THE EFFECTIVENESS OF STRUCTURED INTERVENTION PROGRAMME FOR STROKE (SIPS) IN IMPROVING STROKE AWARENESS AND REDUCING STROKE RISK AMONG ADULT POPULATION IN MALAYSIA: A CLUSTER RANDOMISED CONTROLLED TRIAL

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DECLARATION

I, MOHAMAD ZARUDIN BIN MAT SAID, declare that the work in this dissertation titled “The Effectiveness of Structured Intervention Programme for Stroke (SIPS) in Improving Stroke Awareness and Reducing Stroke Risk Among Adult Population in Malaysia: A Cluster Randomised Controlled Trial” has been carried out by me. The information derived from the literature has been duly acknowledged in the text, and a list of references is provided. No part of this dissertation was previously presented in any other institution.

MOHAMAD ZARUDIN BIN MAT SAID **MARCH 2022**

LIST OF PAPERS

The following articles were published/submitted and partly drafted for submission at the Web of Sciences (WOS) Journal and/or presented in various conferences nationally/internationally.

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The Effectiveness of Stroke Riskometer™ in Improving Stroke Risk Awareness in Malaysia: A Study Protocol of a Cluster-Randomised Controlled Trial

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A Cluster-Randomised Controlled Trial Evaluating the Effectiveness of Stroke Riskometer™ in Improving Stroke Risk Awareness in Adults: A Preliminary Study

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Zarudin Mat Said, Kamarul Imran Musa, Tengku Alina Tengku Ismail, Anees Abdul Hamid, Ramesh Sahathevan, Zariah Abdul Aziz, Valery Feigin

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LIST OF ABBREVIATIONS

ABCD	Attitudes and Beliefs about Cardiovascular Disease
ABCD-*M*	Malay Version of Attitudes and Beliefs about Cardiovascular Disease
AIC	Akaike Information Criterion
ANOVA	Analysis of variance
AOR	Adjusted Odd Ratio
APP	Application
AUT	Auckland University of Technology, New Zealand
BIC	Bayesian Information Criterion
BMI	Body Mass Index
CFA	Confirmatory factor analysis
CFI	Comparative fit index
CI	Confidence interval
CONSORT	Consolidated Standards of Reporting Trial
CSV	Comma-separated values
CVD	Cardiovascular disease
CVI	Content Validity Index
DALY	Disability-adjusted life year
DBP	Diastolic blood pressure
FAST	Face drooping, Arm weakness, Speech difficulty, Time to call
FL	Factor loading
FMS	Family medicine specialist
FVI	Face Validity Index
GBD	Global Burden of Diseases, Injuries, and Risk Factors Study

GDP	Gross domestic product
GEE	Generalised estimating equation
GLMM	Generalised linear mixed model
GP	General practitioner
HBM	Health Belief Model
HC	Health centre
HRQol	Health-related quality of life
ID	Identifier
IHD	Ischemic heart disease
IQR	Interquartile range
ITT	Intention to treat analysis
ITU	International Telecommunication Union
JEPeM	Human Research Ethics Committee of USM
KK	Klinik kesihatan
LMIC	Lower- and middle-income country
MAR	Missing at random
MCAR	Missing completely at random
MCMC	Malaysian Communications and Multimedia Commission
MOH	Ministry of Health, Malaysia
MREC	Medical Research and Ethics Committee's
NCD	Non-communicable disease
NHS	National Health Service
PAR	Population attributable risk
RCT	Randomised Controlled Trial
RI	Random intercept

RM ANOVA	Repeated measures analysis of variance
RM	Malaysian ringgit
RMSEA	Root Mean Square Error of Approximation
RS	Random slope
SBP	Systolic blood pressure
SD	Standard deviation
SIPS	Structured Interventional Programme for Stroke
SMS	Short message service
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trial
SRMR	Standardised Root Mean Square Residual
TIA	Transient ischemic attack
TLI	Tucker-Lewis index
TTM	Transtheoretical Model
UKMMC	Universiti Kebangsaan Malaysia Medical Centre
USD	United States dollar
USM	Universiti Sains Malaysia
WHO	World Health Organisation
ZMS	Zarudin Mat Said

