



Faculty of Medicine and Health Sciences

**Treatment Satisfaction and Health-related Quality of Life of
Non-Valvular Atrial Fibrillation Patients on
Long-Term Warfarin Based on Time in Therapeutic Range**

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Treatment Satisfaction and Health-related Quality of Life of
Non-Valvular Atrial Fibrillation Patients on
Long-Term Warfarin Based on Time in Therapeutic Range

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DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Malaysia Sarawak. Except where due acknowledgements have been made, the work is that of the author alone. The thesis has not been accepted for any degree and is not concurrently submitted in candidature of any other degree.



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ABSTRACT

Warfarin use in non-valvular atrial fibrillation (NVAF) poses challenges. This study evaluates patients' time in therapeutic range (TTR), treatment satisfaction, and HRQoL on long-term warfarin therapy for NVAF. Treatment satisfaction and HRQoL were compared based on TTR level. This cross-sectional study was conducted among NVAF patients on long-term warfarin attending the anticoagulant clinic of a tertiary cardiology referral centre in Sarawak from 1st June 2018 to 31st May 2019. TTR was calculated using the Rosendaal technique, and treatment satisfaction was assessed by the Duke Anticoagulation Satisfaction Scale (DASS) and HRQoL with Short Form-12 version 2 Health Survey (SF-12v2). This study includes 300 patients, with a mean TTR score of $47.0 \pm 17.3\%$. The HRQoL components were physical component summary (PCS) and mental component summary (MCS) with scores of 47.0 ± 9.0 and 53.5 ± 9.6 , respectively. The treatment satisfaction components namely, limitations (L), hassles and burdens (H&B), and positive physiological impacts (PPI) were 18.0 ± 10.0 , 15.6 ± 9.1 , and 21.6 ± 5.9 respectively. Good TTR ($\geq 60\%$) patients 24.3% (n=73) with a mean TTR of $70.2 \pm 8.7\%$, while 227 (75.7%) patients with poor TTR with a lower mean of $39.5\% \pm 11.9\%$. There was no significant difference between good and poor TTR patients in DASS score ($p=0.779$). Similarly, no significant differences were found in DASS subdimensions ($p=0.502-0.699$). Likewise, there was also no significant difference in the score of PCS ($p=0.150$), MCS ($p=0.919$), and each domain of SF-12v2 ($p=0.184-0.684$) between good and poor TTR, except for social functioning ($p=0.019$). Most NVAF patients on long-term warfarin therapy in this study had poor TTR, but TTR levels did not influence their treatment satisfaction and HRQoL. Achieving a good TTR does not compromise treatment satisfaction and HRQoL. Thus, steps should be taken to improve INR control.

Keywords: Non-valvular atrial fibrillation, time in therapeutic range, treatment satisfaction, health-related quality of life

Kepuasan Rawatan dan Kualiti Hidup Pesakit Fibrilasi Atrium Bukan Valvular yang Menggunakan Warfarin Dalam Jangka Panjang Berdasarkan Masa dalam Julat Terapeutik

ABSTRAK

Penggunaan Warfarin di kalangan pesakit fibrilasi atrium bukan injap (NVAF) menimbulkan cabaran kepada mereka. Kajian ini menilai masa pesakit dalam julat terapeutik (TTR), kepuasan rawatan, dan HRQoL pesakit-pesakit NVAF yang mengambil warfarin dalam jangka panjang. Kepuasan rawatan dan HRQoL dibandingkan berdasarkan tahap TTR. Kajian keratan rentas ini telah dijalankan di kalangan pesakit NVAF yang mengambil warfarin, menghadiri klinik antikoagulan di sebuah pusat rujukan kardiologi tertuari di Sarawak dari 1 Jun 2018 hingga 31 Mei 2019. TTR dikira menggunakan teknik Rosendaal, dan kepuasan rawatan dinilai oleh Skala Kepuasan Antikoagulasi Duke (DASS) dan HRQoL dengan Kajian Kesihatan Borang Pendek-12 versi 2 (SF-12v2). Kajian ini merangkumi 300 pesakit, dengan purata skor TTR $47.0 \pm 17.3\%$. Komponen HQRoL adalah ringkasan komponen fizikal (PCS) dan skor ringkasan komponen mental (MCS), dengan markah 47.0 ± 9.0 and 53.5 ± 9.6 . Komponen kepuasan rawatan adalah batasan (L), kerumitan dan beban (H&B), dan kesan fisiologi positif (PPI) masing-masing dengan markah 18.0 ± 10.0 , 15.6 ± 9.1 , dan 21.6 ± 5.9 . Pesakit TTR yang dalam kawalan baik ($\geq 60\%$) 24.3% ($n=73$) dengan purata TTR sebanyak $70.2 \pm 8.7\%$, manakala 227 (75.7%) pesakit dengan TTR kawalan lemah yang jauh lebih rendah sebanyak $39.5\% \pm 11.9\%$. Tiada perbezaan ketara antara pesakit TTR yang dalam kawalan baik dan lemah dalam skor DASS ($p=0.779$). Begitu juga, tiada perbezaan ketara ditemui dalam subdimensi DASS ($p=0.502-0.699$). Begitu juga, tidak ada perbezaan yang signifikan dalam skor PCS ($p = 0.150$), MCS ($p = 0.919$), dan setiap domain SF-12v2 ($p = 0.184-0.684$) antara TTR yang dalam kawalan baik dan lemah, kecuali fungsi sosial ($p = 0.019$). Kebanyakan pesakit NVAF yang

mengambil warfarin dalam jangka panjang dalam kajian ini mempunyai TTR dalam kawalan lemah, tetapi tahap TTR tidak mempengaruhi kepuasan rawatan mereka dan HRQoL. Mencapai TTR yang baik tidak menjejaskan kepuasan rawatan dan HRQoL. Oleh itu, langkah-langkah perlu diambil untuk meningkatkan kawalan INR.

Kata kunci: *Fibrilasi atrium bukan valvular, masa dalam julat terapeutik, kepuasan rawatan, kualiti hidup yang berkaitan dengan kesihatan*

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LIST OF ABBREVIATIONS

AF	Atrial Fibrillation
ACTS	Anti-Clot Treatment Scale
AHA/ACC/HRS	American College of Cardiology, American Heart Association, and Heart Rhythm Society
ANCOVA	Analysis of Covariance
BP	Bodily Pain
DASS	Duke Anticoagulation Satisfaction Scale
DOAC	Direct Oral Anticoagulant
GH	General Health
HRQoL	Health-related Quality of Life
H & B	Hassles & Burdens
L	Limitation
INR	International Normalised Ratio
INSAM	International Study of Anticoagulant Management
MCS	Mental Component Summary
MH	Mental Health
MTAC	Medication Therapy Adherence Clinic
NSAID	Nonsteroidal Anti-Inflammatory Drugs
NVAF	Non-Valvular Atrial Fibrillation
OAC	Oral Anticoagulant
ORBIT-AF	Outcome Registry for Better Informed Treatment Atrial Fibrillation
OTC	Over-the-Counter
PCS	Physical Component Summary
PF	Physical Functioning

PPI	Positive Physiological Impacts
QoL	Quality of Life
RE	Role Emotional
RP	Role Physical
SD	Standard Deviation
SF	Social Functioning
SF-12v2	Short Form 12 version 2
SF36	Medical Outcome Study 36-Items Short-Form Survey
TIA	Transient Ischemic Attack
TTR	Time in Therapeutic Range
TSQM	Treatment Satisfaction Questionnaire for Medication
VKA	Vitamin K Antagonist
VT	Vitality
WMTAC	Warfarin Medication Therapy Adherence Clinic

CHAPTER 1

INTRODUCTION

1.1 Study Background

Atrial Fibrillation (AF) is the dominant chronic cardiac dysrhythmia, imposing susceptibility to diverse cardiovascular disorders, notably heart failure, besides non-cardiovascular complications including stroke and cognitive impairments such as dementia (Zhou et al., 2019). It represents a major global healthcare burden frequently encountered in clinical practice. In the Global Burden of Disease Study, it was reported that AF affected 37.6 million people globally in 2017, with 287,200 deaths reported (Institute for Health Metric and Evaluation, 2018; Roth et al., 2018). However, this figure is likely underestimated as many patients remain unaware of their AF until they experience an ischemic thromboembolic stroke or systemic thromboembolism (Alshehri, 2019). The mortality rate is approximately five to six percent within the first year after the initial manifestation of AF (Bassand et al., 2016). AF is also expected to increase significantly due to improved detection and longer life expectancy (Cavallari & Patti, 2020). In each passing decade, the risk of developing AF doubles, reaching 20% by the age of 80 (Magnani et al., 2016). Thromboembolic events, particularly stroke, are five times more likely to occur in association with AF (Wolf et al., 1991). In the absence of anticoagulant therapy, the risk of stroke among individuals with AF varies from 1.9% to 18.2% (Pearce et al., 2000). In addition to the severe morbidity and high mortality rate, AF is also associated with impaired quality of life (QoL) globally (Chugh et al., 2014). There are numerous causes of AF, including hypertension, diabetes, congestive heart failure, coronary heart disease, obesity, rheumatic heart disease, and valvular heart disease (Rahman et al., 2014).

According to the guidelines from the American College of Cardiology, American Heart Association, and Heart Rhythm Society (AHA/ACC/HRS) (2019), Valvular AF is AF occurring in the presence of moderate-to-severe mitral stenosis (which may require surgical intervention), or the presence of a mechanical heart valve. On the other hand, Non-Valvular Atrial Fibrillation (NVAf) is AF that develops in the absence of moderate-to-severe mitral stenosis or a mechanical heart valve (January et al., 2019).

Warfarin, a Vitamin K antagonist (VKA) continues to be the most commonly prescribed oral anticoagulant (OAC) for stroke thromboprophylaxis in patients with AF despite availability of novel/non VKA/direct OAC (DOAC) in the past few years (Zirlik & Bode, 2017). Some medical practitioners regard warfarin as the "gold standard" in management of AF patients (Fareed, 2015; Mearns et al., 2014). While warfarin has effectively reduced risk of thromboembolism in AF patients, attaining and sustaining optimal therapeutic levels can be difficult (Kimmel et al., 2007). Serious warfarin adverse effects include intracranial haemorrhage, gastrointestinal bleed, haematosis & intraocular bleeding (Patel et al., 2022). To mitigate these risks, patients may need to make lifestyle and diet modifications, particularly by limiting vitamin K-rich foods and alcohol consumption (Card et al., 2020; Middeldorp et al., 2020). Certain OTC drugs, NSAIDs (ibuprofen and naproxen) and herbals/vitamins can interact with warfarin and affect its efficacy, which is measured by the level of International Normalised Ratio (INR) (Pharmaceutical Services Program, 2020). Due to its wide drug-drug and food interactions, it can increase the risk of adverse effect or reduce efficacy of anticoagulant effect of warfarin (Patel et al., 2022). Hence, it is crucial to routinely assess the INR level to verify that it falls within the

therapeutic interval of 2.0-3.0 (Wyse, 2007). If the INR level is outside the therapeutic range, appropriate warfarin dose adjustment is required to prevent thromboembolic or haemorrhagic complications (Clark, 2018). The frequency of clinic visits may vary among patients, with more frequent visits initially to closely monitor the patient's INR until the target therapeutic range is achieved. Once the INR level stabilizes, longer intervals of four to twelve weeks appointments can be considered (Pharmaceutical Services Program, 2020).

The proportion of time during which a patient's INR values remained within the target range or desired range of 2.0-3.0 is time in therapeutic range (TTR) (White et al., 2007). The Rosendaal method is an INR-specific incidence rate used to calculate the TTR value to determine the optimal intensity of anticoagulation (Rosendaal et al., 1993). Higher values of TTR are indicative of more favourable treatment outcomes, characterized by reduced occurrences of stroke, major haemorrhagic events, and mortality (White et al., 2007). The measurement of time spent within the TTR is crucial in assessing the efficacy of anticoagulation treatment for patients with NVAf on long-term warfarin therapy.

Treatment satisfaction refers to the individuals' assessment of various aspects of treatment process and its outcomes, including their expectations, preferences, and overall satisfaction. In the case of long-term warfarin, patients often face the need for lifestyle changes, the risk of bleeding, and a lack of easily measurable benefits from the treatment, which can compromise their HRQoL (Cherian et al., 2017). Managing the satisfaction with treatment regimen is crucial for patients with chronic illnesses such as AF (Bartlett et al., 1984). Research has shown that better understanding, higher adherence to treatment,

increased satisfaction, and reduced anxiety related to warfarin are all linked to significantly improved INR control (Suárez Fernández et al., 2018).

The concept health-related Quality of Life (HRQoL) was developed to focus more specifically on the impact of illness, including the side effects of treatment, on an individual's overall quality of life. HRQoL measures an individual's satisfaction or happiness with their life as indicated by the level of their physical, mental, emotional, or social functioning (Ware Jr & Sherbourne, 1992). It is used to assess how an individual's health has changed over time due to illness, disability, or dysfunction. As advancements in healthcare have led to increased life expectancies, HRQoL has become an emerging area of focus among patients on warfarin.

This study explores the specific patient population at a tertiary hospital in Kota Samarahan, Sarawak. This study investigated how their sociodemographic and clinical characteristics influenced treatment satisfaction and HRQoL of NVAf patients on long-term warfarin based on TTR. By capturing the outcomes, researchers can understand and tailor the unique needs of NVAf patients on long-term warfarin. By focusing specifically on this population, distinct requirements and challenges faced by this patient population can be identified, and the impact of warfarin on patient treatment satisfaction and HRQoL. Recognizing patients' perceptions of their treatment satisfaction and HRQoL is essential when evaluating the effectiveness of the treatment. By shedding light on the findings of this research and valuable insights can be made in optimizing care and improving outcomes in this population.

1.2 Problem Statement

In patients with NVAf, the consistent and lifelong use of warfarin is necessary. However, the use of warfarin poses challenges due to various reasons. Firstly, warfarin has a narrow therapeutic index, necessitating regular monitoring of the INR to prevent complications (Hawes, 2018; Witt et al., 2016). Secondly, warfarin's daily maintenance dose can differ between patients and even within the same patients (Holbrook et al., 2005). The inconsistent achievement of optimal TTR has been a concern in managing patients on warfarin (Wallentin et al., 2013). Effective anticoagulation management on maintaining therapeutic levels, and regular monitoring, is crucial for enhancing HRQoL (European Heart Rhythm et al., 2010). Thirdly, the consumption of certain foods, drugs, and alcohol can influence the metabolism of warfarin. Consuming foods with vitamin K can counteract the effect of warfarin by promoting clotting and leading to fluctuation in INR levels (Holbrook et al., 2005). Inconsistent TTR due to dietary factors can lead to poor treatment satisfaction (D. L. Ng et al., 2019). Patients often struggle with dietary restrictions further compounded by the need for INR monitoring and dosage adjustments. Fourthly, genetic factors have been found to impact the warfarin metabolism. Patients may require lower or higher doses of warfarin to achieve the same anticoagulation effect due to the CYP2C9 and VKORC1 genotypes in patients' genetic variations (M. Wadelius et al., 2007).

Understanding and evaluating the specific dimensions affected by warfarin is crucial for improving patient care and tailoring interventions accordingly. Maintaining consistent TTR is essential for improving HRQoL by reducing the risk of stroke and bleeding complications, major concerns for NVAf patients (Varona et al., 2020). Balancing

standardized treatment with the need for individualized care is challenging, requiring nurses to have the skills and resources to tailor interventions appropriately (van Servellen, 1988).

Globally, the assessment of TTR, HRQoL, and treatment satisfaction in NVAF patients has a notable gap in the literature, with a particular lack of local data. The treatment satisfaction of existing studies focuses on overall satisfaction (Elbur et al., 2015; Eltayeb et al., 2017; Ucar & Arslan, 2021). Limited studies compare the treatment satisfaction of patients with good and poor TTR control. Few studies focus on the HRQoL of patients on warfarin or compare between warfarin and DOACs (Corbi et al., 2011b; D. L. Ng et al., 2019; Tan et al., 2018). None have explored the HRQoL of NVAF patients on long-term warfarin based on their TTR. This gap is critical as HRQoL encompasses both physical and physiological well-being, both of which are significantly affected by the challenges of managing chronic conditions like NVAF.

1.3 Significance of Study

This research aims to contribute to a better comprehension regarding the impact of TTR on treatment satisfaction and HRQoL among individuals with NVAF patients on long-term warfarin in this region. The findings may assist healthcare professionals in identifying and addressing specific challenges faced by patients, as well as developing targeted interventions to enhance HRQoL and improve patient-centered care. Ultimately, the research aims to optimise treatment approaches and support strategies for NVAF patients undergoing long-term warfarin, leading to improved overall well-being and patient outcomes. Furthermore, the knowledge gained from this study can be integrated into promoting positive

changes in patients' lives and guiding nursing actions toward individuals undergoing anticoagulation therapy (Corbi et al., 2011b). The individual's perspective on their health status and the effects of their illness on their physical, function and emotional well-being is crucial for ensuring the effectiveness of the provided treatment.

According to Wilson and Cleary's Model, the biological and physiological status of patients (stable INR levels), reduces symptoms such as bleeding and thromboembolic events, and improves functional status which is measured by treatment satisfaction and HRQoL (Wilson & Cleary, 1995). High TTR levels demonstrated increased patient satisfaction (Samsa et al., 2004).

1.4 Research Questions

The research questions that will guide this study are as follows:

1. What is the sociodemographic and clinical characteristics of NVAf patients on long-term warfarin?
2. What is the difference between the sociodemographic and clinical characteristics of NVAf patients on long-term warfarin based on their TTR?
3. Is there any difference in the treatment satisfaction of NVAf patients on long-term warfarin based on their TTR?

4. Is there any difference in the HRQoL of NVAF patients on long-term warfarin based on their TTR?

1.5 Research Objectives

The research objectives for this study are as follows:

1. To describe the sociodemographic and clinical characteristics of NVAF patients on long-term warfarin.
2. To compare the treatment satisfaction and HRQoL of patients with NVAF who are undergoing long-term warfarin based on their TTR.

