PROBABILITY OF CARDIOVASCULAR DISEASE (CVD) EVENTS AMONG FAMILY MEMBERS OF STROKE SURVIVORS IN KELANTAN

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UNIVERSITI SAINS MALAYSIA

2025

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by

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The thesis submitted in fulfilment of the requirements

for the Degree of

Doctor of Public Health (Epidemiology)

2025

ACKNOWLEDGEMENT

Alhamdulillah, I have concluded this dissertation with gratitude to Allah for His assistance and achievement. I want to express my profound thanks and appreciation to the persons who have significantly contributed to and supported me in various capacities during the execution of this study.

This hard work would be unfeasible without the support and encouragement of my supervisor, Prof. Dr. Kamarul Imran Musa, Department of Community Medicine, School of Medical Sciences, Universiti Sains Malaysia, and my co-supervisor, Dr. Wan Nor Arifin Bin Wan Mansor, Department of Biostatistics and Research Methodology Unit, School of Medical Sciences, Universiti Sains Malaysia. Commendations to them for facilitating this study effort, their skill, benevolence, and, above all, their patience.

I would like to express my gratitude to all my esteemed colleagues and lecturers at the Department of Community Medicine who indirectly contributed to this research effort

This effort would undoubtedly be futile without the support of my cherished parents, wife, and family. I extend my utmost thanks to all of them.

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DECLARATION

I, Mohd Izrul Isham Bin Rosidi, declare that the work presented in this thesis is originally mine. The information derived from other sources is clearly indicated in the thesis.

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LIST OF PAPERS AND CONFERENCES

During the Doctor of Public Health (DrPH) program, the following articles were finally drafted for submission to the selected Journal and/or presentation at the international level. The thesis comprises the three drafted papers corresponding to the three study objectives.

Final draft papers for submission:

Bibliometric Analysis of Global Research Trends on Cardiovascular disease Risk Among Family Members of Stroke Patients

Mohd Izrul Isham Rosidi[1], *Kamarul Imran Musa[1], WN Arifin[2]

Distribution Of Cardiovascular disease (CVD) Risk Among Family Members of Stroke Survivors in Kelantan; A Descriptive Analysis

Mohd Izrul Isham Rosidi[1], *Kamarul Imran Musa[1], WN Arifin[2]

The Relationship Between CVD Risk Factors And CVD Risk Scores Among Family Members Of Stroke Survivors In Kelantan

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Conferences presentation:

1. 4th International Conference on Dental, Medical and Health Sciences (ICDMHS), 24-26 September 2024

- Factors Associated with CVD Risk Score Among Family Members of Stroke Survivors in Kelantan; an Ordinal Logistic Regression **(oral presenter)**

2. Johor Public Health Symposium 2024, 9 October 2024

- Bibliometric Analysis of Global Research Trends on Cardiovascular disease Risk Among Family Members of Stroke Patients **(poster presenter)**

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LIST OF ABBREVIATIONS

AIC	Akaike information criterion
BMI	Body Mass Index
CDC	Center for Disease Control
CI	Confidence interval
CPG	Clinical Practice Guideline
CVD	Cardiovascular disease
FRS	Framingham Risk Score
IQR	Interquartile range
LR	Likelihood ratio
NCD	Non-communicable disease
POM	Proportional Odds Model
PPOM	Partial Proportional Odds Model
SBP	Systolic blood pressure
SD	Standard deviation
SE	Standard error
STEPS	WHO STEPwise approach to NCD risk factor surveillance
var	variable
VIF	Variance inflation factor
WHO	World Health Organization

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ABSTRAK

KEBARANGKALIAN KEJADIAN PENYAKIT KARDIOVASKULAR (CVD)

DALAM KALANGAN AHLI KELUARGA MANGSA STROK DI KELANTAN

Pengenalan: Penyakit kardiovaskular (*CVD*) termasuk strok, masih menjadi bebanan di peringkat global. Kajian menunjukkan bahawa sejarah keluarga yang positif akan meningkatkan lagi risiko untuk menghidap *CVD*. Kalkulator risiko *CVD* seperti kalkulator *Framingham Risk Score (FRS)* dapat membantu untuk mengukur risiko ini, sekaligus menyerlahkan kesan faktor risiko seperti *BMI*, kolesterol *LDL* dan tekanan darah. Pada masa yang sama, pendekatan *family-centered* kian mendapat perhatian, terutamanya dalam pencegahan strok dalam kalangan ahli keluarga. Walaupun begitu, masih terdapat kekurangan kajian berkaitan bidang tersebut di Kelantan dan Malaysia.

Objektif: Kajian ini bertujuan untuk mengenalpasti trend penerbitan, dan tema-tema yang berkaitan dengan risiko *CVD* dalam kalangan ahli keluarga mangsa strok di peringkat global. Selain itu, ia bertujuan untuk menilai taburan risiko *CVD* menggunakan *FRS* dan menganalisis hubung kait antara risiko *CVD* daripada *WHO STEPS questionnaires* dan skor risiko *CVD* dalam populasi tempatan di Kelantan.