LIST OF SYMBOLS

>	More than
<	Less than
=	Equal to
≥	More than and equal to
≤	Less than and equal to
α	Alpha
β	Beta
Θ	Theta
n	Number of populations
%	Percentage
χ^2	Pearson chi-square

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ABSTRAK

KEBERKESANAN PROGRAM INTERVENSI BERSTRUKTUR UNTUK PENYAKIT STROK (SIPS) DALAM MENINGKATKAN KESEDARAN DAN MENGURANGKAN RISIKO PENYAKIT STROK DALAM KALANGAN ORANG DEWASA DI MALAYSIA: UJI KAJI KAWALAN RAWAK SECARA KLUSTER

Latar belakang: Strok ialah masalah kesihatan awam yang besar dengan kadar kematian yang membimbangkan, beban morbiditi dan hilang upaya di seluruh dunia. Senario ini adalah bukti kukuh bahawa strategi pencegahan utama yang digunakan pada masa ini tidak cukup berkesan. Aplikasi Stroke Riskometer™ adalah strategi pencegahan penyakit strok baharu yang berpotensi merapatkan jurang antara pendekatan populasi secara besar-besaran dan berisiko tinggi yang boleh mendorong dan memperkasakan orang ramai untuk mengurangkan risiko penyakit strok dan kardiovaskular (CVD).

Objektif: Kajian ini bertujuan untuk menilai keberkesanan aplikasi Stroke Riskometer™ yang merupakan sebahagian daripada Program Intervensi Berstruktrur untuk penyakit strok (SIPS) dalam meningkatkan kesedaran ke atas penyakit strok dan dan mengurangkan risiko strok dalam kalangan penduduk dewasa di Malaysia.

Kaedah: Uji kaji kawalan rawak (RCT) secara kluster yang selari telah dijalankan di Kelantan, Malaysia, dengan tempoh susulan selama enam minggu.

Keseluruhan 116 peserta telah dibahagi secara rawak sama ada kumpulan intervensi (n = 58) yang dilengkapi dengan aplikasi Stroke Riskometer™ yang percuma dan risalah maklumat atau kumpulan kawalan (n = 58) yang hanya menerima pengurusan standard. Hasil utama kajian ialah tahap kesedaran ke atas risiko penyakit strok yang dinilai menggunakan soal selidik risiko ABCD-*M* pada permulaan kajian, 2-4 minggu dan minggu keenam selepas pembahagian rawak. Hasil sekunder kajian ialah kebarangkalian menghidapi penyakit strok untuk tempoh 5 dan 10 tahun akan datang yang diukur menggunakan aplikasi Stroke Riskometer™ (kumpulan kawalan akan menggunakan penilaian sama yang telah diterjemahkan ke dalam set soalan). Model pintasan rawak kesan campuran linear digunakan untuk menilai kesan intervensi ke atas kesedaran strok (diukur dengan skor ABCD-*M*), kebarangkalian risiko strok 5 dan 10 tahun menggunakan pakej *lme4*, *geepack* dan *nlme*. Prinsip niat untuk merawat dan tahap keertian pada 5% telah digunakan.

Keputusan: Purata umur peserta ialah 32 (SD 10.0) tahun. Tiada perbezaan yang signifikan dalam ciri asas antara peserta kecuali pendapatan bulanan. Kesedaran risiko penyakit strok berjaya dipertingkatkan sebanyak kira-kira 10%–12%, dengan kumpulan intervensi telah mencapai peningkatan seawal minggu ketiga kajian. Kebarangkalian menghidapi penyakit strok bagi kumpulan intervensi telah berkurangan dengan ketara (–26.3%) bersama-sama dengan peningkatan beberapa faktor risiko: Indeks Jisim Badan (–18.5%), tekanan diastolic darah (–19%), diet sihat (19%), aktiviti fizikal (22%). Walau bagaimanapun, tiada perbezaan yang ketara antara kumpulan intervensi (Kesedaran: $\beta = 1.25$; 95% CI, –1.42–3.92; Kebarangkalian (5 tahun): $\beta = –0.14$; 95% CI, –0.47–0.18; Kebarangkalian (10 tahun): $\beta = 0.03$; 95% CI, –0.40–0.46).