Specific aims include:

- 2.1 To compare the sociodemographic and clinical characteristics of NVAF patients on long-term warfarin based on their TTR.
- 2.2 To compare the treatment satisfaction of NVAF patients on long-term warfarin based on their TTR
- 2.3 To compare the HRQoL of NVAF patients on long-term warfarin based on their TTR.

1.6 Chapter Summary

Warfarin remains a common choice of oral anticoagulants among patients with NVAf to prevent thromboembolic events. The use of warfarin can be challenging for patients. This study aims to gain knowledge regarding the impact of long-term warfarin on treatment satisfaction and HRQoL in the local setting based on TTR.

CHAPTER 2

LITERATURE REVIEW

2.1 Overview

This chapter provides a comprehensive overview of existing research concerning the treatment satisfaction and HRQoL of patients with AF on long-term anticoagulants. This section strives to analyze relevant studies, highlighting their main findings, limitations, and research gaps. The chapter begins by discussing AF, its prevalence worldwide. This section then examines the findings on treatment satisfaction of patients receiving long-term anticoagulation therapy. It advances to HQRoL findings of patients on long-term warfarin.

2.2 A Global Prevalence of Atrial Fibrillation (AF)

Atrial fibrillation (AF) prevalence rates reveal variation across different regions and populations. Globally, the prevalence of AF was estimated at 0.51% of the worldwide population. Over the past two decades, there has been a notable increase of 17% to 33% in the prevalence of AF compared to (Lippi et al., 2021). AF rates were reported higher in Western countries, such as North America and Europe, compared to other regions (Wong et al., 2017). However, it is observed that developing countries such as Brazil, China, India, and Indonesia, undergoing demographic and epidemiological transitions, have increased AF prevalence (Rahman et al., 2014). According to the Framingham Heart Study (FHS), the prevalence of AF has tripled over 50 years (Kornej et al., 2020). In the United States, at least three to six million people suffer from AF. It is projected to reach six to 16 million by 2050. In Europe, the prevalence of AF in 2010 was nine million and is expected to rise rapidly in

2060, with 14 million individuals with AF. It is also expected to reach at least 72 million individuals with AF in Asia (Kornej et al., 2020). Although the prevalence of AF appears to be higher in Western countries compared to Asian countries, Asia has a substantially higher population of AF individuals than Europe or North America (Chao et al., 2021).

Research on the prevalence and incidence of AF have been extensively studied in the United States and Europe, comparatively limited to other regions. The highest burden of AF is observed in countries with a high sociodemographic index, although the most significant recent increase in AF cases has occurred in countries with a middle sociodemographic index. Projections for the future indicate that the total burden of AF may increase by more than 60% by the year 2050 (Lippi et al., 2021). It is predicted that five to 16 million in the United States will be affected by 2050 (Kodani & Atarashi, 2012). In the Asia Pacific region, studies on AF have been widely conducted in Japan, Taiwan, and China (Chao et al., 2021). The prevalence rate of AF in Japan in 2015 was 1.4% (Kodani et al., 2019). It is expected to increase by more than one million by 2050 (Kodani & Atarashi, 2012). However, there is notably limited research available from countries in Southeast Asia. (Chao et al., 2021).

2.3 Treatment Satisfaction of Long-term Warfarin Therapy

Various research has investigated the treatment satisfaction associated with long-term anticoagulation therapy across patient populations. These findings have been varied, with some patients expressing high satisfaction (Shilbayeh et al., 2018; Ucar & Arslan, 2021). Conversely, other studies have revealed patients with moderate or ambivalent

satisfaction levels towards the treatment (Eltayeb et al., 2017; Wang et al., 2014; Yildiz & Dayapoglu, 2017). Long-term anticoagulation treatment comes with challenges that can induce dissatisfaction and reduce quality of life (QoL) (Samsa et al., 2004). Enhancing patient care has emerged as a top priority to attain high satisfaction levels. Remarkably, treatment satisfaction has been found to significantly influence health outcomes (Kugbey et al., 2019). Another study also reported that higher levels of satisfaction with anticoagulation treatment are associated with improved treatment adherence, subsequently resulting in an overall enhancement of quality of life (QoL) (Wang et al., 2014).

2.3.1 Factors Influencing Treatment Satisfaction

Patients' satisfaction with their treatment is often influenced by positive outcomes and symptom relief (Hansson & Berglund, 1987; Volpicelli Leonard et al., 2020). Patients with better clinical outcomes in maintaining a therapeutic level of INR consistently with lower thromboembolic events and major bleeds demonstrated higher satisfaction (Suárez Fernández et al., 2018). Additionally, treatment satisfaction showed a positive relationship with the effectiveness of the treatment perceived by patients with chronic illness (Volpicelli Leonard et al., 2020). This implies that if patients perceive the treatment as having no negative effects on their daily life, it contributes to higher satisfaction. Certain aspects of sociodemographic and clinical characteristics may influence treatment satisfaction (Al-Jabi et al., 2022).

Few studies have shown that gender differences affect treatment satisfaction levels. It was reported that female patients exhibit greater dissatisfaction with warfarin treatment in

comparison to male patients (Elbur et al., 2015). Another study also identified that female patients experience more problems with warfarin compared to male patients (Eltayeb et al., 2017). Similar to the previous study, another study showed that male patients perceived better satisfaction than female patients (Ucar & Arslan, 2021). Higher treatment satisfaction was also reported with increasing age; older patients were generally more satisfied compared to the younger group (Alexander C. Perino et al., 2019; Riva et al., 2020). Likewise, the financial burden associated with treatment costs can greatly impact patients' satisfaction levels. It is reported that patients with better income levels encountered less burden of warfarin treatment as it requires long-term treatment and requires laboratory control (Ucar & Arslan, 2021). The overall cost incurred with warfarin due to frequent therapeutic monitoring, despite its lower price, can lead to a financial burden to the patients (Sterne et al., 2017). A finding reported that reducing the cost of travelling could increase the level of satisfaction with the warfarin treatment (Khiralla et al., 2022). The level of education also significantly influences treatment satisfaction. Patients with higher education tend to be more satisfied with the treatment compared to those with lower education (Eltayeb et al., 2017). Similar findings reported that higher education level patients had higher satisfaction due to better knowledge and ability to comprehend information on treatment received (Ucar & Arslan, 2021). Treatment satisfaction influence by gender, employment status, monthly income and education status ($p < 0.05$) (Tan et al., 2018).

It is paramount for healthcare providers and policymakers to understand the factors that may hinder treatment satisfaction and how it influences patients' outcomes. These factors may be varied from one individual to another and from one patient population to another. It may also be similar between a few groups of the patient population. The

healthcare provider should actively perform the role of empowering patients through the provision of comprehensive information and awareness of treatment (Al-Jabi et al., 2022). Enhanced communication in patient care contributes to improved clinical outcomes and increased levels of patient satisfaction (Trummer et al., 2006). Emphasising patients' satisfaction is a step towards achieving better healthcare outcomes and fostering stronger patient-provider relationships.

2.3.2 Assessment Tools for Treatment Satisfaction

Several tools have been developed to assess the treatment satisfaction of patients on anticoagulation. Over the years, the development of the tools used to measure treatment satisfaction has evolved. It shifted from general patient satisfaction to more disease-specific tools. This transition aims to better capture the specific aspects of patients' satisfaction across different conditions (Castro & Wang, 2023). Tools to measure treatment satisfaction for medication are the Treatment Satisfaction Questionnaire for Medication (TSQM) for generic tools, and some are specifically constructed for anticoagulation therapy, like Duke Anticoagulation Satisfaction Scale (DASS) and Anti-Clot Treatment Scale (ACTS). TSQM is a widely validated tool designed as a generic tool to assess patients' satisfaction with medication across multiple domains, such as effectiveness, side effects, convenience, and global satisfaction (Delestras et al., 2013). It can be used across various medications, and it is short and easy for patients to complete (Atkinson et al., 2004). However, it does not address specific issues unique to anticoagulation therapy.

Disease-specific tools tailored to assess treatment satisfaction in patients with anticoagulation therapy are ACTS and DASS. ACTS focuses on the impact of treatment on daily life, convenience, and satisfaction. ACTS is a 15-item scale that is used to measure satisfaction which assesses the burden and benefits of the anticoagulation treatment (Cano et al., 2012). ACTS is able to accurately reflect patients' satisfaction with anticoagulation treatment (Shilbayeh & Ibrahim, 2020). However, ACTS does not measure the psychological impact of the therapy.

DASS is a tool to assess satisfaction and QoL with anticoagulation for all models of medical care that can evaluate patients' satisfaction with anticoagulation and aid with identifying areas of anticoagulation that may prevent patients from obtaining therapeutic PT-INR range (Samsa et al., 2004). The questionnaire items were specifically designed to align with three primary dimensions relevant to anticoagulation therapy, namely: limitations (e.g., physical activity restrictions due to bleeding concerns, dietary constraints), hassles and burdens (encompassing daily inconveniences like medication adherence and occasional challenges such as waiting for blood tests during provider visits), and positive psychological impacts (e.g., a sense of reassurance due to anticoagulation therapy) (Samsa et al., 2004). Compared to other tools, DASS provides a more detailed evaluation of the satisfaction and quality of life impacts. This approach allows for a deeper understanding of the patient's experience with anticoagulation therapy, beyond what is captured by more generic tools like TSQM or even other anticoagulation-specific tools like ACTS.

The strengths of DASS lie in its comprehensive coverage of the dimensions critical to anticoagulation therapy, making it particularly sensitive to the specific challenges and benefits experienced by patients (Samsa et al., 2004). This specificity enhances its utility in clinical settings for tailoring patient care and improving therapeutic outcomes. However, its detailed and specific nature might also be a limitation, as it may not be as broadly applicable or as easy to administer in settings where a quicker, more general assessment is needed. Compared to the TSQM, which offers a broad view of medication satisfaction across different conditions, DASS is less versatile but more detailed in the context of anticoagulation, specifically warfarin. While several tools are available to assess treatment satisfaction, DASS is suitable for its thorough and specific focus on the multifaceted impacts of anticoagulation therapy including regular INR monitoring, dietary restriction, and the risk of bleeding which are comprehensively addressed by DASS (Samsa et al., 2004). This makes it a robust tool for gaining comprehensive insights into patients' experiences, which is crucial for improving patient care in anticoagulation management. The dimensions measured in treatment satisfaction instruments are integral in understanding patients' experiences and perspectives comprehensively. A range of assessment tools, each with its unique strengths and limitations, to assess the treatment satisfaction of patients. The changes from using generic tools to disease-specific tools are due to the need for more precise and relevant data specific to the disease, treatments, and patient populations. The awareness of patient-centered care emphasizes the importance of patient satisfaction as a key indicator of healthcare quality and outcome which incorporates the patients' perspectives into treatment evaluations (Castro & Wang, 2023).

2.4 Measuring Health-related Quality of Life (HRQoL)

Health-related quality of life (HRQoL) is vital in comprehending the holistic impact of a disease on an individual's overall well-being and addressing specific areas of concern. It refers to an individual's perspective and ability to cope with the burden of symptoms, functional constraints, and prognosis while also encompassing their perceptions of general health and well-being (Rumsfeld et al., 2013).

In a study conducted by Radaideh and Matalqah in 2018, it was reported that patients on warfarin therapy displayed good HRQoL. A study investigating HRQoL in the Asian population in Singapore showed relatively higher HRQoL as the participants reported low levels of symptoms and severity (Tan et al., 2018). In Pakistan, patients with AF reported overall satisfactory HRQoL (Iqbal et al., 2020). However, HRQoL was found to be influenced by demographic and clinical factors (Radaideh & Matalqah, 2018).

2.4.1 Factors Influencing Health-related Quality of Life (HRQoL)

The characteristics positively impacted HRQoL, including younger age, higher education level, and employment status. Conversely, factors such as being female and having a history of previous haemorrhagic episodes, whether minor or major bleeding, were associated with reduced HRQoL (Radaideh & Matalqah, 2018). Similarly, gender differences affect HRQoL as female patients experienced reduced HRQoL compared to male participants (Tan et al., 2018). Elderly patients also reported lower HRQoL than the younger group (Corbi et al., 2011a; Radaideh & Matalqah, 2018; Tan et al., 2018).

2.4.2 Assessment Tools for Health-related Quality of Life (HRQoL)

Numerous assessment instruments were developed to measure HRQoL, both generic and disease-specific, related to health status and symptom impact instruments (Zhang et al., 2020). The generic instrument includes Medical Outcome Study 36-Items Short-Form Survey (SF-36), the most common generic instrument used to investigate HRQoL (Ware & Sherbourne, 1992). This instrument assesses eight domains, namely, physical functioning, role-physical, bodily pain, and general health perceptions, which yield a Physical Component Summary and Mental Component Summary consisting of social functioning, general mental health, and role-emotional and vitality (Zhang et al., 2020). This tool measures thoroughly the eight health domains, allowing a detailed analysis of the patients' health status. However, due to its length and complexity with 36 items, it can be time consuming and may impose a higher burden, especially on elderly patients (Ware & Sherbourne, 1992).

A simplified version of SF-36, the Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12v2) serves as an equivalent substitute for SF-36 with shorter and less time-consuming (Lam et al., 2013; Linde et al., 2009). While SF-36 offers a comprehensive assessment of the physical and mental health component, SF-12v2 provides similar results with fewer questions, making it more practical in clinical settings (Gandek et al., 1998; Ware & Sherbourne, 1992). The strength of SF-12v2 is despite fewer items, it contains all eight domains of SF-36 and it captures the physical and mental component summary effectively (Linde et al., 2009). A study by Ware et al. stated that the simplified version of SF-12 reduced the length of the questionnaire with minimal loss of measurement precision (Ware et al., 1996). It is also a more feasible tool and time-efficient compared to SF-36. Additionally,

SF-12v2 has been validated as an effective substitute for SF-36, ensuring that it still provides meaningful insights into patients' HQRoL (Linde et al., 2009; Ware & Sherbourne, 1992). SF-12v2 demonstrated strong psychometric properties with good internal consistency and construct validity making it comparable to SF-36 (Fleishman et al., 2010).

Disease-specific HRQoL instruments such as the Atrial Fibrillation Severity Scale (AFSS) are utilized to assess how patients perceive the frequency of episodes and the severity of symptoms related to AF with seven items (Zhang et al., 2020). Assessing disease-specific HRQoL instruments like AFSS allows precise symptoms and impacts of specific conditions. While allowing detailed insight into the specific condition, it may lack of comprehensive scope of general HRQoL measures and does not cover a broad range of physical and mental health domains compared to SF12-v2.

2.5 Measuring Time in Therapeutic Range (TTR)

Time in therapeutic is calculated by determining the percentage of time that a patient's INR values remain within therapeutic range, between 2.0 to 3.0 (White et al., 2007). The optimal range for patients with NVAf prescribed on warfarin should be maintained between 2.0 to 3.0 (Fuster et al., 2001). Any INR value exceeding 3.0 puts patients at risk of experiencing haemorrhage (Hylek et al., 1996). Conversely, an INR below 2.0 increases the likelihood of patients at risk of stroke (Jones et al., 2005). TTR is expressed as percentage, indicating a higher percent for better anticoagulation control and associated with reduced risk of both thrombotic and bleeding complications (Caldeira et al., 2014). TTR is an important measure as it directly correlates with patients' outcomes. Achieving an optimum

TTR is the primary goal in anticoagulation management to optimize patients' safety and efficacy of treatment (Connolly et al., 2008). A study by Schmitt et al., in 2003 compares three methods of calculating TTR, namely, Fraction of INR's, Cross-section-of-the-files, and Rosendaal method. Both Fraction of INR's and Cross-section-of-the-files involve simple arithmetic calculation. This method is straightforward but does not consider the actual days within the target range. The methods also do not describe the full variability of INR values over time, leading to inaccuracy of the TTR measurement (Schmitt et al., 2003). It often provides an incomplete state of patient management and may result in suboptimal clinical outcomes (Tadesse et al., 2022). The Rosendaal method involves more complex calculations. However, it takes into consideration the actual days patients are in the target range. The Rosendaal method is preferred over the traditional methods due to accuracy, precision, and standardization (Schmitt et al., 2003). This method also offered time-sensitive measures that better reflect the anticoagulation control over time (Grzymala-Lubanski et al., 2017).

TTR plays an antecedent role in treatment satisfaction and HRQoL. The impact of TTR on treatment satisfaction shows that TTR above 60% significantly experiences fewer adverse events which may positively influence their treatment satisfaction (Asarcıklı Lale et al., 2013; Connolly et al., 2008). Patients with stable TTR also require fewer clinic visits and dose adjustments which enhances their satisfaction (Connolly et al., 2008). The impact of TTR on HRQoL shows that better anticoagulation control improves physical functioning and reduces the impact of illness on daily activities as well as lower levels of anxiety (Minjie et al., 2023). Consistent INR control provides physiological comfort to patients, reducing anxiety about adverse reactions of warfarin. Maintaining an optimal TTR is important in

enhancing patients' treatment satisfaction and HRQoL. This can also improve patient health experience and satisfaction with treatment.

2.5.1 Good vs. Poor Control of Time in Therapeutic Range

Higher TTR aims for optimal anticoagulation control and best clinical outcomes. However, achieving high TTR may not be feasible for all patients. For instance, Asarcıklı Lale et al identified 60% as an optimal benchmark that strikes between achieving effective anticoagulation and minimizing the risk of adverse events (Asarcıklı Lale et al., 2013). Good anticoagulation control in the US Veterans was defined at 65% and above (Liu et al., 2018). A study by Connolly et al suggested a minimum TTR threshold of 58%.

The determination of good TTR control variants between populations. Asians often require lower doses of warfarin compared to Western populations due to differences in warfarin sensitivity and metabolism (Johnson, 2008; Takahashi & Echizen, 2001). The genetic polymorphism CYP2C9 influences the hepatic metabolism of the warfarin response which can result in TTR variation (Takahashi & Echizen, 2001). Genetic predisposition, the VKORC1 polymorphisms also show consistently significant influence on warfarin response among Asians, Western, and Black populations (Limdi et al., 2010).

Dietary intake such as vitamin K is not suggested for patients on warfarin as it can fluctuate the INR stability (Schurgers et al., 2004). Asian diets are typically rich in green leafy vegetables high in vitamin K (Chuang et al., 2021). The variability in warfarin dose is

influenced by vitamin K intake (Sconce et al., 2005). Thus, it may interfere with the efficacy of warfarin, leading to challenges in maintaining INR stability.