Materials dan Metodologi: Kajian ini merupakan kajian keratan rentas melibatkan 307 ahli keluarga mangsa strok di Kelantan, dan dijalankan selama setahun (Jun 2023 - Jun 2024). Penyelidikan bermula dengan analisis bibliometrik terhadap penerbitan sedia ada mengenai risiko *CVD* dalam kalangan populasi yang terlibat. *FRS* dikira berdasarkan umur, jantina, status diabetes, rawatan tekanan darah tinggi, status merokok, dan indeks jisim badan (*BMI*). *Ordinal logistic regression* telah digunakan untuk menilai hubung kait

antara faktor risiko *CVD* dalam *WHO STEPS questionnaires* dan skor risiko *CVD*, diikuti dengan ujian *proportional odds assumptions.*

Dapatan kajian: Analisa bibliometrik mendedahkan peningkatan yang konsisten dalam penerbitan mengenai risiko *CVD* dalam kalangan ahli keluarga pesakit strok sejak 1978, dengan kadar pertumbuhan tahunan sebanyak 7.67%. Amerika Syarikat dikenal pasti sebagai penyumbang utama, dengan jurnal "Stroke" menjadi yang paling dominan. Kajian dalam kalangan peserta di Kelantan mendapati bahawa umur median ialah 47 tahun, dengan 60.0% merupakan pasangan kepada pesakit strok. Taburan risiko CVD menunjukkan 57.1% diklasifikasikan sebagai berisiko rendah, 25.7% sebagai risiko sederhana, dan 17.2% sebagai berisiko tinggi. Analisa *Ordinal logistic regression* merumuskan bahawa faktor 'pasangan' dan jantina 'lelaki' adalah masing-masing mempunyai 4.04 dan 4.32 kali nisbah kebarangkalian yang lebih tinggi untuk berada dalam kategori risiko *CVD* yang lebih tinggi.

Kesimpulan: Dapatan kajian ini membuktikan minat kajian yang semakin meningkat berkaitan risiko *CVD* dalam kalangan ahli keluarga pesakit strok, dengan menekankan kepentingan faktor risiko keluarga dalam membangunkan strategi pencegahan yang disasarkan. Kajian ini juga menggariskan pengaruh pelbagai faktor terhadap *FRS*. Memahami hubungan ini adalah penting untuk mencegah dan mengurus kesihatan kardiovaskular dengan berkesan.

Kata Kunci: Penyakit kardiovaskular (CVD), sejarah keluarga, kalkulator *Framingham Risk Score (FRS)*, bibliometrik, *ordinal logistic regression*

ABSTRACT

PROBABILITY OF CARDIOVASCULAR DISEASE (CVD) EVENTS AMONG FAMILY MEMBERS OF STROKE SURVIVORS IN KELANTAN

Introduction: Cardiovascular disease (CVD), including stroke, is still becoming a global burden across the population, and a positive family history does significantly increase the risk. CVD risk calculators such as Framingham Risk Score (FRS) help quantify these risks, highlighting the impact of factors like BMI, LDL cholesterol, and blood pressure. Concurrently, family-centered approaches to cardiovascular health are gaining attention, particularly in stroke prevention among family members. Despite that, there is still a lack of studies related to the field in Kelantan and Malaysia.

Objectives: This study aimed to explore publication trends, and themes related to CVD risk among family members of stroke survivors. Additionally, it sought to assess the distribution of the CVD risk using the Framingham Risk Score and to analyse the relationship between CVD risk factors from WHO STEPS questionnaires and CVD risk scores in local population in Kelantan.

Materials and Methods: A cross-sectional study involved 307 family members of stroke survivors in Kelantan over one year (June 2023 - June 2024). The research began with a bibliometric analysis of existing literature on CVD risk among the population. The Framingham CVD Risk Score was calculated based on age, gender, diabetes status, hypertension treatment, smoking status, and body mass index (BMI). An ordinal logistic regression was employed to evaluate the relationship between CVD risk factors from

WHO STEPS questionnaire and CVD risk scores, followed by assessment for proportional odds assumptions.

Results: The bibliometric analysis revealed a consistent increase in publications on CVD risk among family members of stroke patients since 1978, with an annual growth rate of 7.67%. The USA was identified as the leading contributor, with the journal "Stroke" being the most prolific. Study among the participants in Kelantan reported the median age of 47 years, with 60.0% being spouses to the stroke patients. The CVD risk distribution showed 57.1% classified as low risk, 25.7% as moderate risk, and 17.2% as high risk. Ordinal logistic regression showed that spouse and male gender were associated with 4.04 and 4.32 higher odds to be in higher CVD risk categories respectively.

Conclusion: The findings highlighted the growing scholarly interest in CVD risk among family members of stroke patients, emphasizing the importance of familial risk factors in developing targeted prevention strategies. The local study in Kelantan underscored the influence of various factors on the Framingham CVD Risk Score. Understanding these relationships was crucial for effectively preventing and managing cardiovascular health.

Keywords: Cardiovascular disease (CVD), family history, Framingham, bibliometric, ordinal regression

CHAPTER ONE: INTRODUCTION

1.1 Background on cardiovascular disease (CVD)

CVDs encompass a range of disorders affecting the heart and blood vessels, including coronary artery disease, hypertension, heart failure, and stroke. These conditions were among the leading causes of morbidity and mortality globally, accounting for approximately 31% of all deaths in 2015, which translated to an estimated 17.7 million fatalities (Muneshwar *et al*., 2017). The burden of CVD is not uniformly distributed; it varies significantly between developed and developing countries, influenced by a complex interplay of risk factors, healthcare access, and lifestyle choices.

The global prevalence of CVD has been steadily increasing, driven by urbanization, ageing populations, and lifestyle changes. Major modifiable risk factors include unhealthy diets, physical inactivity, tobacco use, and excessive alcohol consumption (The GBD 2015 Obesity Collaborators, 2017). For instance, a high intake of saturated fats and cholesterol can lead to the development of atherosclerotic plaques, which significantly increases the risk of heart attacks and strokes (Cunha *et al*., 2020). Furthermore, the rise in obesity rates worldwide has been linked to an increase in cardiovascular risk, with studies indicating that nearly half of the excess risk for ischemic heart disease and more than 75% of the excess risk for stroke can be attributed to high body mass index (BMI) (The GBD 2015 Obesity Collaborators, 2017).