Kesimpulan: Penggunaan SIPS telah menunjukkan peningkatan ketara dalam kesedaran risiko strok dan mengurangkan kebarangkalian risiko strok 10 tahun. Aplikasi Stroke Riskometer™ ini merupakan strategi pencegahan primer berasaskan aplikasi besar-besaran yang sangat berpotensi untuk digunapakai bukan sahaja untuk pencegahan penyakit strok dan kardiovaskular tetapi juga untuk pencegahan penyakit tidak berjangkit (NCD) lain di Malaysia dan juga negara berpendapatan rendah dan sederhana yang lain.

KATA KUNCI: Strok, Kesedaran, Risiko Kebarangkalian, Aplikasi Mudah Alih, RCT

Pendaftaran Uji kaji: ClinicalTrials.gov Identifier NCT04529681

ABSTRACT

THE EFFECTIVENESS OF STRUCTURED INTERVENTION PROGRAMME FOR STROKE (SIPS) IN IMPROVING STROKE AWARENESS AND REDUCING STROKE RISK AMONG ADULT POPULATION IN MALAYSIA: A CLUSTER RANDOMISED CONTROLLED TRIAL

Background: Stroke is an enormous public health problem with an alarming mortality rate, the burden of morbidity and disability worldwide. The scenario is strong evidence that currently used primary prevention strategies are not sufficiently compelling. The Stroke Riskometer™ app represents a new stroke prevention strategy potentially bridging the gap between mass and high-risk population approaches that can motivate and empower people to reduce their risk of stroke and cardiovascular disease (CVD).

Objective: This study aimed to evaluate the effectiveness of the Stroke Riskometer™ app as part of the Structured Intervention Programme for Stroke (SIPS) in improving stroke awareness and reducing stroke risk among the adult population in Malaysia.

Methods: A parallel-group cluster randomised controlled trial (RCT) was conducted in Kelantan, Malaysia, with a six-week follow-up. Total 116 participants were randomised to either the intervention group (n = 58) equipped with free Stroke Riskometer™ app and informational leaflets or the control group (n = 58) that received standard management. The primary outcome was stroke risk awareness level assessed using the ABCD-*M* risk questionnaire at the baseline, 2–4 weeks and sixth-week post-intervention. The secondary outcome measure was the 5- and 10-years stroke risk probability measured using the Stroke Riskometer™ app (the

control group will use the same assessment translated into the question set). Linear mixed-effect random intercept models were used to assess the effect of the intervention on the stroke awareness (measured by ABCD-*M* score), 5- and 10-year stroke risk probability using the *lme4*, *geepack* and *nlme* packages. The intention-to-treat principle and the level of significance at 5% were used.

Results: The mean age of participants was 32 (SD 10.0). There were no significant differences in baseline characteristics except monthly income. The risk awareness was successfully improved by about 10%–12%, with the intervention group achieved as early as the third week. The risk probability of the intervention group was significantly reduced (–26.3%) together with the improvement of several risk factors: body mass index (–18.5%), diastolic blood pressure (–19%), healthy diet (19%), physical activity (22%). However, there was no significant difference between the intervention group (awareness: $\beta = 1.25$; 95% CI, –1.42–3.92; probability (5 years): $\beta = –0.14$; 95% CI, –0.47–0.18; probability (10 years): $\beta = 0.03$; 95% CI, –0.40–0.46).

Conclusion: The SIPS has shown significant improvement in stroke risk awareness and reduced the 10-years stroke risk probability. The Stroke Riskometer™ app is a potentially effective mass app-based primary prevention strategy that can be used not only for stroke and CVD prevention but also for primary prevention of other non-communicable diseases (NCDs) in Malaysia and other low- and middle-income countries as well.