A TTR of 60% or higher is often used as a benchmark for optimal anticoagulation control as when the TTR falls below 58%, the clinical advantage of warfarin therapy does not surpass dual antiplatelet therapy (Connolly et al., 2008). Within the context of this particular study, a TTR value of 60% was identified as the threshold for defining a good TTR. Controlled TTR patients had higher satisfaction than uncontrolled TTR patients (TTR <65%) (Varona et al., 2020). Patients with uncontrolled anticoagulation (TTR <65%) had lower HRQoL compared to patients with controlled anticoagulation (Varona et al., 2020).

2.5.2 Time in Therapeutic Range in Atrial Fibrillation Patients

A mean TTR of 51% was reported in the study with 127,385 NVAf patients among US veterans (Liu et al., 2018). A national data registry of NVAf patients in Turkey in 2015 with one- and five-year follow-ups reported that the general population TTR rate was 40% (Güzel et al., 2022). A higher mean TTR was reported in a study in Australia with 82% (Bernaitis et al., 2017). A study in Sarawak reported mean TTR of 66%, Kuala Lumpur with 60.6% and Pulau Pinang average TTR of 65.9% (Edwards et al., 2014; Hien et al., 2017; Hooi et al., 2021). Similar to the finding, good QoL reported in patients with good TTR (>60%) (Sridharan et al., 2020). However, it was observed that there was no correlation reported between general health status and INR control (Hasan et al., 2015).

2.6 Research Gap

The existing studies explore the aspects of either treatment satisfaction or HRQoL among patients on warfarin (Eltayeb et al., 2017; Shilbayeh et al., 2018; Ucar & Arslan, 2021; Wang et al., 2014; Yildiz & Dayapoglu, 2017). At the same time, few studies compare the treatment satisfaction or HRQoL of NVAf patients based on different treatments such as VKA and DOACs (Fang et al., 2021; D. L.-C. Ng et al., 2019a). There is a notable gap in the literature regarding comparing treatment satisfaction and HRQoL based on their TTR level. Existing literature strongly suggests that maintaining a high TTR reduces complications and enhances treatment satisfaction and HRQoL. However, there were limited studies that provide detailed insight into the treatment satisfaction and HRQoL of NVAf patients on long-term warfarin. Hence, the treatment satisfaction and HRQoL based on good and poor TTR control should be explored.

2.7 Conceptual Framework

Figure 2.1 shows the conceptual framework on the relationship between the TTR and treatment satisfaction and figure 2.2 on relationship between TTR and HRQoL. The TTR patients determine the level of treatment satisfaction and HRQoL. Patients with good TTR control are more likely to be satisfied with their treatment and have positive HRQoL. Likewise, patients with poor TTR control are more likely to be dissatisfied with the treatment and perceived negatively towards their HRQoL.

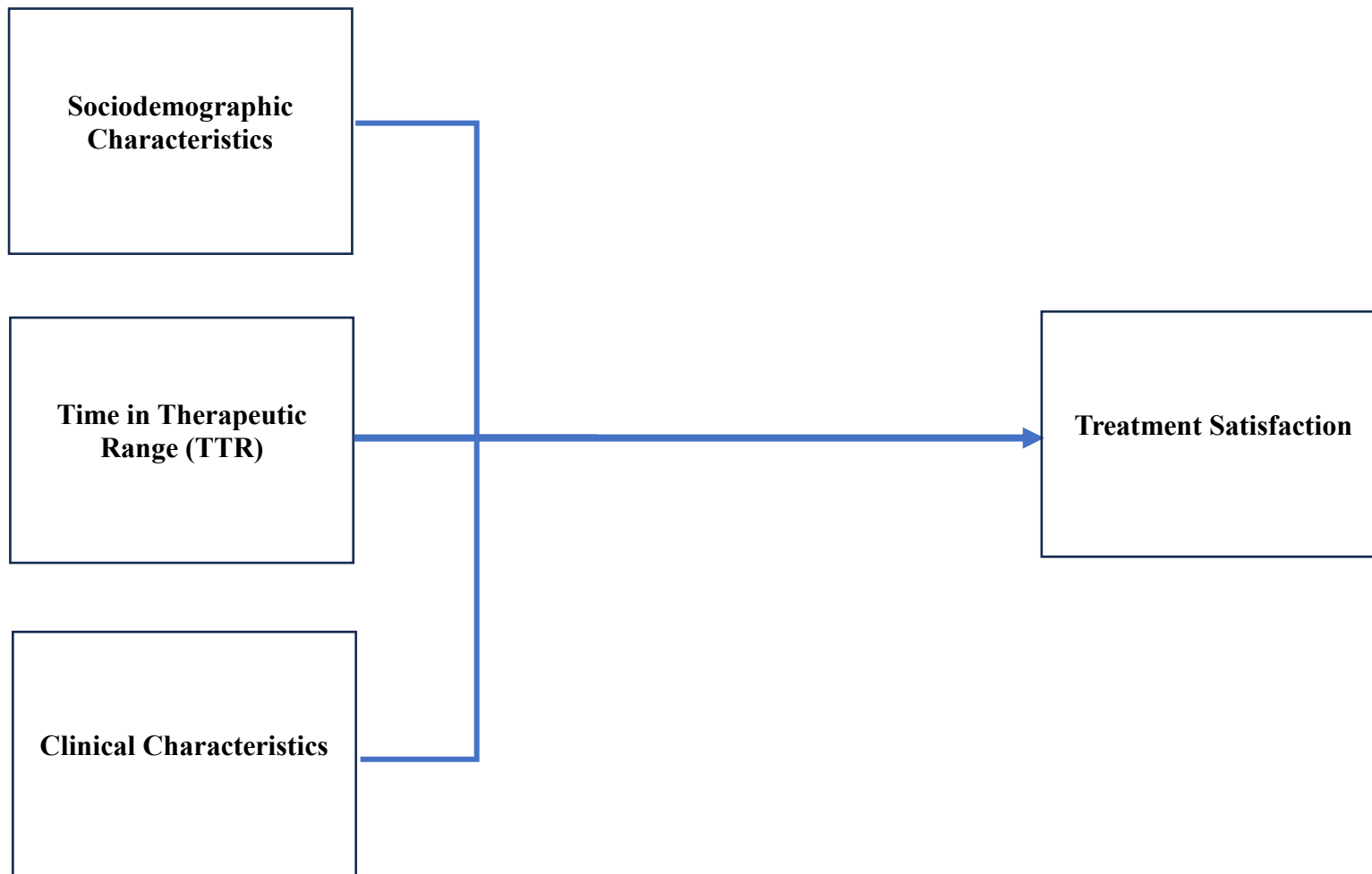


Figure 2.1: Conceptual Framework on Relationship Between TTR and Treatment Satisfaction

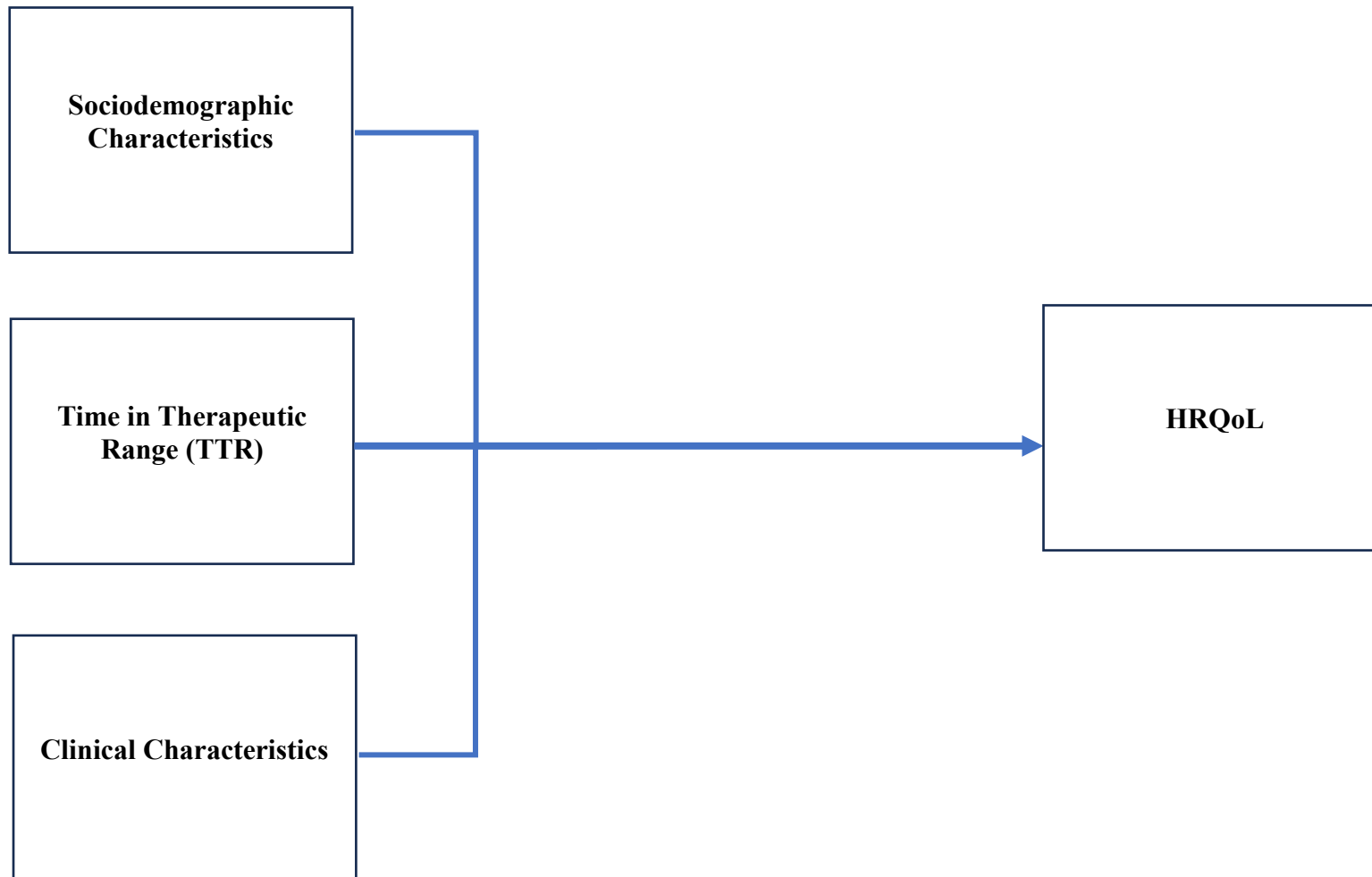


Figure 2.2 : Conceptual Framework on Relationship Between TTR and HRQoL

2.8 Chapter Summary

There are limited literatures addressing treatment satisfaction and HRQoL of NVAf patients receiving long term warfarin based on their TTR. There is also no local data available.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Overview

This chapter deliberates in detail the research methodology applied in conducting this research. Six sections on research methodology are comprehensively described in this chapter. The first section explains on research design chosen for this research. Subsequently, this chapter discusses on research settings of the 300 participants recruited in this study. Sample selection recruitment is described subsequently in the research design section. This chapter will also consist of data collection procedures such as research tools, reliability and validity of the instruments used in this study. The data analysis procedures, which include statistical analysis used in the study, conceptual framework and ethical consideration of this research, will also be covered in this chapter.

3.2 Research Design

This is a cross-sectional study where NVAF patients on long-term warfarin were recruited once during their INR clinic visit.

3.3 Research Setting

This study was conducted in the Warfarin Medication Therapy Adherence Clinic (WMTAC) Specialist Out-patient Clinic of Sarawak Heart Centre, located in the division of

Kota Samarahan, Sarawak. It is one of the centers providing outpatient anticoagulant treatment under the Pharmaceutical Services.

3.4 Population

This study involves patients with NVAF who were on warfarin and INR monitoring, attending WMTAC at Sarawak Heart Centre, Kota Samarahan, Sarawak.

3.5 Selection Criteria

The selection criteria in this study were as below.

3.5.1 Inclusion Criteria

The inclusion criteria for this research are all NVAF patients aged 18 years and above and have been on warfarin therapy for at least past six months.

3.5.2 Exclusion Criteria

In this research, the exclusion criteria for patients were incomplete INR records; concurrent use of anti-platelet therapy; a history of crossover from direct oral anticoagulants (DOACs); presence of co-existing valvular heart disease or mechanical heart valves; hospital admission for any reason other than complications related to warfarin therapy within one month prior to the interview; and inability to answer the questionnaire independently.

3.6 Sampling

3.6.1 Sample Size Calculation

Cross Sectional Study for Qualitative Variables was used. The Formula used as below;

$$n = \frac{Z_{1-\alpha/2}^2 p(1-p)}{d^2}$$

Equation 3.1

In equation 3.1, n is the estimated sample size, $Z_{1-\alpha/2}$ was constant 1.96 and the precision (d) is 0.05. Based on a previous study for Asian, the prevalence was 16.7%. Using this equation as a basis, a total of 217 respondents should be recruited for this study. An additional 30% was added as a non-response rate. However, a larger sample size contributed to the robustness and generalisability of the findings. Hence, 300 respondents were recruited for this study.

3.6.2 Sampling Method

A total of 300 respondents were recruited using a systematic random sampling method. In this research, every k^{th} number of AF patients on long-term warfarin registered at the registration counter during the WMTAC Sarawak Heart Centre were recruited using the following formula;

$$k = \frac{N}{n}$$

Equation 3.2

k = skip interval

N = population size

n = sample size

In this method, the first number, r , is obtained by electing a number between one and k . The k th value is selected after a random start. In this research, the $r=2$. $N=1800$ population, $n=300$. $k = 6$. This method was chosen as it is feasible for the structure of the appointment system, inexpensive and straightforward. It also prevents bias as every sixth number of registered patients could not be controlled. If the sixth number refused to participate, the next sixth was approached in this study. All patients were given an equal chance of being selected in the sample every time the clinic operates, which avoids arrangement in the selection. The sample frame for this study was the patients' appointment list on every clinic visit.

Patients recruitment algorithm as below;

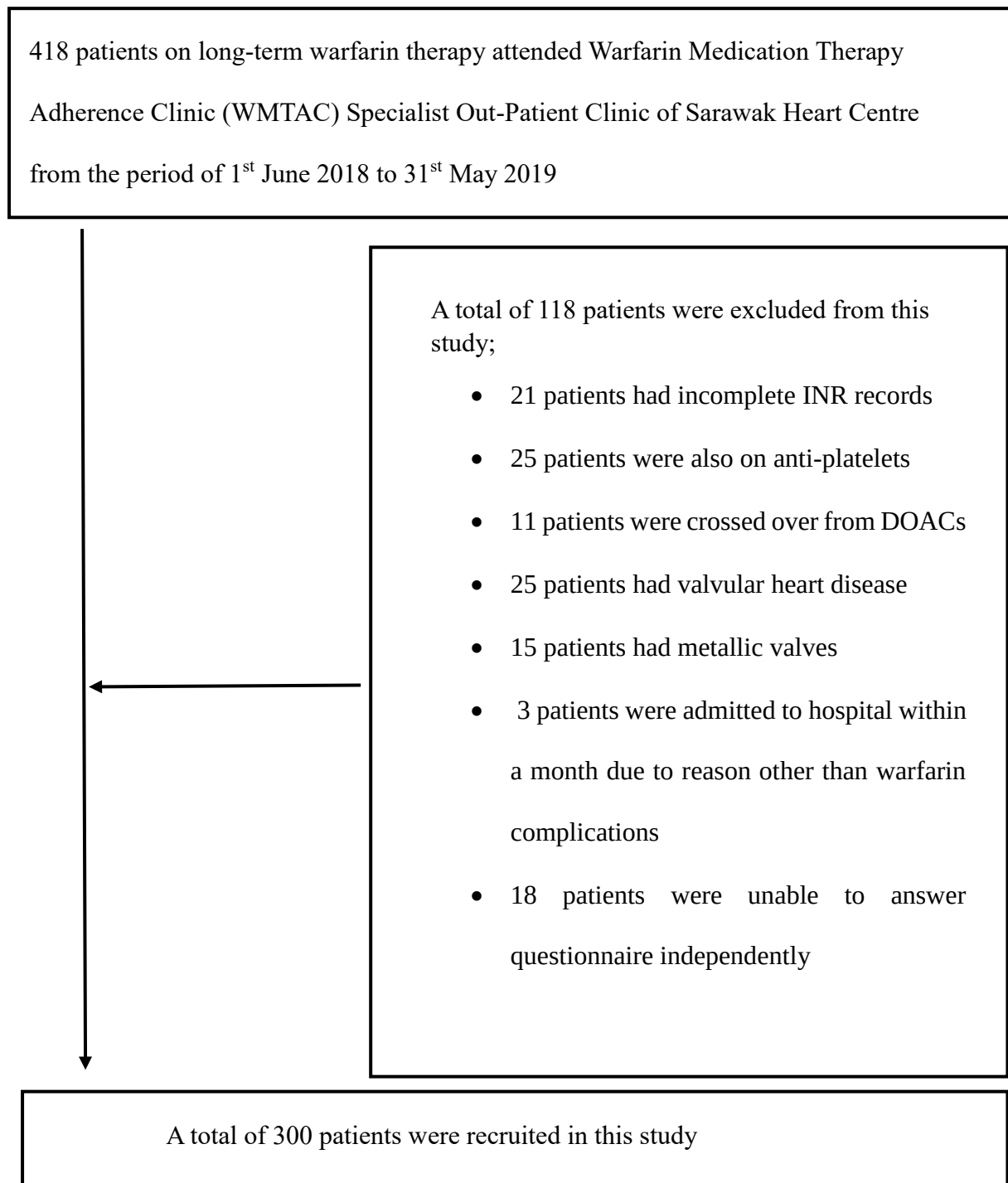


Figure 3.1: Algorithm of Patients' Recruitment in this Study

3.7 Research Tools

The questionnaire consists of three sections. The first section covers the sociodemographic data and clinical data of the respondents. The sociodemographic data includes age, gender, marital status, ethnicity, education level, occupation sector, family income group, estimated cost incurred during follow-up, diet and alcohol intake. Clinical data obtained include (the date of warfarin initiation, previous hospitalisation due to complications of warfarin, comorbidities and level of INR reading past six months to a year).