In addition to lifestyle factors, socioeconomic determinants play a crucial role in the prevalence of CVD. Populations in low- and middle-income countries often face higher rates of CVD due to limited access to healthcare, inadequate health education, and a lack of preventive measures (Muneshwar *et al*., 2017). The World Health Organization

(WHO) has recognized the urgent need for comprehensive strategies to address these disparities, advocating for policies that promote healthy lifestyles and improve healthcare access.

In Malaysia, CVD represents a significant public health challenge following global trends. The country has witnessed a rising prevalence of CVD, driven by similar risk factors such as unhealthy diets, sedentary lifestyles, and increasing rates of obesity and diabetes (Erwin *et al*., 2023). According to the National Health and Morbidity Survey (NHMS), CVD was the leading cause of death in Malaysia, accounting for approximately 34% of total deaths in 2019 (NHMS, 2019). The increasing burden of CVD is particularly concerning given Malaysia's rapidly ageing population and the associated rise in non-communicable diseases.

The Malaysian healthcare system faces challenges managing CVD, including improving public awareness and education regarding risk factors and preventive measures. Studies have shown that many Malaysians remain unaware of their cardiovascular risk profiles, which can lead to late diagnoses and poor health outcomes (Agbana *et al*., 2016). Furthermore, the prevalence of hypertension and diabetes among Malaysian adults has reached alarming levels, with estimates suggesting that nearly one in three adults is hypertensive and one in five has diabetes (Erwin *et al*., 2023).

Efforts to combat CVD in Malaysia have included government initiatives promoting healthier lifestyles, such as the National Strategic Plan for Non-Communicable Diseases (NSP-NCD) (Muneshwar *et al*., 2017). This plan emphasizes the importance of early detection, risk factor modification, and promoting physical activity and healthy eating. However, despite these efforts, the prevalence of CVD continues to rise, highlighting the need for more effective interventions and public health strategies.

The modifiable risk factors for CVD are well-documented and include hypertension, dyslipidaemia, obesity, diabetes, and lifestyle choices such as smoking and physical inactivity (Erwin *et al*., 2023). Addressing these risk factors is crucial for reducing the incidence of CVD. For instance, clinical interventions targeting high blood pressure and cholesterol levels have proven effective in mitigating cardiovascular risk (The GBD 2015 Obesity Collaborators, 2017). Additionally, lifestyle modifications, including regular physical activity and a balanced diet, can significantly lower the risk of developing CVD.

In Malaysia, public health campaigns are essential to educate the population about the importance of lifestyle changes. Studies have shown that interventions such as structured teaching programs on healthy living can significantly improve cardiovascular risk factors, including reductions in BMI, total cholesterol, and blood pressure. Furthermore, community-based programs that promote physical activity and healthy eating can empower individuals to take charge of their health and reduce their risk of CVD.

1.2   Bibliometric Analysis

Bibliometric analysis is a quantitative research method that utilizes statistical techniques to analyse published literature, providing insights into the structure, dynamics, and trends within specific fields of study. This analytical approach has gained significant traction across various disciplines, including medicine, social sciences, and technology, as it allows researchers to objectively assess academic productivity, collaboration patterns, and the impact of scholarly work (Demiray & Alkan, 2022). The term "bibliometrics" was

first introduced by Pritchard in 1969, and it encompasses a range of methodologies aimed at measuring and analysing the characteristics of literature, such as publication counts, citation frequencies, and authorship patterns (Erdoğmuş & Korkmaz, 2022).

The primary objective of bibliometric analysis is to provide a comprehensive overview of a research domain, enabling scholars to identify key contributors, influential publications, and prevailing trends. Researchers can systematically evaluate the scientific output and impact of individual researchers, institutions, or countries by employing bibliometric methods. This is particularly valuable in the current age, characterized by an exponential increase in published literature, where navigating vast information can be challenging (SALTALI and Emine ASLANLAR, 2023). Over the decades, bibliometric analysis has evolved, incorporating advanced statistical methods and computational tools to enhance the depth and breadth of literature evaluation.

Bibliometric analysis employs a variety of metrics to assess research performance and impact. The most commonly used indicators are citation counts, the h-index, and the impact factor. Citation counts reflect the total number of times a publication has been cited by other works, directly measuring its influence within the academic community. The h-index, introduced by Jorge Hirsch in 2005, combines productivity and citation impact, providing a balanced assessment of an author's contributions (Tirink, 2022). Nevertheless, the impact factor, calculated based on the average number of citations to articles published in a specific journal, is a proxy for its influence within its field (Kokol & Vošner, 2018).

In recent years, digital databases and bibliometric software, such as VOS viewer and Bibliometrix package in R software, have revolutionized the field. These tools facilitate the visualization of bibliometric data, allowing researchers to create network maps that illustrate relationships between authors, institutions, and keywords (Barajas-

Ochoa *et al*., 2023; Bahoo *et al*., 2020). Such visual representations enhance the interpretability of bibliometric data and enable researchers to effectively identify emerging trends and research hotspots.

1.3   Framingham CVD Risk Score Calculator

The Framingham Cardiovascular Risk Score (FRS) is a widely utilized tool developed to estimate an individual's 10-year risk of developing CVD, including coronary heart disease (CHD) and stroke. Originating from the Framingham Heart Study, which began in 1948 in Framingham, Massachusetts, the FRS was designed to identify key risk factors associated with cardiovascular events and to provide a systematic method for assessing cardiovascular risk in the general population (Xue *et al*., 2013). The study has significantly contributed to our understanding of cardiovascular health, identifying various risk factors such as age, gender, smoking status, blood pressure, cholesterol levels, and diabetes (Gyldenløve *et al*., 2013).