KEYWORDS: Stroke, Awareness, Risk Probability, Mobile Apps, RCT

DISSERTATION OUTLINE

This dissertation is presented in the alternative format for Doctor of Public Health (DrPH), in accordance with the Universiti Sains Malaysia research degree regulations. The dissertation includes a series of research papers/manuscripts either published/submitted or drafted for submission to peer-reviewed journals. This dissertation is divided into six chapters.

Chapter 1 is the introductory chapter of the study with the rationale for conducting this study to the benefits of primary prevention of stroke and CVD, particularly in Malaysia. It also includes the objectives and hypothesis of this research study. At the end of this chapter, the general setting of the study was described together with the flow process for the entire research study.

Chapter 2 comprises the literature review of the study, including the role of personalised risk communication and the evidence of the effectiveness of health-based apps in preventing and controlling stroke and CVD. In addition, the underlying theoretical framework and the methodological challenges were reviewed to establish reliable and robust study methods and tools.

Chapters 3, 4, and 5 are the three major chapters that describe the research study's protocol and results. Further elaboration of the methodology used in both phases of the study was elaborated extensively in these chapters. Chapter 3 elaborates the methods used to conduct the phase two study. It was published in Neuroepidemiology. Chapter 4 provides a detailed process for translating and validating the ABCD risk questionnaire into Malay, which was used in phase two. This chapter has been submitted to the BMC Public Health and is reviewing.

Finally, results of the phased evaluation of the effectiveness of the Stroke Riskometer™ app in an adult population in Malaysia context are detailed in Chapter 5.

Chapter 6 is the chapter on the conclusion from this research study. It includes the strengths and limitations of the study, the recommendations, and the experiences gained from this research study. References and Appendices are included after Chapter 6.

CHAPTER 1: INTRODUCTION

1.1 Introduction

1.1.1 Stroke Burden and Risk Factors

According to World Health Organisation, non-communicable diseases (NCDs) has been responsible for about 41 million deaths each year, equivalent to 71% (77% in low- and middle-income countries (LMICs)) of all deaths worldwide (WHO, 2021b). The highest proportion comes from cardiovascular diseases (CVDs), which primarily consist of ischemic heart disease (IHD) and stroke (17.9 million, 43.7%), followed by cancers (9.3 million, 22.7%), respiratory diseases (4.1 million, 10.0%) and diabetes (1.5 million, 3.7%) (Budreviciute *et al.*, 2020; WHO, 2021b). Stroke or cerebrovascular accident is a global public health problem with significant-high morbidity and disability. Globally, it is the third leading cause of mortality and disability after IHD and neonatal disorder (Pandian *et al.*, 2020; Feigin *et al.*, 2021). It has caused a tremendous burden to the LMICs; for example, more than 78% of stroke disability-adjusted life years (DALYs) came from these countries (O'donnell *et al.*, 2010; Ezejimofor *et al.*, 2016; Dee *et al.*, 2020). In 1990, DALYs from stroke cases was 38 million, but this increased to 125 million in 2019 (Hejazi *et al.*, 2015; Feigin *et al.*, 2021). It is predicted that by 2030, the stroke burden could be enormous; as many as 12 million stroke deaths, 70 million stroke survivors, and more than 200 million DALYs lost from stroke each year (Kim *et al.*, 2015a).

Despite a global decline in the age-standardised stroke mortality rate, the scenario is different in LMICs, where there are escalation trends of age-standardised stroke incidence and a slower decline of age-standardised stroke mortality rates compared to the high-income countries (Ganasegeran *et al.*, 2020; Feigin *et al.*, 2021).