3.7.1 The Rosendaal Method for Time in Therapeutic Range (TTR)

The INR readings past six months to a year were traced from the Anticoagulation Treatment Book (Warfarin). INR readings of the first six weeks of warfarin initiation were excluded as it is the establishment period of adjustment and does not accurately reflect the long-period stability of warfarin. Time of therapeutic range (TTR) for the past six months to a year was recorded and TTR was calculated by using the Rosendaal method. In this method, the target INR was set to 2.0 to 3.0. Then, the INR for the past six months to a year is entered in the calculator to obtain the time in range which is expressed in percentages. The good TTR control is defined at 60% and above and poor TTR as less than 60%.

Validity and Reliability

The Rosendaal method is designed for INR control over time as it is sensitive to fluctuations, precise and is widely used in studies (Ageno et al., 2012; Dlott et al., 2014; Rose et al., 2011; Rosendaal et al., 1993; Siddiqui et al., 2018; Wieloch et al., 2011).

3.7.2 Short Form 12 Version 2 Health Survey (SF-12v2) for Health-related Quality of Life (HRQoL)

The second section comprises of Functional Health and Well-being using Short Form 12 version 2 Health Survey (SF-12v2). This instrument consists of eight components: physical functioning (PF, two items), role limitations due to physical problems (RP, two items), bodily pain (BP, one item), general health perceptions (GH, one item), vitality (VT, one item), social functioning (SF, one item), role limitations due to emotional problems (RE, two items) and mental health (MH, two items).

These eight subscales combine to form the Physical Component Summary (PCS) and Mental Component Summary (MCS). The PCS derived from PF (limitation in moderate physical activities & limitations in climbing several stairs), RP (accomplished less due to physical health & limited work or activities due to physical health), BP (pain interference with work or home activities) and GH (health rating in general). The MCS from SF (interference of physical health or emotional problems with social activities), RE (Accomplished less due to emotional problems), VT (having a lot of energy and MH (feeling calm and peaceful & feeling downhearted and blue).

The response for these items ranges from a three-point Likert scale for questions 2, 3, and 5 option rating scale for the remaining items. The Quality Metric's Health Outcome™ Scoring Software 5.0, was used to obtain Physical Component Summary (PCS) and Mental Component Summary (MCS) from these eight components. The PCS and MCS score range from 0-100. A higher score indicates a better HRQoL.

Validity and Reliability

SF-12v2 is a validated tools measuring generic HRQoL across patients with various diseases, conditions and treatment group available in various languages including English and Malay (QualityMetric, 2023).

Various studies reported good Cronbach Alpha ranging from 0.72 to 0.85 for both PCS and MCS of SF-12v2 (Fong et al., 2021; Kathe et al., 2018).

3.7.3 Duke Anticoagulation Satisfaction Scale (DASS) for Treatment Satisfaction

The third section Duke Anticoagulation Satisfaction Scale (DASS) questionnaire is a disease-specific questionnaire containing 25 items that address patients' treatment satisfaction in three sub-dimensions, namely limitations (L), hassles and burdens (H&B) and positive psychological impacts (PPI) (Samsa et al., 2004).

The first sub-dimension, L derived from nine items; the possibility of experiencing bruising or bleeding restricted physical activities, traveling, medical care needed, working life & daily life, and warfarin restricted food choices, alcoholic beverages, OTC medicines & daily life. The second sub-dimension, H&B from items; warfarin makes difficult in daily responsibilities, complicates changing responsibilities when necessary, warfarin treatment complicated, time lost due to warfarin treatment, frustration, painful and difficult/burden of warfarin treatment. The last sub-dimension, PPI from items; understanding the medical causes of warfarin treatment, reassurance to warfarin treatment, worry if bruising or bleeding

due to warfarin, positive & negative effect of warfarin on life, satisfied with warfarin treatment, comparison of warfarin to other medical treatment and recommend warfarin to someone with the same disease.

These 25 items offered a seven-point Likert scale for each item. The L and H&B are also considered as negative impacts of oral anticoagulant. The total score of DASS range from 25 – 175, with lower value represents a better satisfaction.

Validity and Reliability

DASS is a validated tools to measure patients' satisfaction on anticoagulation therapy (Schoen et al., 2020). DASS is available in various languages including English and Malay. The Malay-validated version complied with the standard procedure in the translation guidelines (Radaideh & Matalqah, 2018).

The internal consistency for DASS was reported Cronbach's Alpha 0.88 for English version (Samsa et al., 2004). For Malay version, the internal consistency was Cronbach's Alpha 0.758.

3.7.4 Pilot Study

A pilot study was done prior to data collection. A total of 30 respondents on warfarin with diseases other than NVAf were recruited.

3.7.5 Operational Definition

Health-related Quality of Life (HRQoL)

Health-related quality of life refers to the patient's perceived physical and mental health aspects of well-being related to the health conditions.

Treatment Satisfaction

Treatment satisfaction comprised the degree of perceived treatment such as limitations (L), hassles and burdens (H&B), and positive psychological impacts (PPI).

Time in Therapeutic Range

The Time of Therapeutic Range (TTR) in this study was classified into two categories: Good Control was defined as 60% or more of the (TTR) value, and Poor Control as less than 60% of the TTR value. Patients TTR was calculated using Rosendaal technique was used to calculate INR for the past six months to a year.

3.8 Data Collection Method

Data collection was done from 1st June 2018 to 31st May 2019. Potential respondents were identified from the patients' registry a day before data collection and approached on the clinic visit day based on the Systematic Random sampling method. The approaches used in data collection for this research include;

1. Self-administered questionnaires for literate patients.
2. Face-to-face interview for illiterate patients.
3. Review of medical and INR records.

The questionnaires were available in English and validated Malay version. Patients were given the option to choose their preferred language.

The sixth number interval patients were approached, and eligible patients who met all the inclusion and exclusion criteria were recruited in this study. Written consent was obtained before the distribution of the questionnaire to the eligible participants. All complete questionnaires answered on site were returned on the same day.

3.9 Data Analysis

In this research, data analysis was performed by using Statistical Package for Social Sciences (SPSS for Windows version 25.0, SPSS Inc., Chicago, IL, USA). Quantitative data were analysed with descriptive statistics of the variables in this study.

Categorical variables was presented as percentage and frequency while continuous variables as mean $\pm$ standard deviation (SD) or median with interquartile range. For between group differences, Chi-square test or Fisher exact test was used to analysed categorical data while independent sample t-test or Mann-Whitney U test was used to analysed continuous variables. The difference in treatment satisfaction and HRQoL between the study group and statistically significant variables as covariates was analysed with Analysis of Covariance (ANCOVA). A p-value less than 0.05 was considered statistically significant.

3.10 Ethical Consideration

Ethical approval acquired from Medical Research and Ethics Committee of National Registry of Malaysia (NMRR-17-1086-34402) and director of the hospital.

Written informed consent was obtained from all participants in this study prior to data collection.

3.11 Chapter Summary

This was a cross-sectional study on NVAf patients who were on long term warfarin, attending anticoagulant clinic of a tertiary referral centre in Sarawak from 1st June 2018 to 31st May 2019. Patients' TTR was calculated by using Rosendaal method, while their treatment satisfaction and HRQoL were assessed usng DASS and SF12v2, respectively.

CHAPTER 4

RESULTS

4.1 Overview

This chapter figured out the results of 300 NVAf respondents on long-term warfarin based on their TTR. The data is presented in descriptive analysis and inferential analysis. This chapter compares the sociodemographic and clinical characteristics of NVAf patients on long-term warfarin based on TTR. Data cleaning was done to remove duplicate or irrelevant entries from the dataset. All data collected in this research had no missing responses.

4.2 Sociodemographic Characteristics of Respondents (N=300)

There were 300 patients recruited, and no patients dropped out of this study. The demographic characteristics are shown in table 4.1. The mean age of all participants (n=300) was 59.7 ± 15.6 years. There were more males (57.3%) compared to females. Most of the respondents were with partners (73.3%). More than half of the respondents were Native Sarawak (53.0%). 80.7% of respondents received formal education. 49% were unemployed. 5% were vegetarian and 2% consumed regular alcohol.

Table 4.1: Sociodemographic Characteristics of Respondents

Sociodemographic	Number (n)	Percentage (%)	Mean	SD
Age				
Years			59.7	15.6
Gender				
Male	172	57.3		
Female	128	42.7		
Marital status				
No partner	80	26.7		
With partner	220	73.3		
Ethnic group				
Malay	67	22.3		
Chinese	68	22.7		
Native	159	53.0		
Others	6	2.0		
Education				
None	58	19.3		
Primary	101	33.7		
Secondary	115	38.3		
College/University	26	8.7		
Occupation				
None	147	49.0		
Government Dependent/ Pensioner	72	24.0		
Private	81	27.0		
Diet				
Non-vegetarian	285	95.0		
Vegetarian	15	5.0		
Alcohol				
No	294	98.0		
Yes	6	2.0		

4.3 Clinical Characteristics of Respondents (N=300)

Hypertension is the most common comorbidities among the patient (58.7%), followed by Congestive Heart Failure (18.0%), Diabetes Mellitus (17.3%), and 3.7% had Stroke/TIA/thromboembolism.

The mean CHA₂DS₂-VASc score was 2.0 ± 1.3 . The mean duration of warfarin treatment was 6.3 ± 6.5 years. Mean TTR was $47.0 \pm 17.3\%$. 18.3% of the respondents reported a history of prior hospitalisation related to warfarin therapy as shown in table 4.2.

Table 4.2: Clinical Characteristics of Respondents

Clinical Characteristics	Number (n)	Percentage (%)	Mean	SD
Comorbidities				
Congestive Heart Failure	54	18.0		
Hypertension	176	58.7		
Diabetes Mellitus	52	17.3		
Stroke/TIA/Thromboembolism	11	3.7		
Vascular Disease	0	0		
Others	67	22.3		
CHA₂DS₂-VASc				
None			2.0	1.3
Treatment Duration				
Years			6.3	6.5
Time in Therapeutic Range				
%			47.0	17.3
Time in Therapeutic Range Control				
Good TTR Control ($\geq 60\%$)	73	24.3		
Poor TTR Control ($< 60\%$)	227	75.7		
Hospitalisation				
No	245	81.7		
Yes	55	18.3		

Abbreviation: TIA, Transient Ischemic Attack

4.4 Time in Therapeutic Range (TTR) of the Respondents (N=300)

Table 4.3 shows the comparison of sociodemographic characteristics and table 4.4 on clinical characteristics between good and poor TTR patients. In this study, 24.3% of the patients had good TTR with a mean score of $70.2 \pm 8.7\%$ while the remaining patients (75.7%) had lower TTR 39.5 ± 11.9 . Respondents with good TTR control had significantly longer treatment duration, 7.8 ± 8.3 years versus 5.7 ± 5.7 years ($p < 0.001$). Patients with poor TTR who did not receive formal schooling were 22.9% (n=52) compared to good TTR with 8.2% (n=6). The respondents' education level was significantly different between the good and poor TTR group ($p = 0.001$). Stroke/TIA/thromboembolism was significant more common among the good TTR group compared to the poor TTR group ($p = 0.0017$). However, the number of these patients was too small. Otherwise, there was no statistical difference between good and poor TTR in term of patients' age, gender, ethnicity, partner status, occupation, diet preferences, alcohol intake, and other comorbidities.

Table 4.3: Comparison of Sociodemographic Characteristics Between Good and Poor TTR

Characteristics	Patients TTR								p-value
	Good (TTR≥60%)				Poor (TTR<60%)				
	Number (n)	Percentage (%)	Mean	SD	Number (n)	Percentage (%)	Mean	SD	
Age									
Years			57.2	15.0			60.5	15.7	0.559
Gender									
Male	39	53.4			133	58.6			0.438
Female	34	46.6			94	41.1			
Marital status									
No partner	18	24.7			62	27.3			0.420
With partner	55	75.3			165	72.7			
Ethnic group									
Malay	15	20.6			52	22.9			0.095
Chinese	24	32.9			44	19.4			
Native	32	43.8			127	55.9			
Others	2	2.7			4	1.8			

The *p*-value in bold are statistically significant

Table 4.3 continued

Characteristics	Patients TTR								<i>p</i> -value
	Good (TTR≥60%)				Poor (TTR<60%)				
	Number (n)	Percentage (%)	Mean	SD	Number (n)	Percentage (%)	Mean	SD	
Education									
None	6	8.2			52	22.9			0.001
Primary	19	26.0			82	36.1			
Secondary	41	56.2			74	32.6			
College/University	7	9.6			19	8.4			
Occupation									
None	30	41.1			117	51.5			0.269
Government Dependent/ Pensioner	19	26.0			53	23.3			
Private	24	32.9			57	25.1			
Diet									
Non-Vegetarian	69	94.5			216	95.2			0.829
Vegetarian	4	5.5			11	4.8			
Alcohol									
No	71	97.3			223	98.7			0.604
Yes	2	2.7			4	1.8			

The *p*-value in bold are statistically significant

Table 4.4: Comparison of Clinical Characteristics Between Good and Poor TTR

Characteristics	Patients TTR								<i>p</i> -value
	Good (TTR≥60%)				Poor (TTR<60%)				
	Number (n)	Percentage (%)	Mean	SD	Number (n)	Percentage (%)	Mean	SD	
Comorbidities									
Congestive Heart Failure	16	21.9			38	16.7			0.317
Hypertension	36	49.3			140	61.7			0.062
Diabetes Mellitus	11	5.1			41	18.1			0.557
Stroke/TIA/Thromboembolism	6	8.2			5	2.2			0.017
Vascular Disease	0	0			0	0			NA
Others	12	16.4			55	24.2			0.164
CHA₂DS₂-VASc									
None			1.8	1.1			2.0	1.4	0.204
Treatment Duration									
Years			7.8	8.3			5.7	5.7	<0.001

Abbreviation: SD, standard deviation; TIA, Transient Ischemic Attack

The *p*-value in bold are statistically significant

Table 4.4 continued

Characteristics	Patients TTR								<i>p</i> -value
	Good (TTR≥60%)				Poor (TTR<60%)				
	Number (n)	Percentage (%)	Mean	SD	Number (n)	Percentage (%)	Mean	SD	
Time in Therapeutic Range									
%			70.2	8.7			39.5	11.9	NA
Hospitalisation									
No	58	79.5			187	82.4			0.574
Yes	15	20.5			40	17.6			
The <i>p</i> -value in bold are statistically significant									

4.5 Treatment Satisfaction of the Respondents

4.5.1 Descriptive Analysis of Treatment Satisfaction (N=300)

The first nine items of the questionnaire were on L of the respondents. The highest mean score (SD) was 3.1 ± 2.0 on “warfarin treatment restricts food choices.” More than one-third, $n=104$ (34.7%), of the respondents answered, “not at all.” The lowest mean score (SD) for limitations is “possibility of experiencing bruising or bleeding restrict in traveling” with 1.9 ± 1.4 . Only three respondents answered, “a lot,” while another three chose “very much.” In L, this dimension’s mean score (SD) was 18.0 ± 10.0 .

The subsequent eight questions on H&B. The highest mean score (SD) in this dimension on the question “warfarin treatment complicates changing responsibilities, when necessary,” with 2.3 ± 1.7 compared to the lowest mean (SD) on the question “painful due to warfarin treatment” with 1.4 ± 1.1 . More than half, 51.3% ($n=154$), responded “not at all,” while only three percent ($n=9$) answered “very much” on the question “warfarin treatment complicates changing responsibilities, when necessary.” For “painful due to warfarin treatment,” the majority (82.3%, $n=247$) responded “not at all.” In H&B dimension, the mean score (SD) was 15.6 ± 9.1 .

For the final eight questions on PPI, the highest score (SD) was on the question “recommend warfarin treatment to someone who has to start due to disease or treatment,” with 4.5 ± 2.1 . A total of 80 participants (26.7%) responded “very much” to this item. This dimension’s lowest mean (SD) was “difficult of warfarin treatment compared to other

medical treatments” with 1.8 ± 1.4 . Only two (0.7%) respondents answered, “very much” compared to 70.3% (n=211) who responded, “not at all.” PPI scored 21.7 ± 5.8 , and the total DASS score for this study was 55.2 ± 21.3 as presented on table 4.6.