The primary purpose of the Framingham Risk Score is to assist healthcare providers in stratifying patients based on their cardiovascular risk, thereby guiding preventive strategies and interventions. By quantifying the risk of CVD, the FRS enables clinicians to make informed decisions regarding lifestyle modifications, pharmacotherapy, and further diagnostic evaluations for at-risk patients (Xue *et al*., 2013). The ability to predict cardiovascular events accurately is crucial, as early intervention can significantly reduce morbidity and mortality associated with CVD. The Framingham Risk Score calculator incorporates several clinical parameters, including age, sex, total cholesterol, high-density lipoprotein (HDL) cholesterol, systolic blood pressure, smoking status, and

diabetes mellitus. Each of these factors is assigned a specific weight based on its association with cardiovascular risk, allowing for a comprehensive assessment of an individual's likelihood of experiencing a cardiovascular event within the next decade (Hossian *et al*., 2022). This systematic approach has made the FRS a cornerstone in cardiovascular risk assessment and management.

The FRS has been extensively applied in various clinical and research settings to evaluate cardiovascular risk across diverse populations. For instance, studies have demonstrated the utility of the FRS in specific patient populations, such as individuals living with HIV, where it has been used to assess the impact of antiretroviral therapy on cardiovascular risk (Falcone *et al*., 2011). Additionally, the FRS has been employed in studies examining the relationship between chronic inflammatory diseases, such as psoriasis, and cardiovascular risk, highlighting its versatility in different clinical contexts (Gyldenløve *et al*., 2013). Moreover, the FRS has been validated in numerous cohorts worldwide, demonstrating its effectiveness in predicting cardiovascular events in diverse ethnic and demographic groups. For example, research has shown that the FRS can accurately stratify risk in populations with varying prevalence of traditional cardiovascular risk factors, reinforcing its applicability in global health settings (Geldsetzer *et al*., 2018). This adaptability is particularly important in addressing the rising burden of CVD in low- and middle-income countries, where tailored risk assessment tools are essential for effective public health interventions (Geldsetzer *et al*., 2018).

1.4   WHO STEPwise approach to NCD risk factor surveillance (STEPS)

The World Health Organization (WHO) STEPwise approach to surveillance (STEPS) is a systematic framework designed to collect, analyse, and disseminate data on non-communicable disease (NCD) risk factors. The STEPS is launched in 2003 to provide a standardized method for assessing the prevalence of NCDs and their associated risk factors across diverse populations and settings. This approach is particularly crucial in the context of the global rise in NCDs, which are responsible for approximately 71% of all deaths worldwide, with CVD being the leading cause (Bahendeka *et al*., 2016). The STEPS questionnaire is a vital tool for public health researchers and policymakers, enabling them to gather comprehensive data to inform effective interventions and health policies.

The WHO STEPS questionnaire is divided into three distinct STEPs, each focusing on different aspects of NCD risk factors. The first step involves collecting demographic information, including age, sex, and socioeconomic status, which are essential for understanding the context of health behaviours and outcomes (Teshome *et al*., 2017). The second step assesses behavioural risk factors such as tobacco use, physical activity, dietary habits, and alcohol consumption. This STEP is critical for identifying lifestyle factors that contribute to the development of NCDs (Ngaruiya *et al*., 2021). Finally, the third step includes clinical measurements, such as blood pressure, body mass index (BMI), and blood glucose levels, which provide objective data on the biological risk factors associated with NCDs (Bahendeka *et al*., 2016). The STEPS questionnaire's flexibility allows for additional questions tailored to specific populations or research objectives, making it adaptable to various cultural and regional contexts (Manjrekar *et al*.,

2014). This adaptability is particularly important in addressing the diverse risk profiles of different communities and ensuring that the data collected is relevant and actionable.

The WHO STEPS questionnaire has been widely adopted in numerous countries to assess the prevalence of NCD risk factors and inform public health strategies. For example, the national NCD risk factor survey in Palau utilized the STEPS methodology to collect data on obesity and other risk factors, contributing to the development of targeted interventions to address the growing burden of NCDs in the region (Hasegawa *et al*., 2023). Such applications underscore the significance of the STEPS questionnaire in informing public health policies and guiding resource allocation.

In Malaysia, the WHO STEPS questionnaire has been instrumental in assessing the prevalence of NCD risk factors and informing health policies. The Malaysian Ministry of Health adopted the STEPS approach as part of its National Health and Morbidity Survey (NHMS) in 2006, which aims to monitor the population's health status and identify emerging health issues. For instance, the NHMS 2006 utilized the STEPS questionnaire to assess the prevalence of hypertension and its associated risk factors among Malaysian adults. The findings indicated a rising trend in hypertension prevalence, highlighting the urgent need for targeted interventions to address this public health challenge. The data collected through the STEPS approach has also informed the development of national health policies aimed at reducing the burden of NCDs in Malaysia (Ministry of Health (Malaysia), World Health Organization (WHO). Malaysia STEPS Noncommunicable Disease Risk Factors Survey 2005-2006)

1.5   Relationship between CVD risk factors and CVD risk score

Cardiovascular risk factors are critical determinants of an individual's likelihood of developing CVD. Traditional risk factors such as hypertension, hyperlipidaemia, diabetes, and lifestyle choices like smoking and physical inactivity have been extensively studied and are well-established contributors to cardiovascular morbidity and mortality (Kaffashian *et al*., 2011). The Framingham Risk Score quantifies these risk factors, allowing for a better understanding of an individual's cardiovascular health. For instance, studies have shown that elevated levels of low-density lipoprotein (LDL) cholesterol and systolic blood pressure significantly increase the FRS, thereby indicating a higher risk of future cardiovascular events (Kamuhu *et al*., 2021; Crowson *et al*., 2012). Moreover, emerging research has begun to explore the relationship between additional factors, such as psychological distress and systemic inflammation, and cardiovascular risk. For example, studies have indicated that conditions like depression can independently elevate cardiovascular risk, potentially influencing the FRS (Kirağ & Çalişkan, 2020; Paraswati *et al*., 2020). This evolving understanding of risk factors underscores the importance of a comprehensive approach to cardiovascular risk assessment, integrating both traditional and emerging factors.

