because I have been prescribed warfarin by my doctor or care for someone who is taking warfarin. My participation in this research will involve completing questionnaires and providing feedback about a warfarin pamphlet. The meeting will take place in a room at the Castle Hill Medical Centre for up to around one hour with a follow up interview of half an hour two weeks later.

I am aware that I can contact Angela Yiu or her supervisor, Associate Professor Beata Bajorek, if I have any concerns about the research. I also understand that I am free to withdraw my participation from this research project at any time I wish, without consequences, and without giving a reason.

I agree that the research data gathered from this project may be published in a form that does not identify me in any way.

_____ ___/___/___
Signature (participant)

_____ ___/___/___
Signature (researcher or delegate)

NOTE:
This study has been approved by the University of Technology, Sydney Human Research Ethics Committee. If you have any complaints or reservations about any aspect of your participation in this research, which you cannot resolve with the researcher, you may contact the Ethics Committee through the Research Ethics Officer (ph: +61 2 9514 9772 Research.Ethics@uts.edu.au) and quote the UTS HREC reference number. Any complaint you make will be treated in confidence and investigated fully and you will be informed of the outcome.

7.4. Data collection form

Participant code _ _/_ _/_ _

P
: Evaluation of a Warfarin Action Plan for Australian

	DATA COLLECTION

Data Collection Site: Castle Hill Medical Centre

Investigators:

Beata Bajorek (Pharmacy Practice, University of Technology of Sydney, Supervisor)
Angela Yiu (Pharmacist, Student/Project Officer)

DATA COLLECTION REQUIREMENTS

- Patients will be initially identified by Dr Steven Lee (Director of Castle Hill Medical Centre) and Dr Robert Elliott. The identification process will involve a search through the medical centre database (electronic record) for patients currently prescribed warfarin.
- The identified patients (around 40 to 50 patients) will be sent a letter in the post by the medical centre inviting them to participate in the study (i.e. to receive a copy of the WAP and provide feedback). If patients do not respond, the patient's doctor and a nurse will call them. Patients will be able to express their interest in participating by contacting the medical centre or project pharmacist using the contact details provided on the Participant Information sheet.
- At the on-site appointment the project officer will explain the project steps and ask participants to provide informed signed consent. Baseline data will be collected at this stage. For example baseline warfarin knowledge, health literacy and background information. At this initial appointment the participant will receive a copy of the WAP to take home and review and an appointment follow up made. The duration of the initial interview will be up to one hour.

- If participants are unable to attend the appointment on site, baseline data will be obtained via the telephone, email and post. Approximately two weeks from the initial baseline appointment, participants will be contacted for follow up for feedback on the WAP. The mode of contact and feedback will be either face-to-face in the medical centre or in exceptional circumstances such as little mobility over the phone. The feedback will be audio recorded with the patient's permission. Records for patients < 65 years of age will be excluded from the review. (i.e./ only records for patients ≥ 65 years of age will be selected).

- Participants will be asked to present to the medical centre at a stated date and time (a specific day will be scheduled as a pilot study day where the project officer will be on site to speak to the participant).

Data entry completed (tick box) [__]

• Part 1 : PATIENT DEMOGRAPHICS

1(a)	Participant number:	
1(b)	Patient's Initials:	
1(c)	Age (years):	(Date of birth) / /
1(d)	Gender:	1 Male 2 Female
1(e)	Residential Postcode:	| | | | | Suburb:
1(f)	Telephone Number of participant:	
1(g)	Country of birth:	
1(h)	Carer:	1 Yes 2 No
1(i)	Aboriginal or Torres Strait Islander:	1 Yes 2 No
1(j)	Speak English at home:	1 Yes 2 No
1(k)	Other language/s spoken at home:	
1(l)	Lives alone:	

1(m)	Dose administration aid:	1 2 Yes No
1(n)	Uses medicine list	1 2 Yes No
1(o)	Has impaired hearing	1 2 Yes No
1(p)	Has impaired vision	
1(q)	Highest level of education:	1 Primary school or less 2 High school (not completed) 3 High school completed 4 TAFE/Trade 5 University
1(r)	Employment:	1 Employed 2 Retired 3 Other
1(v)		

• Part 2: SUMMARY OF Warfarin

2(a)	Indication for warfarin:	1 Atrial Fibrillation 2 Stroke 3 Deep vein thrombosis 4 Pulmonary embolism 5 Antiphospholipid syndrome 6 Valve replacement 7 Other (specify)
2(b)	Duration of warfarin:	
2(c)		
2(d)		
2(e)		
2(f)		

2(g) _____

Additional Comments:

•Part 3: MEDICAL HISTORY - Presence of Coexisting Medical Conditions

Medical Conditions			Present	Past History	Diagnosed at AF	No / Unknown
4(a)	**Cardiovascular:**	Hypertension	1	2	3	4
4(b)		Coronary Artery Disease	1	2	3	4
4(c)		Ischaemic Heart Disease	1	2	3	4
4(d)		Congestive Heart Failure	1	2	3	4
4(e)		Mitral Valve Disease	1	2	3	4
4(f)		Other Cardiac Arrhythmia	1	2	3	4
4(g)		Other (specify)	1	2	3	4
4(h)	**Vascular:**	Thromboembolus	1	2	3	4
4(i)		Stroke (CVA)	1	2	3	4
4(j)		Transient Ischaemic Attack (TIA)	1	2	3	4
4(k)		Intracranial Haemorrhage	1	2	3	4
4(l)		Other (specify)	1	2	3	4
4(m)	**Haematological**	Underlying Coagulopathy	1	2	3	4
4(n)		Haemorrhagic Disorder	1	2	3	4
4(o)		Anaemia	1	2	3	4
4(p)		Other (specify)	1	2	3	4
4(q)	**Gastrointestinal:**	Ulceration / Ulcer Disease	1	2	3	4
4(r)		Gastrointestinal bleeds	1	2	3	4
4(s)		Other (specify)	1	2	3	4
4(t)	**Respiratory:**	Chronic Obstructive Airways	1	2	3	4
4(u)		Asthma	1	2	3	4
4(v)		Other (specify)	1	2	3	4
4(w)	**Endocrine:**	Thyroid Disease	1	2	3	4
4(x)		Diabetes Mellitus	1	2	3	4
4(y)		Other (specify)	1	2	3	4
4(z)	**Neuropsychological:**	Seizure Disorder	1	2	3	4

4(aa)		Dementia/Confusional States	1	2	3	4
4(bb)		Cognitive impairment	1	2	3	4
4(cc)		Psychiatric Disorder	1	2	3	4
4(dd)		Hearing Loss/Visual Impairment	1	2	3	4
4(ee)		Parkinson's Disease/Gait Disorder	1	2	3	4
4(ff)		Depression/anxiety	1	2	3	4
4(gg)	**Organ Failure:**	Liver failure	1	2	3	4
4(hh)		Renal failure	1	2	3	4
4(ii)	**Social Factors:**	Smoker	1	2	3	4
4(jj)		Alcohol abuse	1	2	3	4
4(kk)	**Pain:**	Back pain	1	2	3	4
4(ll)	**Oncology**	Cancer	1	2	3	4
4(mm)	**Other (specify)**		1	2	3	4

Additional Comments:

• Part 4: MEDICINE HISTORY

	Is the patient using any agent/s from the following medication categories:	Yes	No	No/ of Agents	Comments
	General:				
5(a)	Analgesic	1	2		
5(b)	Anti-inflammatory	1	2		
5(c)	Gastrointestinal	1	2		
5(d)	Respiratory	1	2		
5(e)	Central Nervous System	1	2		
5(f)	Endocrine	1	2		
5(g)	Dermatological	1	2		
5(h)	Antimicrobial	1	2		

5(i)	Antiarrhythmic	1	2	
5(j)	Heart rate control	1	2	
5(k)	Antithrombotic	1	2	
5(l)	Antihypertensive	1	2	
5(m)	Diuretics	1	2	
5(n)	Antianginal	1	2	
5(o)	Vitamains/Supplements	1	2	
5(p)	Topical agents (creams, ointments, lotions, patches)	1	2	
5(q)	Inhalers, puffers, sprays, sublingual tablets	1	2	
5(r)	Over-the-counter medicines	1	2	
5(s)	Complementary medicines (vitamins, herbal or natural therapies)	1	2	
5(t)	Other (specify)	1	2	
5(u)	Total number of medications	1	2	
5(v)	Total number of long term medications	1	2	

Additional Comments:

7.5. Warfarin Knowledge Questionnaire

QUESTIONNAIRE ABOUT WARFARIN KNOWLEDGE

QUESTIONS	ANSWERS (checked against WAP)
1) Why are you taking warfarin?	
2) If you have 5mg tablets of warfarin, and were told to take 7.5mg a day, how many of the 5mg pills should you take every day?	____ pills
3) The best thing to do if you miss a dose of warfarin is to? (Please select the correct or best answer) a) double up the next day b) take the next scheduled dose and tell your health care provider c) call your healthcare provider immediately d) discontinue warfarin altogether	
4) Why is it important to get all of the blood tests that your doctor orders for you?	
5) A patient with an INR value below their "target INR range": (Please select the correct or best answer) a) is at an increased risk of bleeding b) is at an increased risk of having a clot c) is more likely to have a skin rash from warfarin d) is more likely to experience side effects from warfarin	
6) Why is it important to keep your diet consistent (i.e. to eat the same types of food every day)?	
7) What might happen if someone takes too much warfarin?	

8) What can you do to let your health care providers know you are taking warfarin?	
9) Why is it important to let your doctor know about any other medications you are taking (including over-the-counter and herbal products)?	
10) A person on warfarin should seek immediate medical attention: (Please select the correct or best answer) a) if they skip more than two doses of warfarin in a row b) if they notice blood in their stool when going to the bathroom c) if they experience a minor nose bleed d) If they develop bruises on their arms or legs e) I don't know	

References to question

Question 1,4,6,7, 9

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Question 2

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Question 3, 5, 10

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Note: Each question gives one point score

7.6. Interview schedule

What are your thoughts about the information presented in this leaflet?

What things do you MOST like about this leaflet?

What things do you LEAST like about this leaflet?

How does this leaflet compare with other types of information and resources you have received about warfarin therapy?

How could we make this leaflet better so that people can make the most use from it?

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