Table 4.5: Descriptive Analysis of DASS

Limitations		Responses (%)							Mean	SD
		1	2	3	4	5	6	7		
1.	Possibility of experiencing bruising or bleeding restrict participation in physical activities	66.3	8.3	6.0	13.7	2.3	2.7	0.7	1.9	1.4
2.	Possibility of experiencing bruising or bleeding restrict in travelling	68.0	7.3	5.7	12.0	5.0	1.0	1.0	1.9	1.4
3.	Possibility of experiencing bruising or bleeding restrict the medical care needed	64.3	7.3	7.7	12.7	4.0	2.3	1.7	2.0	1.5
4.	Possibility of experiencing bruising or bleeding restrict in working life	72.7	8.3	6.7	9.3	1.7	0	1.3	1.6	1.2
5.	Consider all above, possibility of experiencing bruising or bleeding restrict daily life	70.7	9.7	5.7	9.7	2.7	1.3	0.3	1.7	1.3

Table 4.5 continued

Limitations		Responses (%)							Mean	SD
		1	2	3	4	5	6	7		
6.	Warfarin treatment restrict in food choices	34.7	13.0	9.3	16.0	11.3	7.7	8.0	3.1	2.0
7.	Warfarin treatment restrict in drinking alcoholic beverages wanted	84.0	3.7	2.0	4.3	2.3	2.0	1.7	1.5	1.3
8.	Warfarin treatment restrict in using over-the-counter medicines	62.0	4.0	8.0	13.7	3.7	5.0	3.7	2.2	1.8
9.	Consider all above, warfarin treatment affect daily life	61.3	11.0	4.3	14.0	3.0	3.7	2.7	2.1	1.7

Table 4.5 continued

Hassles & Burdens		Responses (n%)							Mean	SD
		1	2	3	4	5	6	7		
10.	Warfarin treatment make difficult in daily responsibilities	61.3	17.7	3.7	10.3	1.3	3.3	2.3	1.9	1.5
11.	Warfarin treatment complicate changing responsibilities when necessary	51.3	16.3	8.3	13.0	3.0	5.0	3.0	2.3	1.7
12.	Warfarin treatment complicated	67.3	11.3	3.3	12.0	1.0	3.3	1.7	1.9	1.5
13.	Time lost due to warfarin treatment	60.0	13.7	3.7	13.7	2.7	4.7	1.7	2.1	1.6
14.	Frustration to warfarin treatment	55.3	24.3	2.7	13.0	2.0	0.3	2.3	1.9	1.4
15.	Painful due to warfarin treatment	82.3	5.7	3.7	6.0	0.7	0.7	1.0	1.4	1.1
16.	Consider all above difficult/burden warfarin treatment	54.7	17.0	7.0	11.3	3.3	4.0	2.7	2.1	1.6
17.	Confidence in handling warfarin treatment	63.7	11.3	8.3	9.7	0.3	2.0	4.7	2.0	1.6

Table 4.5 continued

Positive Physiological Impacts		Responses (%)							Mean	SD
		1	2	3	4	5	6	7		
18.	Understand medical causes of warfarin treatment	37.0	30.0	16.0	11.3	2.7	2.7	0.3	2.2	1.3
19.	Reassurance to warfarin treatment	43.7	29.3	5.7	17.3	1.0	2.3	0.7	2.1	1.3
20.	Worry if bruises or bleeding due to Warfarin treatment	57.7	12.0	3.7	12.7	4.7	5.7	3.7	2.3	1.8
21.	Consider all above, warfarin treatment have positive effect on life	22.7	32.0	13.0	19.3	2.7	4.7	5.7	2.8	1.7
22.	Consider all above, warfarin treatment have negative effect on life	21.3	15.7	5.0	17.0	10.3	21.7	9.0	3.8	2.1
23.	Consider all above, satisfied with warfarin treatment	36.3	39.3	5.0	14.7	1.7	1.3	1.7	2.2	1.3
24.	Difficult of Warfarin treatment compared other medical treatment	70.3	7.7	3.3	13.7	1.7	2.7	0.7	1.8	1.4
25.	Recommend warfarin treatment to someone who has to start due to disease or treatment	16.7	7.3	5.0	23.3	2.0	19.0	26.7	4.5	2.1

Table 4.6: DASS Score of Respondents

DASS Parameter	Mean	SD
Total	55.2	21.3
Limitations	18.0	10.0
Hassles & Burden	15.6	9.1
Positive Physiological Impact	21.6	5.9

Abbreviation: SD, standard deviation; DASS, Duke Anticoagulation Satisfaction Scale

4.5.2 The Relationship Between the Level of TTR and Treatment Satisfaction of Respondents (N=300)

The mean DASS score for this study was 55.2 ± 21.3 (Table 4.6). The mean DASS score was not significantly different between good and poor TTR (54.6 ± 21.9 vs. 55.4 ± 21.2 , $p=0.779$), even after adjusted for treatment duration (55.0 ± 2.5 vs. 55.2 ± 1.4) and education level (53.9 ± 2.5 vs. 55.6 ± 1.4) as shown in table 4.7, table 4.8 and table 4.9. There was also no significant differences in each of the subdimension scores between good and poor TTR patients ($p=0.502 - 0.699$). The subdimension scores between the two groups were still not significantly different after adjusted for treatment duration ($p=0.612 - 0.998$) and education level ($p= 0.419- 0.864$). Table 4.8 and 4.9 shows comparison of DASS score between patient with good and poor TTR adjusted for duration of warfarin treatment and education level respectively.

Table 4.7: Comparison of DASS Score Between Patients with Good and Poor TTR without Adjustment

DASS Parameter	Patients TTR (Mean, SD)		<i>p</i> value
	Good (TTR≥60%)	Poor (TTR<60%)	
Total	54 ± 21.9	55.4 ± 21.2	0.779
Limitations	18.4 ± 10.5	17.9 ± 9.8	0.699
Hassles & Burden	14.9 ± 8.4	15.8 ± 9.4	0.502
Positive Physiological Impact	21.3 ± 6.3	21.8 ± 5.8	0.531

Abbreviation: SD, standard deviation; DASS, Duke Anticoagulation Satisfaction Scale

Table 4.8: Comparison of DASS Score Between Patients with Good and Poor TTR
Adjusted for Duration

DASS Parameter	Patients TTR (Mean, SD)		<i>p</i> value
	Good (TTR≥60%)	Poor (TTR<60%)	
Total	55.0 ± 2.5	55.2 ± 1.4	0.922
Limitations	18.5 ± 1.2	17.8 ± 0.7	0.998
Hassles & Burden	15.1 ± 1.1	15.7 ± 0.6	0.655
Positive Physiological Impact	21.3 ± 0.7	21.7 ± 0.4	0.612

Abbreviation: SD, standard deviation; Duke Anticoagulation Satisfaction Scale

*Adjusted with ANCOVA test

Table 4.9: Comparison of DASS Score Between Patients with Good and Poor TTR
Adjusted for Education

DASS Parameter	Patients TTR (Mean, SD)		<i>p</i> value
	Good (TTR≥60%)	Poor (TTR<60%)	
Total	53.9 ± 2.5	55.6 ± 1.4	0.563
Limitations	17.8 ± 1.2	18.0 ± 0.7	0.864
Hassles & Burden	14.8 ± 1.1	15.8 ± 0.6	0.419
Positive Physiological Impact	21.3 ± 0.7	21.7 ± 0.4	0.589

Abbreviation: SD, standard deviation; Duke Anticoagulation Satisfaction Scale

*Adjusted with ANCOVA test

4.6 Health-related Quality of Life (HRQoL) of the Respondents

4.6.1 Descriptive Analysis of Health-related Quality of Life (HRQoL) (N=300)

The descriptive results of the Short Form-12 version 2 (SF-12v2) assessment of the HRQoL of NVAf patients on long-term warfarin are shown in table 4.10. The SF-12v2's twelve items were divided into eight subscales to sum a total score of 100. The higher the score, the better the patient's quality of life.

For overall health scale, GH, the mean score with standard deviation was 3.1 and 0.9. Only two respondents, or 0.7% of the total respondents, classified their GH as poor. The next question on “limitation in moderate physical activities” under subscale of Physical Functioning (PF), the mean score $\pm$ SD was 2.4 ± 0.70 . Over fifty percent of the respondents, 152 (50.7%) reported ‘no, not limited at all’ for limitation in moderate physical activities e.g.; moving table, pushing vacuum cleaner, bowling or golf. Question 3 on “limitation in climbing several flights of stairs” the mean score $\pm$ SD was 2.4 ± 0.7 . Half of the respondents stated “no, not limited at all” for this question, and only 45 respondents (15.0%) answered “yes, limited a lot”.

The mean score SD for on RP “during the past four weeks, how much time had accomplished less than ones’ would like with work or other regular daily activities as result of physical health?” was $3.9 \pm (1.1)$. Only 7 respondents (2.3%) answered “all of the time”. The next question was also on RP on “during the past four weeks, how much time had limited in the kind of work or other activities as a result of physical health?” had mean score SD of

3.9 $\pm$ (1.2). Almost half of the respondents 45.0% (n=135) reported “none of the time”, followed by 77 respondents (25.7%) “some of the time”, 49 respondents (16.3%) with “a little of the time”, 10.0% (n=30) “most of the time” and only 9 respondents (3.0%) “all of the time”. The mean score $\pm$ SD for Question 6 under subscale RE was 4.3 $\pm$ (1.0) Nearly two-thirds of the respondents, 63.3% (n=190) reported “none of the time” followed by “some of the time” 47 respondents (15.7%), 42 respondents (14.0%) “a little of time”. Question 7 also on RE had similar responds with 190 respondents (60.7%) answered “none of the time”.

The subscale BP on how much pain interferes work and house activities and greater than half (53.7%) answered “not at all”. Question 9,10 and 11 on feeling for the past four weeks. The mean score for question on MH on feeling calm and peaceful, most (39.7) answered were all the time followed closely by 92 respondents (30.7) “most of the time”. The mean score and standard deviation was 3.9 ($\pm$ 1.2). The following question was on having a lot of energy for the past four weeks, majority (33.3%) also reported all the time. The mean score $\pm$ SD for feeling downhearted and blue was under subscale MH, with mean score 4.3 (1.0) the second highest mean score compared to other items. The final question on Social Functioning (SF) more than half (58%, n=174) reported none of the time.

Question 1 to 5 and 8 were Physical Component Summary (PCS) and question 6, 7, 9 to 12 were from Mental Component Summary (MCS). The mean score for Physical Component Scale (PCS) derived from GH, PF, RP, and BP and Mental Component Scale from RE, MH, VT, and SF was 47.0 $\pm$ 9.0 and 53.5 $\pm$ 9.6 respectively. In table 4.11, the

highest mean score among the eight subscales was VT with 56.3 ± 11.3 , and the lowest was PF with 47.0 ± 10.6 .

Table 4.10: Descriptive Analysis of HRQoL

SF-12v2 item	Responses (%)					Mean	SD
	1	2	3	4	5		
Health rating in general (GH)	0.7	24.7	45.7	19.7	9.3	3.1	0.9
Limitations in moderate physical activities (PF)	13.3	36.0	50.7	-	-	2.4	0.7
Limitations in climbing several flights of stairs (PF)	15.0	35.0	50.0	-	-	2.4	0.7
Accomplished less due to physical health (RP)	2.3	9.3	27.3	17.3	43.7	3.9	1.1
Limited in kind of work inside or outside home (RP)	3.0	10.0	25.7	16.3	45.0	3.9	1.2
Accomplished less due to emotional problems (RE)	2.3	4.7	15.7	14.0	63.3	4.3	1.0
Not careful (work or activities) due to emotion (RE)	2.0	6.7	16.7	14.0	60.7	4.3	1.1
Pain interference work inside or outside home (BP)	3.3	9.0	15.3	18.7	53.7	4.1	1.2
Feel calm and peaceful (MH)	6.3	7.0	16.3	30.7	39.7	3.9	1.2
Having a lot of energy (VT)	4.3	9.7	27.7	25.0	33.3	3.8	1.2
Feel downhearted and blue (MH)	1.3	4.3	16.0	20.7	57.7	4.3	1.0
Interference of physical health or emotional problems with social activities (SF)	4.3	7.0	20.0	10.7	58.0	4.1	1.2

Abbreviation: HRQoL, Health-related Quality of Life; SD, standard deviation; SF-12v2, Short Form-12 version 2; GH, General Health; PF, Physical Functioning; RP, Role Physical; RE, Role Emotional; BP, Bodily Pain; MH, Mental Health; VT, Vitality; SF, Social Functioning

Table 4.11: SF-12v2 Score of Respondents

SF-12v2 Parameters	Mean	SD
Physical Component Summary	47.0	9.0
Mental Component Summary	53.5	9.6
Physical Functioning	47.0	10.6
Role Physical	48.2	9.6
Bodily Pain	49.6	10.5
General Health	47.6	9.7
Vitality	56.3	11.3
Social Functioning	49.0	10.7
Role Emotional	48.8	10.7
Mental Health	53.8	9.9

Abbreviation: SD, standard deviation; SF-12v2, Short Form-12 version 2

4.6.2 The Relationship Between the Level of TTR and HRQoL of Respondents (N=300)

The mean SF-12v2 scores for PCS and MCS between good and poor control TTR are presented in table 4.12. There was no significant difference between the good and poor TTR group for both PCS (48.3 ± 8.7 vs. 46.5 ± 9.1 , $p=0.150$) and MCS (53.4 ± 8.6 vs. 53.6 ± 9.7 , $p=0.919$) and each domain of the HRQoL subscales ($p=0.184-0.684$) except for SF (51.5 ± 7.9 vs. 48.2 ± 11.3 , $p=0.019$). The mean score for PCS (48.2 ± 1.1 vs. 46.6 ± 0.6 , $p=0.175$) and MCS (53.5 ± 1.1 vs. 53.5 ± 0.6 , $p=0.998$) remained not significant different between good and poor TTR patients even after adjusted for treatment duration and education level. Each domain of SF-12v2 also showed no significant difference between the two groups, even after adjustment except for SF after adjusted for treatment duration (51.9 ± 1.3 vs. 48.1 ± 0.7 , $p=0.014$). Table 4.12 shows comparison of SF-12v2 score between good and poor TTR group without adjustment. Table 4.13 shows comparison of SF12v2 scores after adjusted for treatment duration and table 4.14 shows comparison of Sfl2v2 score after adjusted for education level.

Table 4.12: SF-12v2 score between Good and Poor TTR without Adjustment

SF-12v2 Parameters	Patients TTR		<i>p</i> value
	Good (TTR $\geq$ 60%)	Poor (TTR<60%)	
Physical Component Summary	48.3 $\pm$ 8.7	46.5 $\pm$ 9.1	0.150
Mental Component Summary	53.4 $\pm$ 8.6	53.6 $\pm$ 9.7	0.919
Physical Functioning	48.0 $\pm$ 10.9	46.7 $\pm$ 10.5	0.358
Role Physical	48.6 $\pm$ 8.8	48.1 $\pm$ 9.9	0.684
Bodily Pain	51.1 $\pm$ 9.5	49.2 $\pm$ 10.7	0.184
General Health	47.9 $\pm$ 9.5	47.5 $\pm$ 9.8	0.730
Vitality	56.9 $\pm$ 11.5	56.1 $\pm$ 11.3	0.602
Social Functioning	51.5 $\pm$ 7.9	48.2 $\pm$ 11.3	0.019
Role Emotional	48.2 $\pm$ 10.7	49.0 $\pm$ 10.7	0.563
Mental Health	53.4 $\pm$ 9.3	54.0 $\pm$ 10.1	0.634

Abbreviation: SD, standard deviation; 95% CI, 95% confidence interval; SF-12v2, Short Form-12 version 2