A strong family history of stroke serves as a notable risk factor for the potential development of acute CVD or stroke later. Nevertheless, this genetic factor is often interacting with various other elements. While the primary focus has been on modifiable environmental influences like smoking, physical inactivity, and alcohol consumption, it is acknowledged that stroke also possesses a genetic component that may interact with these environmental factors. A study indicates that the risk ratio of stroke, following multifactorial adjustment for factors such as age, smoking, blood pressure, cholesterol,

diabetes, and education, linked to a positive parental history of stroke was found to be 1.89 (p=0.004) for men and 1.80 (p=0.007) for women. The link between a parental history of stroke and the risk of stroke was more pronounced in individuals aged 25 to 49 years compared to those who were older. The presence of coronary disease in parental history did not correlate with stroke risk in men; however, in women, it exhibited a borderline significant relationship with the risk of ischemic stroke. This indicated that a favorable parental history of stroke was a predictor of stroke risk, independent of other risk factors.

Recent advancements in cardiovascular studies underscore the significance of family-centered approaches, which consider the health of both patients and their family members. This method holds significant relevance in the realm of stroke, as family members frequently take the responsibilities of caregiving while also facing a heightened risk for comparable health concerns. By concentrating on the cardiovascular health of family members of stroke patients, it is possible to create targeted interventions that tackle both primary prevention (in the general population) and secondary prevention (for those with a family history). The incorporation of family-centered care within stroke rehabilitation and prevention programs in Malaysia remains at an early stage of development. Although certain studies have examined the psychosocial effects of stroke on families, investigations into the cardiovascular health of family members are still scarce. Filling this gap in knowledge may result in more effective strategies to prevent the emergence of CVD among family members, thereby decreasing the overall impact of strokes.

Family-based interventions have demonstrated potential on a global scale. A study conducted in Canada revealed that interventions aimed at the whole family, including

lifestyle modification programs and consistent health screenings, notably decreased the occurrence of CVD (Lalonde *et al*., 2015). The findings indicate that a comparable strategy may prove advantageous in Malaysia, where family dynamics play a crucial role in caregiving and healthcare decision-making.

1.6   Problem Statement

Many published scholarly articles regarding CVD involve the general population and certain populations globally. Despite that, there is still a lack of evidence or published literature on the probability of developing CVD events among the family members of stroke survivors in Kelantan, specifically, and in Malaysia, generally.

Moreover, CVD risk calculators such as Framingham's have been extensively used in Malaysia for various purposes. This could provide fundamental data and information regarding the Malaysian CVS risk profile. However, there has been no recent update on CVD risk among family members of stroke survivors, especially using a valid and robust CVD risk calculator in Kelantan.

Furthermore, the WHO STEPS questionnaires have been widely used as a standardised tool to measure and quantify the CVD risk across the world population. However, the relationship between the CVD risk among the family members of stroke survivors and the 'WHO STEPS questionnaire is also not well studied and understood, especially in Kelantan.

1.7   Rationale of Study

The study's findings will provide information on the trend and pattern of literatures on CVD risk among family members of stroke survivors. The information is useful for researchers and academia to focus on the demanding and emerging topics related to the field. Next, the study will evaluate the performance matrices of the FRS calculator when used among family members of stroke survivors in Kelantan. This will help policymakers and stakeholders assess the CVD risk and develop the appropriate measures according to the need and priority. Finally, it will also provide an estimate of CVD risk among family members of stroke survivors in Kelantan. The health policymaker can use this data to study the magnitude and distribution of CVD risk among family members of stroke survivors in Kelantan. Hence, a suitable approach or intervention, such as the 'family-based approach,' can be used to prevent and control the incidence of CVD among family members of stroke survivors in Kelantan.

1.8   Research Questions

1. What are the research trends, patterns, and emerging themes related to CVD risk among family members of stroke survivors worldwide?

2. What are the distributions of CVD categories ("low," "moderate" and "high") events among the family members of stroke survivors in Kelantan?

3. What is the relationship between CVD risk factors from WHO STEPS questionnaires and CVD risk among family members of stroke survivors in Kelantan?

1.9 Research Objectives

1.9.1 General Objective

To determine the probability of cardiovascular disease (CVD) events among family members of stroke survivors in Kelantan, Malaysia.

1.9.2 Specific Objectives

1. To identify the global publication trends, and themes related to the CVD risk among family members of stroke survivors and its application towards local setting in Kelantan.

2. To determine the distribution of CVD risk among family members of stroke survivors in Kelantan using BMI-based Framingham Risk Score calculator.

3. To estimate the relationship between CVD risk factors from WHO STEPS questionnaires and CVD risk scores among family members of stroke survivors in Kelantan.