In Malaysia, stroke is the third leading cause of mortality and the most common cause of adult disability (Tan *et al.*, 2014; Wan-Arfah *et al.*, 2018; Ganasegeran *et al.*, 2020). Recently, the age-standardised stroke mortality rates were estimated at 103 per 100,000 in men and 97 per 100,000 in women (Ganasegeran *et al.*, 2020). A population-based study done in Penang showed the overall age-standardised stroke incidence in Malaysia was at 67 cases per 100,000 population with more than half (53.1%) were males and nearly a quarter (23.7%) were recurrent strokes (Kooi *et al.*, 2016). In most cases, it is affecting those aged 60 years or older; however, the incidence in young adults (18–50 years) is also large (10–15% of all reported stroke patients), and the number is increasing (Maaijwee *et al.*, 2014; Lutski *et al.*, 2017; Ganasegeran *et al.*, 2020). Recent researches have shown that the mean age of the first stroke is declining, and its incidence rate is increasing at among the younger populations, primarily in lower-income countries (21.3%; 17.3% globally) (Avan *et al.*, 2019; Hathidara *et al.*, 2019; Boot *et al.*, 2020; Yahya *et al.*, 2020). Recent data in Malaysia has revealed a significant increase in the stroke incidence among young adults, predominantly in men (53.3%) (Hwong *et al.*, 2021). In addition, the high proportion of the risk factors for stroke (i.e., hypertension, obesity and sedentary lifestyle) in the young adults in Malaysia reflect higher future stroke incidence among this group (Kooi *et al.*, 2016; Hwong *et al.*, 2021).

Young stroke will negatively impact the physical, psychological, social, and economical components rendering them unproductive during their youth (Yamamoto, 2012). In addition, young stroke patients have higher risks for unemployment, long-term cognitive impairment, depression, and anxiety (Maaijwee *et al.*, 2016). The resulting functional disabilities and psychiatric morbidities will affect the patient and the family, community and increase the high economic burden to the government (Ganasegeran *et al.*, 2020).

The most intensive international study of risk factors for acute stroke (INTERSTROKE) and the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) reported that the main risk factors stroke events were due to modifiable risk factors (O'Donnell *et al.*, 2016; Feigin *et al.*, 2021). This shows immense potential to combat stroke by reducing the modifiable risk factor exposure (O'Donnell *et al.*, 2016; Feigin *et al.*, 2021). The modifiable risk factors include hypertension or blood pressure of 140/90 mmHg or higher, diabetes mellitus, lipid disorder by evidenced of apolipoprotein (Apo) B/Apo A1 ratio, obesity, physical inactivity, poor diet quality, smoking status, alcohol use status, psychosocial factors and cardiac causes (i.e., atrial fibrillation or flutter, previous myocardial infarction, prosthetic heart valve, rheumatic heart disease). These modifiable risk factors are collectively associated with about 90% of the population attributable risk (PAR) for stroke cases. The remaining risk was due to ethnic, gender and age groups (O'Donnell *et al.*, 2016). The risk factors are shared between stroke and CVDs and other major NCDs, which means stroke intervention and prevention programmes may also positively reduce the burden for other NCDs.

Primary prevention for both stroke and CVD includes measures to reduce the exposure to metabolic risk factors (e.g., screening for and proper management of blood pressure and weight), behavioural risk factors (e.g., smoking cessation, healthy diet, physical activity), and environmental and occupational risk factors (e.g., measures to reduce air pollution and lead exposure). These measures must be implemented and strengthened to reduce stroke morbidity and mortality (Feigin *et al.*, 2021).

1.1.2 Personalised Risk Communication on Stroke

The development and implementation of population-level preventions and efforts to reduce poverty and socioeconomic inequities are important to reduce the burden of stroke, CVD, and other NCDs. But, primary prevention measures at the individual level is equally important (Feigin *et al.*, 2021). Risk communication is a critical component of preventive strategies, it involves (1) risk identification and assessment, (2) improving the accuracy of risk-benefits perceptions of the diseases, (3) combination of appropriate management and behavioural changes (Hill *et al.*, 2011; Powers *et al.*, 2011; Lundgren and McMakin, 2018). Personalised risk communication of stroke and CVD risk promotes identifying risk factors and accurately estimating the risk, producing a modest improvement in the accuracy of risk-benefits perceptions and motivating the patient's intention of starting a specific risk-reduction behaviour (Hill *et al.*, 2011; Powers *et al.*, 2011). The individualised stroke risk assessment in a general population is crucial because it provides additional primary prevention strategies and engages them actively in stroke risk reduction (Goldstein *et al.*, 2006; Nobel *et al.*, 2014).

It may be helpful for healthcare providers and treating physicians to estimate risk for an individual patient, especially those at high risk (Meschia *et al.*, 2014; Nobel *et al.*, 2014).