The *p*-value in bold are statistically significant

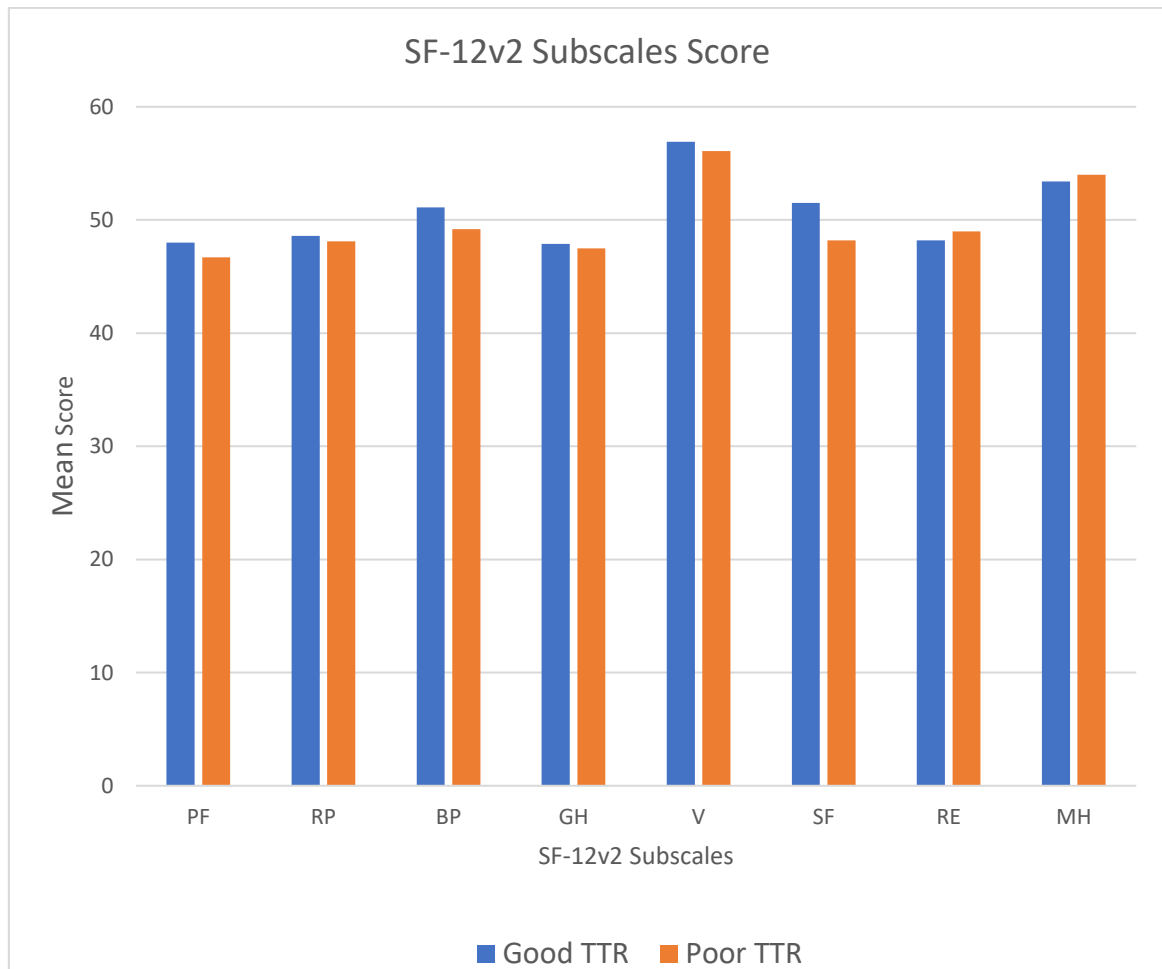


Figure 4.1: Comparison of SF-12v2 Subscales Between the Study Group

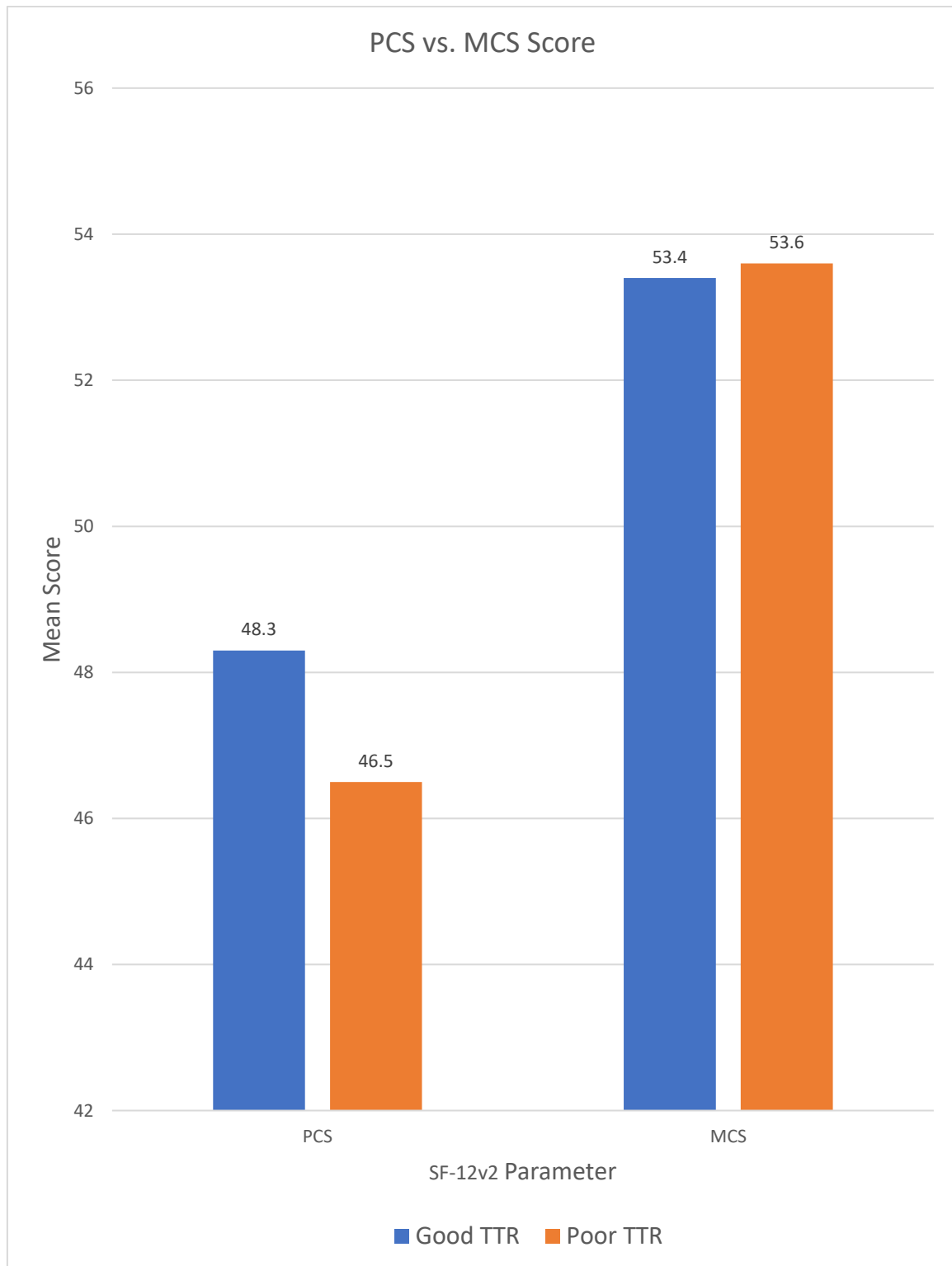


Figure 4.2: Comparison of SF-12v2 Parameters Between the Study Group

Table 4.13: SF-12v2 score between Good and Poor TTR Adjusted for Duration

SF-12v2 Parameters	Patients TTR		<i>p</i> value
	Good (TTR $\geq$ 60%)	Poor (TTR<60%)	
Physical Component Summary	48.2 $\pm$ 1.1	46.6 $\pm$ 0.6	0.175
Mental Component Summary	53.5 $\pm$ 1.1	53.5 $\pm$ 0.6	0.998
Physical Functioning	47.9 $\pm$ 1.2	46.7 $\pm$ 0.7	0.399
Role Physical	48.6 $\pm$ 1.1	48.1 $\pm$ 0.6	0.698
Bodily Pain	51.0 $\pm$ 1.2	49.2 $\pm$ 0.7	0.207
General Health	47.9 $\pm$ 1.2	47.5 $\pm$ 0.7	0.737
Vitality	57.0 $\pm$ 1.3	56.1 $\pm$ 0.8	0.561
Social Functioning	51.9 $\pm$ 1.3	48.1 $\pm$ 0.7	0.014
Role Emotional	48.1 $\pm$ 1.3	49.0 $\pm$ 0.7	0.523
Mental Health	53.5 $\pm$ 1.2	54.0 $\pm$ 0.7	0.714

Abbreviation: SD, standard deviation; 95% CI, 95% confidence interval; SF-12v2, Short Form-12 version 2

*Adjusted with ANCOVA test

The *p*-value in bold are statistically significant

Table 4.14: SF-12v2 score between Good and Poor TTR Adjusted for Education

SF-12v2 Parameters	Patients TTR		<i>p</i> value
	Good (TTR $\geq$ 60%)	Poor (TTR<60%)	
Physical Component Summary	47.7 $\pm$ 1.1	46.7 $\pm$ 0.6	0.395
Mental Component Summary	53.6 $\pm$ 1.1	53.5 $\pm$ 0.6	0.951
Physical Functioning	47.4 $\pm$ 1.2	46.9 $\pm$ 0.7	0.704
Role Physical	48.2 $\pm$ 1.1	48.2 $\pm$ 0.6	0.968
Bodily Pain	50.5 $\pm$ 1.2	49.4 $\pm$ 0.7	0.446
General Health	48.1 $\pm$ 1.2	47.4 $\pm$ 0.7	0.639
Vitality	57.1 $\pm$ 1.3	56.0 $\pm$ 0.8	0.505
Social Functioning	51.0 $\pm$ 1.2	48.3 $\pm$ 0.7	0.069
Role Emotional	48.2 $\pm$ 1.2	49.0 $\pm$ 0.7	0.607
Mental Health	53.4 $\pm$ 1.2	54.0 $\pm$ 0.7	0.661

Abbreviation: SD, standard deviation; 95% CI, 95% confidence interval; SF-12v2, Short Form-12 version 2

*Adjusted with ANCOVA test

4.7 Chapter Summary

This study includes 300 patients, with a mean TTR score of $47.0 \pm 17.3\%$. The Physical Component Summary (PCS) and Mental Component Summary (MCS) scores for limitations (L), hassles and burdens (H&B), and positive physiological impacts (PPI) were 18.0 ± 10.0 , 15.6 ± 9.1 , and 21.6 ± 5.9 respectively. Good TTR ($\geq 60\%$) patients 24.3% (n=73) with a mean TTR of $70.2 \pm 8.7\%$, while 227 (75.7%) patients with poor TTR had a lower mean of $39.5\% \pm 11.9\%$. There was no significant difference between good and poor TTR patients in DASS score ($p=0.779$). Similarly, no significant differences were found in DASS subdimensions ($p=0.502-0.699$). Likewise, there was also no significant difference in the score of PCS ($p=0.150$), MCS ($p=0.919$), and each domain of SF-12v2 ($p=0.184-0.684$) between good and poor TTR, except for social functioning ($p=0.019$).

CHAPTER 5

DISCUSSION

5.1 Overview

This chapter thoroughly discusses treatment satisfaction and HRQoL of NVAF patients on long-term warfarin based on their TTR, incorporating findings from this study and comparing them with existing literature.

5.2 Discussion

This study reported a mean TTR of 47.0% which falls below the recommended target of at least 60% for effective warfarin management (Connolly et al., 2008). These findings suggest suboptimal anticoagulation control among respondents. The lower mean TTR observed in this study aligns with findings from Peninsular Malaysia (52%) and other Asian studies, such as those in Hong Kong (38.8%), Singapore (58%) where NVAF patients also exhibited low mean TTRs and smaller proportion of patients achieving good TTR control (Bernaitis et al., 2017; Chan et al., 2016; Hien et al., 2017). Comparatively, other studies indicated that patients from the Western region had better TTR than the Asian patient population. The mean TTR reported was 57.0-68.9%, from the International Study of Anticoagulant Management (INSAM), and 55.4% from the Global Anticoagulant Registry in the Field (GARFIELD) AF study which is higher compared to this study (Ansell et al., 2007; Haas et al., 2016). The proportion of patients with good TTR ($\geq 60\%$) was 47.7-75.1% in INSAM and 41.1% with TTR $\geq 65\%$ in GARFIELD. Despite this, the subgroup analysis showed that only 16.7% of the Asian cohort had good TTR control compared to the 49.4%

European cohort in the GARFIELD study, highlighting regional disparity in anticoagulation management (Haas et al., 2016). Further analysis comparing warfarin control between Australia and Singapore, and a higher proportion of good control ($TTR \geq 65\%$) at 86% vs. 46% (Bernaitis et al., 2017). These figures are substantially higher compared to the 24.3% of patients with good control ($TTR \geq 60\%$) in the current study. Similarly, a study in Korea reported that only 27% of NVAf patients achieved good TTR ($\geq 60\%$) whereas a Hong Kong study reported a lower mean TTR of 38.8% with only 14.8% achieving good TTR control ($\geq 65\%$) (Chan et al., 2016; Oh et al., 2018).

The mean TTR of good control patients ($TTR \geq 60\%$) in this study was reported at 70.2% vs. 39.5% among poor control TTR. A substantial proportion (75.7%) of NVAf patients in this study are at risk for thromboembolic events and bleeding complications. Compared to a study among US veterans where the good vs poor control TTR at 77% vs. 38% (Liu et al., 2018). The mean TTR of poor control in the present study was slightly higher than the retrospective study in the USA. However, the proportion of patients with good control TTR in this study was higher than in the present study, 65% vs 24.3%. Hence, the lower mean TTR and lower good TTR among patients in this present study were similar to those in other Asia studies. The rationales underlying the variation include that Asians may have different dietary habits and genetic profiles, such as polymorphisms of VKOR1 and CYP2C9 genes (Holbrook et al., 2005; Lam & Cheung, 2012; Mia Wadelius et al., 2007). The INSAM study and a meta-analysis by van Walraven et al. demonstrated that the most influential predictor of patients' TTR was the clinical setting of warfarin given (Ansell et al., 2007; van Walraven et al., 2006).

Despite the poor TTR observed in this study, treatment satisfaction among the respondents was generally good (55.2 ± 21.3). This study's treatment satisfaction findings were independent of patients' TTR. It was consistent with the findings from the previous study. In the Outcome Registry for Better Informed Treatment of AF (ORBIT-AF) study (A. C. Perino et al., 2019). Similarly, comparable results were observed among NVAf patients in Korea (Oh et al., 2018). In contrast, controlled TTR patients had higher general satisfaction versus uncontrolled TTR patients (TTR <65%) (Varona et al., 2020). Likewise, a study in Spain reported a post hoc analysis (ALADIN and ESPARTA) exhibited significantly higher scores with better satisfaction in good TTR ($\geq 50\%$) of NVAf patients ($p=0.024$) (Suárez Fernández et al., 2018). However, the cut-off point of good TTR which was $\geq 50\%$ differed from the commonly used in other literature (60-65%); therefore, we cannot directly compare it with the present study.

Regardless of the patient TTR receiving warfarin for NVAf in this present study, the SF-12v2 score in PCS and MCS were 47.0 ± 9.0 and 53.5 ± 9.6 , was notably lower in comparison to Malaysia's general population (SF-36, 66.7-86.0) (Azman et al., 2003). This observation implies a significant reduction, thus poorer in HRQoL of the present study. To date, no published data is available that compares the HRQoL of adult patients on warfarin for NVAf based on their TTR. Most existing studies either compare the HRQoL of patients on warfarin versus those on DOAC or in a longitudinal approach. In real-world situations, there were no significant differences documented in HRQoL of patients receiving warfarin versus DOAC (Alegret et al., 2014; Benzmira et al., 2018; Contreras Muruaga et al., 2017; D. L.-C. Ng et al., 2019a). The lack of literature comparing patient HRQoL based on TTR underscores this study's novelty and importance. In this present research, in regard to lower

TTR (47.0% vs. 54.9%) compared to the similar subgroup of patients reported in Peninsular Malaysia, this study, however, displayed a slightly higher value in subscales of HRQoL except SF (D. L.-C. Ng et al., 2019b). This study had approximately one-fourth (24.3%) of respondents with good TTR. A higher level of education is the independent predictor of better TTR. The rationale for better social functioning among patients with good TTR in this study could be their higher education level (Berkman et al., 2011; Cutler & Lleras-Muney, 2010; Ross & Mirowsky, 2010).

Notably, the study found no significant differences in treatment satisfaction and HRQoL across different TTR levels, except social functioning, which was better among patients with good TTR. This current study concludes that a significant proportion (75.7%) of NVAf patients attending SHC exhibited suboptimal anticoagulant control. Hence, there is a clear need for targeted interventions to improve anticoagulation control. This poor TTR control may be linked to the lower level of education (Berkman et al., 2011; Cutler & Lleras-Muney, 2010; Ross & Mirowsky, 2010). To address this, patients with poor TTR must receive consistent and tailored educational interventions from healthcare providers during their follow-up appointments. These interventions should be maintained regardless of the duration of warfarin therapy, as continuous education can reinforce understanding and better clinical outcomes (Bhattad & Pacifico, 2022). Patients should be reassured that achieving a higher TTR is important with improved clinical outcomes as fewer complications which may enhance overall well-being. Even if achieving good TTR does not compromise their treatment satisfaction and HRQoL.

To the best of our knowledge, this is the first study to compare the HRQoL of NVAf patients on long-term warfarin based on their TTR. We conducted a comprehensive analysis of each domain of DASS and each subscale of SF-12v2 to provide a more detailed comparison. Our analysis of treatment satisfaction and HRQoL accounted for treatment duration and education level as potential confounding factors to mitigate the impact of bias on the results.

5.3 Chapter Summary

Most NVAf patients on long-term warfarin therapy in this study had poor TTR, but TTR levels did not influence their treatment satisfaction and HRQoL. Situating these findings with a broader context of existing studies provides valuable insights into the complexities of patients on long-term warfarin.

CHAPTER 6

CONCLUSION AND RECOMMENDATIONS

6.1 Overview

This chapter concludes the overall summary of this study. This chapter started with recommendations for future researchers for this study to solidify its implications for future research. Subsequently, limitations of the study were also outlined, acknowledging areas that could be improved. Ultimately, this chapter summarised the significant contributions of this study to its respective fields.

6.2 Limitation

This present study had few limitations. Firstly, it was conducted at a single centre, thus limiting the generalisation of the results. Secondly, the design of study used was cross-sectional. Hence, it might not be able to completely capture the treatment satisfaction and HRQoL as it may vary over time. Thirdly, HAS-BLED score and severity of bleeding for patients was not assessed. Most patients were unable to recall their non-significant minor bleeding incidents accurately. Fourthly, patients on anti-platelet with vascular disease were excluded. Fifthly, the TTR was calculated solely using the Rosendaal technique, unlike the traditional method. The former method assumes the changes between consecutive INR measurements are linear over time, whereas the latter only consider the INR value at a time. Finally, reporting treatment complications depended on patients' memory, introducing the possibility of recall bias, although efforts were made to mitigate this by cross-referencing with available medical records.

6.3 Recommendations

Achieving a good TTR for patients on long-term warfarin necessitates a collaborative endeavor among healthcare professionals. Each healthcare team, including physicians, pharmacists, and nurses, contributes their specialised knowledge and skills to monitor and manage patients' therapy effectively, minimise complications, and optimise outcomes. Nurses should reinforce patients' education on warfarin by providing comprehensive information and educational materials that elucidate the significance of TTR and its impact on treatment effectiveness. Additionally, nurses should empower patients to take an active role in their care and establish support programs that encompass emotional and physiological assistance and a peer support network to share experiences and coping strategies. By prioritising patients' education, empowerment in self-care, and providing a robust support system, the TTR of patients on long-term warfarin can ultimately improve.

Conducting multicentre research in the future may also be applicable to have a larger sample size, broaden the scope of investigations, and the outcome is more likely to generalise the study population. However, conducting a multicentre research set its challenges. Treatment satisfaction, HRQoL, and TTR of patients receiving long-term warfarin may vary over time. Consequently, the value of a longitudinal study lies in its ability to comprehensively monitor these variables across extended durations and evaluate the impact of TTR fluctuation on these parameters.

6.4 Conclusion

The majority of the patients on long-term warfarin for NVAf in the current study exhibit poor TTR control. Their treatment satisfaction and HRQoL appear to be unaffected by their TTR levels. Achieving a good TTR do not compromise the treatment satisfaction and HRQoL. Consequently, it is necessary to implement measures aimed at optimizing INR control.

Enhancing patient education on anticoagulation, focusing on improving comprehension of different dosage forms, medication regimens, and potential side effects, can lead to increased treatment satisfaction. Additionally, empowering patients with the ability to self-manage warfarin may contribute to improvements in their HRQoL.

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APPENDICES

APPENDIX 1

PARTICIPANT INFORMATION SHEET AND INFORMED CONSENT FORM

(for adult subjects and interventional studies)

1. **Title of study:** Quality of life of patients on long term oral anticoagulants
2. **Name of investigator and institution:**

Dr Diana Ng Leh Ching, Universiti Malaysia Sarawak
Natasya Marliana Binti Abdul Malik, Universiti Malaysia Sarawak

3. **Name of sponsor:** Ministry of Higher Education (RAGS grant)

4. **Introduction:**

You are invited to participate in a research study because you are taking long term anticoagulant. The details of the research trial are described in this document. It is important that you understand why the research is being done and what it will involve. Please take your time to read through and consider this information carefully before you decide if you are willing to participate. Ask the study staff if anything is unclear or if you like more information. After you are properly satisfied that you understand this study, and that you wish to participate, you must sign this informed consent form. To participate in this study, you may be required to provide your doctor with information on your health history; you may harm yourself if you are not truthful with the information provided.

Your participation in this study is voluntary. You do not have to be in this study if you do not want to. You may also refuse to answer any questions you do not want to answer. If you volunteer to be in this study, you may withdraw from it at any time. If you withdraw, any data collected from you up to your withdrawal will still be used for the study. Your refusal to participate or withdrawal will not affect any medical or health benefits to which you are otherwise entitled.

This study has been approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia.