CHAPTER TWO: LITERATURE REVIEWS

2.1 Overview of Cardiovascular disease (CVD)

2.1.1 Global Trends in CVD

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality worldwide, accounting for approximately 17.9 million deaths annually, representing 31% of all global deaths (Khan *et al*., 2022). The burden of CVD is not uniformly distributed; it varies significantly across different regions, influenced by factors such as socioeconomic status, lifestyle, and healthcare access. The global trend of CVD has undergone significant changes over the past few decades. The World Health Organization (WHO) reports that the prevalence of CVD has increased, particularly in low- and middle-income countries (LMICs), where rapid urbanization and lifestyle changes have led to concurrent rising rates of risk factors such as obesity, hypertension, and diabetes (Mendoza & Miranda, 2017). According to a study by Elyamani *et al*. (2021), the epidemiological transition theory proposes that as nations move forward in their development, they move away from a predominance of infectious illnesses and toward non-communicable diseases (NCDs), which include CVD.

Recent studies indicate that the prevalence of CVD risk factors is rising globally. For instance, Vandersmissen *et al*. found that high CVD risk is prevalent across various economic sectors, particularly in industries such as transport and construction (Vandersmissen *et al*., 2019). This alarming trend highlights the need for targeted interventions in specific occupational groups. Globally, CVD remains the leading cause of death, with ischemic heart disease and stroke being the most common manifestations (Gao *et al*., 2023). The Global Burden of Disease Study estimated that CVD accounted

for 422.7 million cases and 17.9 million deaths in 2015, with projections indicating that these numbers will rise to 23.6 million deaths annually by 2030 (Khan *et al*., 2022. The increasing prevalence is mainly attributed to risk factors such as hypertension, diabetes, and dyslipidemia (Gao *et al*., 2023). Regarding demographics, CVD affects both men and women, although the risk profiles may differ. For example, women tend to develop CVD later in life compared to men, often after menopause, when the protective effects of estrogen diminish (García *et al*., 2016). Interestingly, the burden of CVD is disproportionately higher in older adults, with age being a significant risk factor (Gao *et al*., 2023).

Besides that, mortality rates from CVD vary significantly across regions, with high-income countries experiencing declines in mortality due to improved healthcare access and preventive measures. This situation might be different in low—and middle-income countries (LMICs), where these countries struggle to combat the high mortality rates due to limited access to healthcare and a higher prevalence of risk factors (Mendoza & Miranda, 2017).

2.1.2 Current Trend of CVD in Malaysia

In Malaysia, CVD is the leading cause of death, accounting for 23.3% of total deaths, highlighting the urgent need for effective public health strategies (BERNAMA, 2024). Interestingly, the epidemiology of CVD in Malaysia reflects global trends driven by increasing rates of risk factors such as hypertension, diabetes, and obesity. The Malaysian Health and Morbidity Survey (NHMS) indicates that approximately 47% of adults have hypertension, and the prevalence of diabetes is around 18% (Khan *et al*.,

2022). These figures emphasize the growing burden of CVD in the country and the need for targeted interventions.

The Malaysian Cohort Project, which includes over 53,000 adults, provides valuable insights into the cardiovascular risk profiles of the population. Findings indicate that sociodemographic factors, such as age, gender, and ethnicity, significantly influence CVD risk, indicating the need for tailored prevention strategies (Borhanuddin *et al*., 2018). Furthermore, lifestyle factors, including dietary habits and physical activity levels, are crucial in determining cardiovascular health (Rippe, 2018). To overcome this, the Malaysian government has implemented various initiatives to reduce the prevalence of CVD risk factors, including health promotion campaigns, screening programs, and establishing national registries for cardiovascular risk evaluation (Khan *et al*., 2022).

2.2   Bibliometric Analysis as An Emerging Research Methodology

In recent years, bibliometric studies have become a popular method of analysing research findings and discoveries to develop themes for research directions. Bibliometric analysis involves the statistical evaluation of published literature to understand the structure and dynamics of research fields. It encompasses various techniques, including citation analysis, co-citation analysis, and co-authorship analysis, to map the intellectual landscape of a specific domain Wu *et al*. 2021, Lu *et al*., 2021).

The effectiveness of bibliometric analysis lies in its ability to provide a comprehensive overview of a research field. Researchers can identify key trends, influential publications, and collaborative networks using quantitative methods. Studies have shown that bibliometric analysis can effectively reveal the growth patterns of

research topics and the impact of specific publications on the field (Kokol *et al.*, 2020; Khan *et al.*, 2016). For instance, bibliometric studies in cardiovascular research have highlighted the increasing focus on specific areas such as heart failure, myocardial infarction, and cardiovascular rehabilitation (Ugolini *et al.*, 2013; Aggarwal *et al.*, 2018).

The advantages of Bibliometric Analysis are that it provides objective measurement for evaluating research output and impact, reducing biases associated with qualitative assessments (Sharma *et al.*, 2019). Second, it offers a comprehensive overview and broad perspective on research trends, allowing for the identification of emerging topics and gaps in the literature (Ellili, 2022). It also facilitates collaboration by mapping co-authorship and citation networks; bibliometric analysis can identify potential collaborators and foster interdisciplinary research (Job et al., 2022) and also supports the policymakers and funding agencies to making informed decisions regarding research priorities and funding allocations (Jamaludin *et al.*, 2023).

However, there are some drawbacks to applying the Bibliometric Analysis technique as bibliometric analysis primarily focuses on quantitative data, which may overlook qualitative aspects of research, such as the societal impact of studies (Song *et al.*, 2023). Besides that, the reliance on citations as a measure of effects can lead to biases, as not all influential work is highly cited, and citation practices vary across disciplines (Dong *et al.*, 2022). Data quality issues can also be a problem as the accuracy of bibliometric analysis depends on the quality of the data sources used. Inconsistent indexing and varying publication practices can affect the reliability of results (Chen *et al.*, 2022). Lastly, the emerging field is mostly to be looked over as the new and rapidly evolving research areas may not be adequately represented in bibliometric analyses

because they are just coming into existence and beginning to display signs of future potential (Ma *et al*., 2021).