Communicating risk to the general population requires simple tools and they must be relevant to the typical individual who is likely to have more than one risk factor or be engaged in risky behaviour (Goldstein *et al.*, 2006; Nobel *et al.*, 2014). Mobile health (mHealth) is an example of such tool and they includes (a) web-based and (b) smartphone-based applications (or known as mobile apps) (Zhang *et al.*, 2017). A few examples of mobile apps are A-CHESS (alcoholism) (Gustafson *et al.*, 2014), My-FitnessPal (dietary changes) (Ipjian and Johnston, 2017), SMART MOVE (physical activity) (Glynn *et al.*, 2014) and smartphone-based coronary heart disease prevention (SBCHDP) (Zhang *et al.*, 2017). Most of these mobile phone apps provide intervention through personalised risk assessment by motivating users to improve their lifestyle and behaviour (Glynn *et al.*, 2014; Gustafson *et al.*, 2014). Mobile apps provide cost-effective, easily accessible, rapid and regular feedback-loop intervention. Good mobile apps offer realistic goal setting, and facility to view updated and relevant clinical management (Glynn *et al.*, 2014; Gustafson *et al.*, 2014; Zhang *et al.*, 2017).

Despite the advantages of mobile apps personalised risk assessment, the actual take up and adoption of this technology in the older population has been low and inconsistent (Wildenbos *et al.*, 2018). This population interact differently with information technology and new intervention. Therefore, the usability and acceptance of this technology must be determined (Aslam *et al.*, 2020).

1.1.3 Stroke Risk Awareness and Its Components

Knowledge and awareness are critical points in managing the risk among the general population, particularly in NCDs. Usually, knowledge of stroke risk refers to identifying the stroke warning signs and risk factors in the population or specific participants (Al Shafaee *et al.,* 2006b; Hickey *et al.,* 2009; Sowtali *et al.,* 2017). The established stroke warning signs in most guidelines are sudden numbness or weakness in the face, arm or leg, especially on one side of the body; sudden confusion or difficulty speaking or understanding speech; sudden trouble seeing in one or both eyes; sudden difficulty in walking, dizziness or loss of balance/coordination; or sudden and severe headache with no known cause (Hickey *et al.,* 2009). While an established list of stroke risk factors in INTERSTROKE and GBD 2019 included hypertension or blood pressure of 140/90 mmHg or higher, diabetes mellitus, lipid disorder, obesity, physical inactivity, poor diet quality, smoking status, alcohol status, psychosocial factors, cardiac causes (i.e., atrial fibrillation or flutter, previous myocardial infarction, prosthetic heart valve, rheumatic heart disease) and transient ischaemic attack (TIA) or prior stroke (O'Donnell *et al.,* 2016; Feigin *et al.,* 2021). However, the NHS Health Check Programme treated a broader and holistic scope of stroke and CVD risk awareness. In that context, stroke and CVD risk awareness refer to the accuracy of the perceived risk of CVD against predicted CVD risk, general knowledge of CVD and what one can do to lower predicted CVD risk (Woringer *et al.,* 2017). While predicted CVD risk refers to one's chance of experiencing a heart attack or stroke, perceived risk of CVD refers to a person's perception of their CVD risk.

The success of any disease control and prevention programme depends on community knowledge and practices regarding the risk factor, treatment and prevention (Sowtali et al., 2016b). Knowledge of stroke risk factors will improve primary prevention through lifestyle modifications and more efficient control of stroke and CVD risk (Lamidi, Rasheed *et al*., 2017). It is expected that high knowledge and awareness of these conditions will prompt people to seek healthcare timely and reduce the possibility of developing complications. Despite various stroke educational campaigns, high-risk prevention strategies, printed-based health education in health clinics and information sharing on social media platforms, knowledge and awareness of stroke risk among the populations are still highlighted as inadequate even if they had experienced the disease (CM, 2014; Foong *et al.*, 2014; Sowtali *et al.*, 2017). Several studies regarding knowledge and awareness of stroke risk highlighted the poor and low level of stroke knowledge mainly influenced by age, gender, education level, income and risk factors (Al Shafaee *et al.*, 2006b; Yang *et al.*, 2013; Sowtali *et al.*, 2017). The younger group (young- and middle-aged) and female stroke patients have a better knowledge of stroke (Sowtali *et al.*, 2016a). At the same time, higher education, income, or socio-economic status are related to better stroke knowledge in most studies conducted (Al Shafaee *et al.*, 2006b; Yang *et al.*, 2013; Sowtali *et al.*, 2017).