5. What is the purpose of the study?

The purpose of this study is to understand the impact of long term oral anticoagulant on quality of life. This research is necessary because the impact of the oral anticoagulant on our local community is not fully studied. It is also necessary to understand whether these impact on quality of life affects their compliance to treatment.

In Malaysia, there will be about 200 subjects. The whole study will last about eight months and your participation will take no longer than 20 minutes during the clinic visit. Participant will only be involved in the survey once throughout the study period.

6. What kind of study products/ procedure will I receive?

Not applicable. This study will not influence the management or treatment you are currently will be receiving. This study will not involve any additional blood test or procedure during the clinic visit.

7. What will happen if I decide to take part?

You will be given questionnaires to answer which will take approximately 15 minutes to complete. The completed questionnaire is to be returned on the day of clinic visit.

8. When will I receive the trial product and how should it be kept?

Not applicable.

9. What are my responsibilities when taking part in this study?

It is important that you answer all of the questions asked by the study staff honestly and completely.

10. What kind of treatment will I receive after my participation in the trial?

Not applicable.

11. What are the potential risks and side effects of being in this study?

There are no potential risks or side effects by participating in this study. All information will be confidential. The results of the study will not be revealed to you and is not relevant to the consent. However, the results may be used during publication without revealing any of the participant's identity.

12. What are the benefits of being in this study?

There may not be any benefits to you. Information obtained from this study will help improve the treatment or management of patients on similar treatments in future.

13. What if I am injured during this study?

Not applicable. There is no risk of injury related to this study.

14. What are my alternatives if I do not participate in this study?

Not applicable. This study will not influence the treatment or management of the attending doctors during the clinic visit.

15. Who is funding the research?

This study is sponsored by Ministry of Higher Education who will pay for all questionnaires materials.

16. Can the research or my participation be terminated early?

Yes. The study doctor may, stop the study or your participation at any time. If the study is stopped early for any reason you will be informed.

17. Will my medical information be kept private?

All your information obtained in this study will be kept and handled in a confidential manner, in accordance with applicable laws and/or regulations. When publishing or presenting the study results, your identity will not be revealed without your expressed consent. Individuals involved in this study and in your medical care, qualified monitors and auditors, the sponsor or

its affiliates and governmental or regulatory authorities may inspect and copy your medical records, where appropriate and necessary.

18. Who should I call if I have questions?

If you have any questions about the study or if you think you have a study related injury and you want information about treatment, please contact the study doctor, Dr Diana Ng Leh Ching at telephone number 082-581000.

If you have any questions about your rights as a participant in this study, please contact: The Secretary, Medical Research & Ethics Committee, Ministry of Health Malaysia, at telephone number 03-2287 4032.

INFORMED CONSENT FORM

Title of Study: Quality of life of patients on long term oral anticoagulants

By signing below I confirm the following:

- I have been given oral and written information for the above study and have read and understood the information given.
- I have had sufficient time to consider participation in the study and have had the opportunity to ask questions and all my questions have been answered satisfactorily.
- I understand that my participation is voluntary and I can at anytime free withdraw from the study without giving a reason and this will in no way affect my future treatment. I am not taking part in any other research study at this time. I understand the risks and benefits, and I freely give my informed consent to participate under the conditions stated. I understand that I must follow the study doctor's (investigator's) instructions related to my participation in the study.
- I understand that study staff, qualified monitors and auditors, the sponsor or its affiliates, and governmental or regulatory authorities, have direct access to my medical record in order to make sure that the study is conducted correctly and the data are recorded correctly. All personal details will be treated as STRICTLY CONFIDENTIAL
- I will receive a copy of this subject information/informed consent form signed and dated to bring home.

Subject:

Signature:

I/C number:

Name:

Date:

Investigator conducting informed consent:

Signature:

I/C number:

Name:

Date:

Impartial witness: *(Required if subject is illiterate and contents of participant information sheet is orally communicated to subject)*

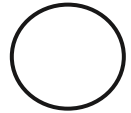
Signature:

I/C number:

Name:

Date:

Section 1



Please mark ☒ that best describe your answer below.

Sociodemographic Data

Date of survey:

1. Age:

2. Gender:

	0	Male
	1	Female

3. Marital status:

	0	Single
	1	Married
	2	Widowed
	3	Divorced/ separated

4. Ethnicity:

	0	Malay
	1	Chinese
	2	Indian
	3	Iban
	4	Bidayuh
	5	Others

5. Education level:

	0	None
	1	Primary
	2	Secondary
	3	College/ University

6. Occupation sector:

	0	None
	1	Government dependent / Pensioner
	2	Private

7. Family income group (Estimated):

	0	Unknown
	1	< RM 1000
	2	RM 1000-3000
	3	RM3000-5000
	4	> RM 5000

8. Estimated cost incurred during follow-up (transportation/ lodging/ meals):

	0	< RM 50
	1	RM 50-99
	2	RM 100-150
	3	> RM 150

9. Diet:

	0	Non-vegetarian/ vegan
	1	Vegetarian/ vegan

10. Regular alcohol intake:

	0	No
	1	Yes

11. Date of warfarin initiation: _____

12. Indication of anticoagulant:

	1	Atrial Fibrillation
	2	Others: _____

13. Previous hospitalisation due to complications of oral anticoagulant?

	0	No
	1	Yes

14. Presence of comorbidities:

	1	Hypertension
	2	Diabetes
	3	Heart failure/ IHD
	4	Stroke
	5	Cancer
	6	Renal impairment
	7	Others: _____ _____

Section 2

Functional Health and Well being

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

Excellent	Very Good	Good	Fair	Poor

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

	Yes, limited a lot	Yes, limited a little	No, not limited at all
Moderate activities (moving table, pushing a vacuum cleaner, bowling or golf			
Climbing several flights of stairs			

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

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Accomplished less than you would like					
Were limited in the kind of works or other activities					

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

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Accomplished less than you would like					
Did work or other activities less carefully than usual					

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

Not at all	A little bit	Moderately	Quite a bit	Extremely

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

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Have you felt calm and peaceful?					
Did you have a lot of energy?					
Have you felt downhearted and depressed?					

7. During the past 4 weeks, how much of the time has your physical health or emotional problems interfere with your social activities (like visiting with friends, relatives, etc)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time

Section 3

Satisfaction with Anticoagulant therapy

When you take warfarin you tend to bleed or bruise more easily. You may limit your activities as a result. Limit means you do less of the activity or no longer perform the activity at all.

1. How much does the possibility of bleeding or bruising limit you from taking part in physical activities (for example, housework, gardening, dancing, sports or anything else you usually do)?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

2. How much does the possibility of bleeding or bruising limit you from travelling?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

3. How much does the possibility of bleeding or bruising limit you from getting the medical care you need (for example visiting dentist, chiropractor or doctor of your choice)?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

4. How much does the possibility of bleeding or bruising limit your ability to work for salary?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

5. Overall, how much does the possibility of bleeding or bruising affect your daily life?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

Being on Warfarin treatment may mean changing some of your habit as well.

6. How much does warfarin limit your choice of food (diet)?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

7. How much does warfarin limit the alcoholic beverages you might wish to drink?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

8. How much does warfarin limit the over-the-counter medications (for examples aspirin, ibuprofen, vitamins) you might wish to take?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

9. Overall, how much does warfarin affect your daily life?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

Daily tasks include remembering to take your medicine at a certain time, taking the correct dose of your medicine not drinking much alcohol, following a moderate diet, avoiding bruising and bleeding and so forth.

Occasional tasks travelling to the clinic for blood check-ups, contacting the clinic in case of bleeding or other important events and so forth.

10. How much hassle (inconvenience) are the daily tasks of warfarin treatment?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

11. How much hassle (inconvenience) are the occasional tasks of warfarin treatment?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

Considering Warfarin treatment as a whole (both daily and occasional tasks) please answer the following

12. How complicated do you find your warfarin treatment to be?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

13. How time-consuming do you find your warfarin treatment to be?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

14. How frustrating do you find your warfarin treatment to be?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

15. How painful do you find your warfarin treatment to be?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

16. Overall, how much of a burden do you find your warfarin treatment to be?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

17. Overall, how confident are you about handling your warfarin treatment?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

These last questions ask what you know and feel about your Warfarin treatment

18. How well do you feel that you understand the medical reason for your warfarin treatment?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

19. How much do you feel reassured because of your warfarin treatment?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

20. How much do you worry about bleeding and bruising?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

21. Overall, how much has warfarin had a positive impact on your life?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

22. Overall, how much has warfarin had a negative impact on your life?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

23. Overall, how satisfied are you with warfarin treatment?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

24. Compared with other treatments you have had, how difficult is your warfarin treatment to manage?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

25. How likely would you be to recommend warfarin treatment to someone else with your disease or medical condition?

Not at all	A little	Somewhat	Moderately	Quite a bit	A lot	Very much

- THANK YOU -

APPENDIX 2

RISALAH MAKLUMAT PESERTA DAN BORANG PERSETUJUAN atau KEIZINAN PESERTA

(untuk subjek dewasa dan penyelidikan intervensi)

1. **Tajuk penyelidikan:** Kesan jangka masa panjang pengambilan ubat antikoagulasi terhadap kualiti hidup
2. **Nama Institusi and Nama Penyelidik**

Dr Diana Ng Leh Ching, Universiti Malaysia Sarawak
Natasya Marliana Binti Abdul Malik, Universiti Malaysia Sarawak

3. **Nama Penaja:** Kementerian Pendidikan Tinggi (Geran RAGS)
4. **Pengenalan:**

Anda telah dijemput untuk menyertai penyelidikan ini kerana anda mengambil ubat antikoagulasi untuk jangka masa panjang. Risalah ini menjelaskan hal-hal berkenaan penyelidikan tersebut dengan lebih mendalam dan terperinci. Amat penting anda memahami mengapa penyelidikan ini dilakukan dan apa yang dilakukan dalam penyelidikan ini. Sila ambil masa yang secukupnya untuk membaca dan mempertimbangkan dengan teliti penerangan yang diberi sebelum anda bersetuju untuk menyertai penyelidikan ini. Jika ada sebarang kemusykilan ataupun maklumat lanjut yang anda ingin tahu, anda boleh bertanya dengan mana-mana kakitangan yang terlibat dalam penyelidikan ini. Setelah anda berpuashati bahawa anda memahami penyelidikan ini, dan anda berminat untuk turut serta, anda dikehendaki untuk menandatangani Borang Persetujuan atau Keizinan Peserta, pada muka surat akhir risalah ini. Untuk menyertai penyelidikan ini, anda perlu memberi doktor anda maklumat sejarah kesihatan ataupun penyakit anda yang lalu/

Penyertaan anda dalam penyelidikan ini adalah secara sukarela. Anda tidak perlu menyertai penyelidikan ini jika anda tidak mahu. Anda juga mempunyai hak untuk tidak menjawab mana-mana soalan yang anda tidak mahu jawab. Anda juga boleh menarik diri daripada penyelidikan ini pada bila-bila masa sahaja. Jika anda menarik diri, segala maklumat yang telah diperolehi sebelum anda menarik diri tetap akan digunakan dalam penyelidikan ini. Jika anda tidak mahu

menyertai ataupun menarik diri dari penyelidikan ini, tindakan anda tidak akan menjejaskan segala hak dan keistimewaan perubatan kesihatan yang selayaknya anda terima.

Penyelidikan ini telah mendapat kelulusan Jawatankuasa Etika dan Penyelidikan Perubatan, Kementerian Kesihatan Malaysia.

5. Apakah tujuan penyelidikan ini dilakukan?

Tujuan penyelidikan ini dilakukan adalah memahami kesan jangka masa panjang antikoagulasi terhadap kualiti hidup. Penyelidikan ini juga diperlukan kerana untuk mengkaji sama ada impak terhadap kualiti hidup mempengaruhi pengambilan ubat tersebut.

Di Malaysia dianggarkan 200 peserta yang akan ambil bahagian . Penyelidikan ini akan berlangsung selama 8 bulan dan tempoh pembabitan anda dianggarkan mengambil masa selama 20 minit semasa hari lawatan klinik untuk sekali sahaja.

6. Apakah produk penyelidikan yang akan saya terima?

Tidak berkenaan. Penyelidikan ini tidak akan mempengaruhi cara rawatan / ubat-ubatan yang akan diberi semasa lawatan klinik.

7. Apakah yang terjadi sekiranya saya bersetuju untuk menyertai penyelidikan ini?

Anda akan diberi soal-selidik, yang mengambil masa kira-kira 15 minit untuk dilengkapkan. Soal-selidik yang telah siap dijawab hendaklah dikembalikan pada hari yang sama semasa lawatan klinik.

8. Bilakah saya akan menerima produk penyelidikan dan bagaimana cara menyimpannya?

Tidak berkenaan.

9. Apakah tanggungjawab saya sewaktu menyertai penyelidikan ini?

Amat penting anda menjawab kesemua soalan yang ditanyakan oleh kakitangan penyelidikan dengan jujur dan lengkap .

10. Apakah jenis rawatan yang akan saya terima selepas menyertai penyelidikan ini ?

Tidak berkenaan.

11. Apakah risiko dan kesan-kesan sampingan menyertai penyelidikan ini?

Tiada pontensi risiko atau kesan sampingan dengan menyertai penyelidikan ini. Semua maklumat yang diperolehi adalah sulit. Segala hasil analisa dan keputusan dalam kajian ini tidak akan dimaklumkan kepada anda dan tidak relevan dengan keizinan anda. Hasil keputusan ini mungkin akan digunakan untuk penerbitan tanpa mendedahkan identiti mana-mana pesakit.

12. Apakah manfaatnya saya menyertai kajian ini?

Penyelidikan ini mungkin akan mendatangkan manfaat ataupun langsung tiada memberi apa-apa manfaat kepada anda. Segala maklumat yang diperolehi daripada penyelidikan ini akan dapat membantu dalam penambahbaikan kaedah rawatan atau pengurusan pesakit yang menerima rawatan yang sama pada masa depan.

13. Apakah yang akan terjadi sekiranya saya tercedera semasa menyertai kajian ini?

Tidak berkenaan. Tiada risiko kecederaan fizikal/badan atau penyakit terhasil secara langsung semasa menyertai penyelidikan ini.

14. Apakah rawatan alternatif lain sekiranya saya tidak menyertai penyelidikan ini?

Tidak berkenaan. Penyelidikan ini tidak akan mempengaruhi cara rawatan penyakit anda.

15. Siapakah yang membiayai penyelidikan ini?

Kajian ini ditaja sepenuhnya oleh Kementerian Pendidikan Tinggi yang akan membayar semua produk penyelidikan.

16. Bolehkah penyelidikan ataupun penyertaan saya ditamatkan lebih awal daripada yang dirancang?

Ya. Doktor penyelidikan atau penaja boleh menamatkan penyelidikan ini ataupun menamatkan penyertaan anda dalam penyelidikan ini pada bila-bila masa.

17. Adakah maklumat perubatan saya akan dirahsiakan ?

Segala maklumat anda yang diperolehi dalam penyelidikan ini akan disimpan dan dikendalikan secara sulit, bersesuaian dengan peraturan-peraturan dan/ atau undang-undang yang berkenaan. Sekiranya hasil penyelidikan ini diterbitkan atau dibentangkan kepada orang ramai, identiti anda tidak akan didedahkan tanpa kebenaran anda terlebih dahulu. Pihak-pihak tertentu seperti individu yang terlibat dalam penyelidikan dan rawatan perubatan anda, juruaudit dan jurupantau yang terlatih, pihak penaja atau pihak gabungannya, pihak berkuasa kerajaan atau undang-undang, boleh memeriksa dan membuat salinan laporan perubatan anda jika berkenaan dan diperlukan.

18. Siakah yang perlu saya hubungi sekiranya saya mempunyai sebarang pertanyaan?

Anda boleh menghubungi doktor penyelidikan ini, Dr Diana Ng Leh Ching pada sambungan telefon, 082-581000 sekiranya anda mempunyai sebarang pertanyaan mengenai penyelidikan.

Jika anda mempunyai sebarang pertanyaan berkaitan dengan hak-hak anda sebagai peserta dalam penyelidikan ini, sila hubungi: Setiausaha, Jawatankuasa Etika & Penyelidikan Perubatan, Kementerian Kesihatan Malaysia, melalui talian telefon 03-2287 4032.

BORANG PERSETUJUAN/ KEIZINAN PESERTA

Tajuk Penyelidikan : Kesan jangka masa panjang pengambilan ubat antikoagulasi terhadap quality hidup

Dengan menandatangani di bawah, saya mengesahkan bahawa :

- Saya telah diberi maklumat tentang penyelidikan di atas secara lisan dan bertulis and saya telah membaca dan memahami segala maklumat yang diberikan dalam risalah ini.
- Saya telah diberikan masa yang secukupnya untuk mempertimbangkan penyertaan saya dalam penyelidikan ini dan telah diberi peluang untuk bertanyakan soalan dan semua persoalan saya telah dijawab dengan sempurna dan memuaskan.
- Saya juga faham bahawa penyertaan saya adalah secara sukarela dan pada bila-bila masa saya bebas menarik diri daripada penyelidikan ini tanpa harus memberi sebarang alasan dan ianya sama sekali tidak akan menjejaskan rawatan perubatan saya pada masa akan datang. Saya tidak mengambil bahagian dalam mana-mana penyelidikan lain pada masa ini. Saya juga memahami tentang risiko dan manfaat penyelidikan ini dan saya secara sukarela memberi persetujuan untuk menyertai penyelidikan ini di bawah syarat-syarat yang telah dinyatakan di atas.
- Saya faham bahawa kakitangan penyelidikan, pemantau dan juruaudit terlatih , pihak penaja atau gabungannya, dan pihak berkuasa kerajaan atau undang-undang, mempunyai akses langsung dan boleh menyemak laporan perubatan saya bagi memastikan penyelidikan ini dijalankan dengan betul dan data direkodkan dengan betul. Segala maklumat dan data peribadi akan dianggap sebagai SULIT.
- Saya akan menerima satu salinan 'Risalah Maklumat Peserta dan Borang Persetujuan atau Keizinan Peserta' yang telah lengkap dengan tarikh dan tandatangan untuk dibawa pulang ke rumah.