2.2.1 Various Tools in Bibliometric Analysis

Recent developments in bibliometric analysis have led to notable progress, particularly with the introduction of diverse software tools that enhance the quantitative evaluation of academic literature. These tools allow for the visualisation and analysis of citation patterns, co-authorship networks, and keyword co-occurrences, offering valuable insights into the evolution of research domains.

One of the most commonly utilised software tools is **VOSviewer**, which focuses on the visualisation of bibliometric networks. This tool enables the creation of maps that utilise citation data, co-authorship, and keyword co-occurrence, which is especially beneficial for identifying trends and relationships within a body of literature (Ayoko *et al*., 2021; Liu, 2023; Zhou *et al*., 2021). VOSviewer is recognised for its impressive graphical features and intuitive interface, enabling the examination of extensive datasets without the need for advanced technical expertise (Liu, 2023). Research has shown its efficacy across multiple domains, such as management studies and environmental science, where it has been utilised to assess the influence of particular research topics and to illustrate the intellectual framework of fields (Ayoko *et al*., 2021; Liu, 2023).

The second tool is "Bibliometrics", an R package that consolidates multiple bibliometric analysis tools into a streamlined, automated workflow, enabling efficient and adaptable analyses of extensive literature (Veloutsou & Liao, 2022; Huang, 2021). This

enables the conduct of comprehensive bibliometric studies, including co-citation and bibliographic coupling analyses, which are essential for understanding the interrelationships between different research outputs. Bibliometrix has been employed in various studies, spanning educational research to the examination of social housing funding, demonstrating its wide-ranging applicability (Kurdi & Kurdi, 2021; Ianchuk, 2021).

Next is "Biblioshiny", also an R-based application that offers a thorough range of statistical methods and visualisations for bibliometric analysis. Biblioshiny stands out for its adaptability and seamless integration with R, facilitating sophisticated data manipulation and analysis (Thangavel & Chandra, 2023; Kaur *et al*., 2022; Alzard *et al*., 2022). This tool facilitates a range of bibliometric techniques, such as performance analysis and science mapping, rendering it ideal for in-depth exploration of research trends and patterns. For example, it has been employed to examine the literature concerning public debt sustainability and COVID-19, showcasing its adaptability across various fields of study (Kaur *et al*., 2022; Alzard *et al*., 2022).

Besides that, "CiteSpace" is another robust tool designed to visualise trends and patterns in scientific literature by employing knowledge mapping techniques. It provides functionalities like keyword-burst analysis, which uncovers emerging research fronts by emphasising keywords that have garnered notable attention over time (Wu & Li, 2022; Li *et al*., 2023). This capability enables individuals to monitor the progression of particular subjects and to pinpoint possible future avenues of inquiry, rendering CiteSpace an essential resource for those seeking to remain at the cutting edge of their disciplines.

In short, the field of bibliometric analysis is enhanced by a range of software tools, each providing unique functionalities that address various analytical requirements.

VOSviewer and Biblioshiny excel in their visualisation features and user-friendliness, whereas CiteSpace and Bibliometrix offer more sophisticated analytical tools. As bibliometric analysis advances, these tools will be essential in influencing the future of research assessment and knowledge mapping across various fields.

2.2.2 Application of Bibliometric Analysis in Healthcare

Bibliometric analysis has been applied to various domains in healthcare, including public health, epidemiology, and clinical research. For instance, bibliometric studies have been conducted to assess research productivity in specific diseases, such as cancer and diabetes, revealing trends in funding, collaboration, and publication patterns (Jin *et al*., 2023; Teles *et al*., 2021). In the context of CVD, bibliometric analysis has been particularly valuable. Studies have mapped the growth of cardiovascular research, identifying key authors, institutions, and journals that contribute to the field (Al-Kindi *et al*., 2015; Ugolini *et al*., 2013). For example, Al-Kindi *et al*. conducted a bibliometric analysis of CVD research in the Middle East, highlighting the region's research output and collaboration patterns (Al-Kindi *et al*., 2015). Similarly, Khan *et al*. analyzed the top-cited articles on cardiovascular magnetic resonance, providing insights into influential studies and emerging trends (Khan *et al*., 2016). In short, bibliometric analysis can help researchers and clinicians identify areas requiring further investigation, such as novel therapeutic approaches, preventive strategies, and health policy implications (Jin *et al*., 2023; Wang *et al*., 2020). As for the present study, we will use the bibliometric analysis method to evaluate the trends, patterns, collaboration, and trending keywords of research activities regarding cardiovascular risks among family members of stroke patients.

2.3   Framingham CVD Risk Score Calculator

The Framingham CVD Risk Score is among the most popular tools in assessing cardiovascular risk, developed from the Framingham Heart Study, which began in 1948. The Framingham Heart Study was initiated to identify common factors contributing to CVD by following a large cohort of participants over several decades. The study's findings led to the development of the Framingham CVD Risk Score, which quantifies the risk of developing cardiovascular events based on several clinical parameters, including age, sex, blood pressure, cholesterol levels, smoking status, and diabetes (Wennman *et al*., 2016). The score was first published in 1998 and has since undergone several revisions to enhance its predictive accuracy (Boulos *et al*., 2017). The original Framingham Risk Score was primarily based on a predominantly Caucasian population, which raises questions about its applicability to diverse ethnic groups. Subsequent studies have sought to recalibrate and validate the score in various populations, including Asia, to ensure its relevance across different demographics (Mettananda *et al*., 2021).

One of the primary advantages of the Framingham CVD Risk Score is its simplicity and ease of use in clinical settings. The score provides a straightforward method for healthcare professionals to estimate an individual's 10-year risk of cardiovascular events, facilitating timely interventions (Wennman *et al*., 2016). Furthermore, the Framingham score has been extensively validated, demonstrating good predictive accuracy in various populations (Nyiambam *et al*., 2020; Bozorgmanesh *et al*., 2011). The Framingham Risk Score also incorporates multiple risk factors, allowing for a comprehensive cardiovascular risk assessment. This multifactorial approach is beneficial in identifying individuals who may benefit from lifestyle modifications or pharmacological interventions to mitigate their risk (Chamnan *et al*., 2009; Wennman *et al*., 2016). The score's widespread

acceptance and use in clinical practice further underscore its utility in guiding CVD prevention strategies.

Despite its advantages, the Framingham CVD Risk Score has notable limitations. One significant drawback is its reliance on data from a predominantly Caucasian population, which may not accurately reflect the cardiovascular risk profiles of individuals from different ethnic backgrounds (Mettananda *et al*., 2021; Chia & Pengal, 2009). For instance, studies have indicated that the Framingham Risk Score may underestimate the risk of cardiovascular events in Asian populations due to differences in risk factor prevalence and the impact of socio-economic factors (Nyiambam *et al*., 2020; Mettananda *et al*., 2021). Moreover, the Framingham score does not account for certain emerging risk factors, such as inflammation markers or advanced imaging techniques, which may provide additional insights into an individual's cardiovascular risk (Crowson *et al*., 2012; Kengne *et al*., 2010). This limitation highlights the need for continuous updates and adaptations of the scoring system to incorporate new evidence and improve its predictive capabilities. For example, Indonesia has created its customised version of the Framingham Risk Score to better fit the characteristics of its populations, referred to as Jakarta Vascular Risk Score (JAKVAS) (Kusmana *et al*., 2019).

2.3.1 Application of the Framingham CVD Risk Score Calculator in Malaysia

The Framingham Risk Score (FRS) has been employed in several research in Malaysia to evaluate cardiovascular risk across diverse groups. Aziz *et al*. conducted a study on the Orang Asli population, using the FRS to assess the cardiovascular risk of individuals based on factors like age, gender, total cholesterol, HDL cholesterol, systolic

blood pressure, and smoking status (Aziz *et al*., 2016). This study emphasized the need to comprehend the distinct cardiovascular risk profiles of indigenous groups in Malaysia, where conventional risk factors may combine variably due to lifestyle and environmental influences. Likewise, Goh *et al*. conducted an independent external validation of the FRS in women, comparing it with the SCORE risk models (Goh *et al*., 2014). Their findings revealed that although the FRS is an effective instrument for forecasting CVD mortality, there were occurrences of overestimation in high-risk populations. This highlights the need for ongoing validation of risk assessment systems across varied populations, especially in Malaysia, where ethnic and lifestyle characteristics may affect cardiovascular risk.

The Framingham Risk Score has been included in public health programs in Malaysia, including the National Health and Morbidity Survey (NHMS). This study utilizes the FRS to assess the prevalence of cardiovascular risk factors in the community, offering essential data for public health planning and intervention efforts (Ko *et al*., 2020). The NHMS data indicate concerning trends in the incidence of hypertension, diabetes, and obesity, which are critical elements of the FRS. Health authorities can utilize the FRS to identify high-risk populations and undertake targeted treatments to alleviate the increasing burden of CVD in Malaysia. Furthermore, the FRS has been essential in evaluating the efficacy of health promotion activities designed to mitigate cardiovascular risk factors. Research has shown that lifestyle adjustments, including dietary alterations and enhanced physical activity, can substantially improve cardiovascular risk profiles as assessed by the FRS (Landim & Victor, 2006). This use of the FRS enables tracking alterations in cardiovascular risk over time, simplifying the assessment of public health measures.

2.3.2　BMI-Based Framingham CVD Risk Score Calculator

Body Mass Index (BMI) is a widely used measure of body fat based on height and weight, and it serves as a useful indicator of obesity-related health risks. Research has demonstrated that higher BMI is associated with increased cardiovascular risk, as it often correlates with other risk factors such as hypertension, dyslipidemia, and diabetes (Cook *et al*., 2012). Integrating BMI into the Framingham risk score allows for a more accessible assessment of cardiovascular risk, particularly in settings where lipid profiles may not be routinely measured (Dehghan, 2023). Moreover, the BMI-based score has been validated in diverse populations, demonstrating its applicability across different demographic groups. For example, a study by Dugas *et al*. highlighted the comparability of lipid-based and BMI-based Framingham risk scores in predicting cardiovascular risk in various settings (Dugas *et al*., 2017). Studies have shown that the BMI-based Framingham CVD risk score can effectively predict cardiovascular risk in various populations. For instance, Rabanal *et al*. found that when BMI was analysed as a continuous variable, it retained a significant association with CVD risk among different ethnic groups in New Zealand (Rabanal *et al*., 2018). Similarly, Ibrahim *et al*. reported that the BMI-based Framingham risk score provided a reliable estimate of coronary heart disease risk among medical students in Saudi Arabia (Ibrahim *et al*., 2014).

The BMI-based Framingham CVD risk score has significant implications for public health and clinical practice. In Malaysia, where CVD is a leading cause of mortality, integrating BMI into risk assessment can enhance early detection and intervention strategies (Sazlina *et al*., 2020). The National Health and Morbidity Survey (NHMS) has highlighted the rising prevalence of obesity and related cardiovascular risk factors in the Malaysian population, underscoring the need for effective risk assessment tools (Sazlina