Subjek :

Tandatangan:

Nombor K/P:

Nama:

Tarikh :

Penyelidik yang mengendalikan proses menandatangani borang keizinan:

Tandatangan:

Nombor
K/P:

Nama:

Tarikh :

Saksi tidak-berpihak/adil: *(Diperlukan; jika subjek adalah buta huruf dan kandungan risalah maklumat peserta disampaikan secara lisan kepada subjek)*

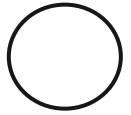
Tandatangan:

Nombor
K/P:

Nama:

Tarikh :

Bahagian 1



Sila tandakan ☒ pada jawapan anda di bawah

Data Sosio-Demografi

Tarikh Survey:

1. Umur:

2. Jantina:

0	Lelaki
1	Perempuan

3. Taraf Perkahwinan:

0	Bujang
1	Berkahwin
2	Balu
3	Berpisah

4. Etnik:

0	Melayu
1	Cina
2	India
3	Iban
4	Bidayuh
5	Lain-lain

5. Taraf Pendidikan:

0	Tiada
1	Sekolah Rendah
2	Sekolah Menengah
3	Kolej/Universiti

6. Sektor pekerjaan:

0	Tidak bekerja
1	Kakitangan Kerajaan / Bersara
2	Swasta

7. Pendapatan isirumah (Anggaran):

0	Tiada pendapatan
1	< RM 1000
2	RM 1000-3000
3	RM3000-5000
4	> RM 5000

8. Anggaran kos rawatan susulan (pengangkutan/tempat tinggal/makan):

	0	< RM 50
	1	RM 50-99
	2	RM 100-150
	3	> RM 150

9. Diet:

	0	Bukan Vegetarian
	1	Vegetarian

10. Kerap mengambil minuman beralkohol:

	0	Tidak
	1	Ya

11. Tarikh mula mengambil warfarin: _____

12. Indikasi mengambil warfarin:

	1	Atrial Fibrillation
	2	Lain-lain _____

13. Sejarah dimasukkan ke wad akibat komplikasi pengambilan warfarin?

	0	Tidak
	1	Ada

14. Masalah Kesihatan lain:

	1	Darah Tinggi (Hypertension)
	2	Kencing Manis (Diabetes)
	3	Lemah Jantung (Heart failure/ IHD)
	4	Lumpuh (Stroke)
	5	Kanser
	6	Masalah Buah Pinggang
	7	Lain-lain _____ _____

Bahagian 2

Kesihatan Am

1. Secara umum, adakah anda akan mengatakan bahawa kesihatan anda adalah:

Paling Baik	Sungguh Baik	Baik	Sederhana	Tidak Baik

2. Soalan-soalan berikut adalah mengenai aktiviti yang mungkin akan anda lakukan pada hari biasa. Adakah anda terbatas dalam sebarang aktiviti berikut kerana keadaan kesihatan anda sekarang? Jika ya sejauh mana?

	Ya, terbatas dengan banyaknya	Ya, terbatas dengan sedikitnya	Tidak, tidak terbatas sama sekali
Aktiviti sederhana seperti mengalih meja, menyapu, bermain badminton atau bercucuk tanam			
Menaiki beberapa larian tangga			

3. Dalam masa 4 minggu yang lalu, berapa kerapkan anda mengalami sebarang masalah berikut apabila anda bekerja atau melakukan aktiviti harian tetap anda yang lain akibat kesihatan fizikal anda?

	Setiap masa	Kebanyakan masa	Kadangkala	Sedikit masa	Tidak sama sekali
Mencapai kurang daripada yang anda ingini					
Terbatas dari segi jenis pekerjaan atau aktiviti lain					

4. Dalam masa 4 minggu yang lalu, berapa kerapkah anda mengalami sebarang masalah berikut apabila anda bekerja atau melakukan aktiviti harian tetap anda yang lain akibat sebarang masalah emosi (seperti berasa murung atau bimbang)?

	Setiap masa	Kebanyakan masa	Kadangkala	Sedikit masa	Tidak sama sekali
Mencapai kurang daripada yang anda ingini					
Bekerja atau melakukan aktiviti lain dengan kurang berhati-hati daripada biasa					

5. Dalam masa 4 minggu yang lalu, sejauh manakan kesakitan telah mengganggu pekerjaan biasa anda (termasuk pekerjaan di luar rumah dan kerja rumah)?

Tidak sama sekali	Sedikit	Sederhana	Agak banyak	Amat sangat

6. Soalan-soalan ini adalah mengenai perasaan dan keadaan anda dalam masa 4 minggu yang lalu. Untuk setiap soalan, sila berikan satu jawapan yang paling hampir dengan keadaan perasaan anda. Dalam masa 4 minggu yang lalu, berapa kerapkah?

	Setiap masa	Kebanyakan masa	Kadangkala	Sedikit masa	Tidak sama sekali
Pernah anda berasa tenang dan aman?					
Adakah anda sungguh bertenaga?					
Pernahkan anda berasa sedih dan murung?					

7. Dalam masa 4 minggu yang lalu, berapa kerapkah kesihatan fizikal atau masalah emosi telah mengganggu aktiviti sosial anda (seperti melawat sahabat handai, sanak saudara, dll)?

Setiap masa	Kebanyakan masa	Kadangkala	Sedikit masa	Tidak sama sekali

Bahagian 3

Tahap kepuasan rawatan Anti-Koagulasi

Penggunaan warfarin boleh menyebabkan risiko untuk berdarah dan lebam. Anda mungkin akan mengurangkan aktiviti-aktiviti untuk mengelakkannya. Kurang bermaksud melakukan kurang daripada sebelum ataupun tidak melakukan aktiviti langsung.

1. Berapa banyak kemungkinan untuk berdarah dan lebam mengurangkan aktiviti-aktiviti fizikal (contoh kerja rumah, bercucuk tanam, menari, bersukan atau aktiviti lain yang kebiasaan dilakukan)?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

2. Berapa banyak kemungkinan untuk berdarah dan lebam mengurangkan anda untuk bercuti?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

3. Berapa banyak kemungkinan untuk berdarah dan lebam mengurangi anda mendapatkan penjagaan kesihatan yang anda perlukan (contoh doktor gigi, ‘chiropractor’ atau doktor pilihan anda?)

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

4. Berapa banyak kemungkinan untuk berdarah dan lebam mengurangi keupayaan berkerja untuk mendapatkan gaji?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

5. Secara keseluruhan, berapa banyak kemungkinan untuk berdarah dan lebam memberi kesan terhadap kehidupan harian anda?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

Pengambilan warfarin menyebabkan perubahan kepada kebiasaan anda

6. Berapa banyak kemungkinan Warfarin mengurangi pilihan makanan anda?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

7. Berapa banyak kemungkinan Warfarin mengurangi pengambilan alkohol yang mungkin anda inginkan?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

8. Berapa banyak kemungkinan Warfarin mengurangi pengambilan ubat ‘over-the-counter’ (Contoh aspirin, ibuprofen, vitamin) yang mungkin anda inginkan?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

9. Secara keseluruhan, berapa banyak kemungkinan Warfarin memberikan kesan terhadap kehidupan harian anda?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

Tugas harian untuk rawatan Warfarin adalah mengingat waktu tertentu untuk mengambil ubat, dos yang betul, menyurangkan pengambilan alkohol, mengamalkan diet sederhana mengelakkan lebam dan berdarah dan sebagainya.

Tugas kadang kala mendapatkan pemeriksaan darah, mendapatkan rawatan sekiranya berdarah atau lain-lain

10. Berapa banyak kerumitan untuk tugas harian dalam rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

11. Berapa banyak kerumitan tugas kadang kala dalam rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

Secara keseluruhannya, rawatan Warfarin (termasuk tugas harian dan tugas kadang kala) sila jawab soalan di bawah

12. Berapa rumitkah rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

13. Berapa banyak rawatan Warfarin memakan masa?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

14. Berapa kecewakah anda dengan rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

15. Berapa sakit anda dengan rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

16. Secara keseluruhan berapa banyak beban anda dengan rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

17. Secara keseluruhan berapakah keyakinan anda dengan rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

Soalan bertanya tentang perasaan anda terhadap rawatan Warfarin

18. Berapa banyak anda memahami sebab perubatan untuk rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

19. Berapa banyak keyakinan anda untuk rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

20. Berapa banyak anda risau tentang berdarah dan lebam?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

21. Secara keseluruhan berapa banyak Warfarin memberi kesan positif dalam hidup anda?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

22. Secara keseluruhan berapa banyak Warfarin memberi kesan negatif dalam hidup anda?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

23. Secara keseluruhan berapa kepuasan anda terhadap rawatan Warfarin?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

24. Jika dibandingkan dengan rawatan lain yang anda terima, berapa rumitkan rawatan Warfarin untuk diurus?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

25. Berapakah kemungkinan untuk anda mengesyorkan rawatan Warfarin kepada orang lain yang menghidap penyakit yang sama seperti anda?

Tidak sama sekali	Sedikit masa	Agak sedikit	Sederhana	Agak banyak	Kebanyakan masa	Setiap masa

-TERIMA KASIH-

APPENDIX 3

Ethical Approval by Medical Research & Ethics Committee



JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN
(*Medical Research & Ethics Committee*)
KEMENTERIAN KESIHATAN MALAYSIA
d/a Institut Pengurusan Kesihatan
Jalan Rumah Sakit, Bangsar
59000 Kuala Lumpur



Tel: 03-2287 4032/2282 0491/2282 9085
03-2282 9082/2282 1402/2282 1449
Faks: 03-2282 0015

Ruj.Kami:KKM/NIHSEC/ P17-1109 (7)
Tarikh: 26-June-2018

DR CHAI CHEE SHEE
UNIVERSITY MALAYSIA SARAWAK (UNIMAS)

DR DIANA NG LEH CHING
UNIVERSITY MALAYSIA SARAWAK (UNIMAS)

DR KUAN JEW WIN
UNIVERSITY MALAYSIA SARAWAK (UNIMAS)

Dato'/ Tuan/ Puan,

Annual Ethical Renewal for 2018

NMRR-17-1086-34402 (IIR)
Protocol No : NMRR-17-1086-34402
Quality of life of patients on long term oral anticoagulants

With reference to the 'Continuing Review Form' submitted 17-June-2018, we are pleased to inform that the conduct of the above study has been granted approval (via Expedited Review by Chairperson) for a year by the Medical Research & Ethics Committee, Ministry of Health Malaysia. Please note that the approval is valid until 25-June-2019. To renew the approval, a completed 'Continuing Review Form' has to be submitted to MREC **within 1 month** before the expiry of the approval.

The MREC, Ministry of Health Malaysia operates in accordance to the International Harmonization Good Clinical Practice Guidelines.

Thank you

"BERKHIDMAT UNTUK NEGARA"

Saya yang menurut perintah,

(DR H.H. SALINA ABDUL AZIZ)
Chairman
Medical Research & Ethics Committee
Ministry of Health Malaysia

HM/Annualrenewal2018/Mrecshare

APPENDIX 4

Application Letter to Director Sarawak Heart Centre, Kota Samarahan Sarawak

Fakulti Perubatan dan Sains Kesihatan
Faculty of Medicine and Health Sciences



UNIMAS/NC-21.06/01-02 (49)

13 Ogos 2018

Dr Mohd Asri Bin Ripin
Pengarah
Pusat Jantung Sarawak
3rd Roundabout
Kuching-Samarahan Expressway
94300 Kota Samarahan

Ybhg Dato'/Tuan/Puan,

PERMOHONAN LANJUTAN KEBENARAN UNTUK MENJALANKAN PENYELIDIKAN DI PUSAT JANTUNG SARAWAK

Dengan hormatnya saya merujuk kepada perkara tersebut di atas

Saya memohon untuk melanjutkan penyelidikan bertajuk 'Quality of life of patients on long term anticoagulants' (NMRR-17-1086-34402(IIR)) sehingga 25 June 2019.

2. Permohonan lanjutan penyelidikan kepada Jawatankuasa Etika Penyelidikan Perubatan JEPP (Medical Research Ethics Committee MREC) telah diluluskan.

3. Bersama ini saya dilampirkan kelulusan oleh MREC untuk rujukan pihak tuan. Kerjasama pihak tuan saya dahului dengan ribuan terima kasih.

Sekian, terima kasih.

Saya yang menurut perintah,

Dr Diana Ng Leh Ching
Ketua Penyelidikan

- ok, tiada halangan untuk
penerbitan
- KES / Medical Research
Ethics Committee
DR MOHD ASRI BIN RIPIN
MD (USMC)
MMC No: 30306
Pengarah Pusat Jantung
Hospital Umum Sarawak

- s.k - Clinicians-in charge, INR Clinic/Cardiology Clinic, Sarawak Heart Centre
- Nursing Sister-in-charge, INR Clinic/Cardiology Clinic, Sarawak Heart Centre
- Matron-in-charge, Emergency Unit & Specialist Out-Patient Clinic, Sarawak Heart Centre



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94300 Kota Samarahan, Sarawak, MALAYSIA
● + 60 82 581 000
● + 60 82 665 152
● www.unimas.my

APPENDIX 5

Permission to use Duke Anticoagulation Satisfaction Scale form Author.

From: Greg Samsa, Ph.D. <greg.samsa@duke.edu>
Sent: 15 February 2018 07:54:16
To: Natasya Marlina binti Abdul Malik
Subject: RE: Permission to use DASS

You are welcome to use the instrument. There is no fee.

Greg Samsa, PhD
Director, Research Integrity Office
Associate Professor, Department of Biostatistics & Bioinformatics
Duke University Medical Center
[11084 Hock Plaza](#)
[Durham NC 27705](#)
[919 613-5212](#)
Greg.Samsa@duke.edu

From: Natasya Marlina binti Abdul Malik [<mailto:amnmarlina@unimas.my>]
Sent: Monday, February 12, 2018 10:58 PM
To: Greg Samsa, Ph.D. <greg.samsa@duke.edu>
Subject: Permission to use DASS

Greetings AP Gregory P. Samsa

I am Natasya Marlina Binti Abdul Malik, MSc (Nursing) student of Universiti Malaysia Sarawak, Malaysia would like to seek permission to use DUKE for my research titled "Quality of Life Patient with Oral Anticoagulants".

Thank You for your consideration

Regards,
Natasya

APPENDIX 6

Permission to use Duke Anticoagulation Satisfaction Scale Malay Version

Permission to use DUKE Malay Translated version

1

L

Laila M. Ali Matalgah <laila.m@yu.edu.jo>
To: Natasya Marlina binti Abdul Malik

Fri 17/08/2018 15:25

Salam alaikm
I don't mind to use it however you have to site the reference of my paper in your future publication.
Good luck in your research
Regards

...

Dr. Laila Matalgah
Assistant Professor of pharmacology and Therapeutics
Department of Basic Medical Sciences
Faculty of Medicine
Yarmouk University

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Natasya Marlina binti Abdul Malik

To: laila.m@yu.edu.jo

Fri 17/08/2018 09:11

Greetings,

I am Natasya Malik, MSc (Nursing) students of Universiti Malaysia Sarawak Malaysia would like to seek permission to use DUKE Malay Translated version for my study titled "Quality of life of patients with oral anticoagulant"

Thanks you for you consideration

Regards,
Natasya

APPENDIX 7

Published Article

Ng et al. *Health Qual Life Outcomes* (2020) 18:347
<https://doi.org/10.1186/s12955-020-01600-z>

Health and Quality
of Life Outcomes

RESEARCH

Open Access



Time in therapeutic range, quality of life and treatment satisfaction of patients on long-term warfarin for non-valvular atrial fibrillation: a cross-sectional study

Diana-Leh-Ching Ng¹, Natasya Marliana Bt Abdul Malik², Chee-Shee Chai¹, Greta-Miranda-Kim-Choo Goh², Seng-Beng Tan³, Ping-Chong Bee³, Gin-Gin Gan³ and Asri B. Said^{1*} 

Abstract

Background: The use of warfarin in patients with non-valvular atrial fibrillation (NVAF) can be challenging. In this study, we evaluate the time in therapeutic range (TTR), health-related quality of life (HRQoL) and treatment satisfaction of patients on long-term warfarin for NVAF. The HRQoL and treatment satisfaction were compared based on the TTR.

Methods: A cross-sectional study was conducted among patients on warfarin for NVAF who attended the anticoagulant clinic of a tertiary cardiology referral center in Sarawak from 1st June 2018 to 31st May 2019. Patients' TTR was calculated by using Rosendaal technique, while their HRQoL and treatment satisfaction were assessed by using Short Form 12 Health Survey version 2 (SF12v2) and Duke Anticoagulant Satisfaction Scale (DASS), respectively.

Results: A total of 300 patients were included, with mean TTR score of $47.0 \pm 17.3\%$. The physical component summary (PCS) and mental component summary (MCS) score of SF-12v2 were 47.0 ± 9.0 and 53.5 ± 9.6 , respectively. The total score for DASS was 55.2 ± 21.3 , while the score for limitations (L), hassles and burdens (H&B) and positive psychological impacts (PPI) were 18.0 ± 10.0 , 15.6 ± 9.1 and 21.6 ± 5.9 , respectively. Seventy-three (24.3%) patients had good TTR ($\geq 60\%$), with mean of $70.2 \pm 8.7\%$; while 227 (75.5%) patients with poor TTR had significantly lower mean of $39.5 \pm 11.9\%$ ($p = 0.006$). There was no significant difference in the score of PCS ($p = 0.150$), MCS ($p = 0.919$) and each domain of SF-12v2 ($p = 0.184$ – 0.684) between good and poor TTR, except for social functioning ($p = 0.019$). The total DASS score was also not significantly different between group ($p = 0.779$). Similar non-significant difference was also reported in all the DASS sub dimensions ($p = 0.502$ – 0.699).

Conclusions: Majority of the patients on long-term warfarin for NVAF in the current study have poor TTR. Their HRQoL and treatment satisfaction are independent of their TTR. Achieving a good TTR do not compromise the HRQoL and treatment satisfaction. Therefore, appropriate measures should be taken to optimise INR control, failing which direct oral anticoagulant therapy should be considered.

Keywords: Warfarin, Time in therapeutic range, Quality of life, Treatment satisfaction, Direct oral anticoagulant

Background

Atrial fibrillation (AF) is the commonest arrhythmia and represents substantial health care burden globally [1]. In 2010, the estimated prevalence of AF was 592 per 100,000

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Full list of author information is available at the end of the article



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