Regarding the perception of the stroke and CVD risks and the benefits of behaviour change, 60% of the general population had false reassurance or false perception of their stroke and CVDs risk either underestimated or overestimated (Webster and Heeley, 2010). It may lead to the adoption and maintenance of unhealthy behaviours and finally contribute to the onset of stroke or other NCDs.

Most studies showed young-aged, hypertension, dyslipidemia, known heart disease, and previous stroke history were significantly associated with the perceived risk of stroke (Harwell *et al.*, 2005; Webster and Heeley, 2010; Yang *et al.*, 2013). Health education that focuses on stroke prevention and risk awareness may help to improve the perceived risk of stroke among the populations (Yang *et al.*, 2013). Intention to change behaviour is closely related to self-efficacy, which is considered a powerful predictor of intention to change in most CVDs studies (Brouwer-Goossensen *et al.*, 2018). It has been found that self-efficacy directly affects health-related behavioural change. The elderly, with high BMI, physically inactive, with a history of vascular disease and/or depression, had lower self-efficacy for health-related behaviour change (Brouwer-Goossensen *et al.*, 2018).

1.1.4 Public Health Interventions for Improving Stroke Risk Awareness

Many efforts were made to improve this issue in response to the importance of stroke risk awareness in reducing the burden. A systematic review on public health interventions for improving stroke risk awareness by Gardois *et al.* revealed that most studies involved community-based health promotion. At the same time, 33% were delivered to individuals (Gardois *et al.*, 2014). In addition, most of these studies targeted the adults (over 18 years) from specific subgroups (i.e., religious members, students or specific genders) than the general population (Jones *et al.*, 2010; Gardois *et al.*, 2014; Olaiya *et al.*, 2017; Vondráčková and Mikulík, 2017; Komolafe *et al.*, 2020). As shown in most studies, targeting the general population is more challenging than having specific subgroups due to high cost and poor sustainability (Jones *et al.*, 2010; Vondráčková and Mikulík, 2017).

Topics of general awareness (Vondráčková and Mikulík, 2017), risk factors and prevention, early signs and symptoms of stroke (Fogle *et al.*, 2008; Jones *et al.*, 2010) were among the specified areas covered in most of the related studies (Gardois *et al.*, 2014; Olaiya *et al.*, 2017).

The interventions were delivered interactively using different methods, including educational videos (Chan *et al.*, 2008; Kalenderian *et al.*, 2009; Villablanca *et al.*, 2009; Jones *et al.*, 2010; Vondráčková and Mikulík, 2017), one-to-one advice sessions (Miller and Spilker, 2003), educational sessions (Kalenderian *et al.*, 2009; Boden-Albala *et al.*, 2010; Mullen Conley *et al.*, 2010; Komolafe *et al.*, 2020), slide presentations (Duraski, 2007; Covington *et al.*, 2010), informative materials (Kleindorfer *et al.*, 2008; Covington *et al.*, 2010; Vondráčková and Mikulík, 2017) and classroom lectures (Morgenstern *et al.*, 2007; Mullen Conley *et al.*, 2010; Gardois *et al.*, 2014; Vondráčková and Mikulík, 2017). The interventions were conducted either in a single session or a repetitive session. The repetitive session usually covers different stroke-related topics for the same participants over weeks, months or even years (Jones *et al.*, 2010; Gardois *et al.*, 2014; Komolafe *et al.*, 2020). As suggested in some studies, repetitive sessions with an optimal time frame were proven effective in optimising the intervention in a limited time (Jones *et al.*, 2010).

Most studies showed significant improvement of overall stroke awareness even using different methods. Beyond that, an increase in knowledge and awareness of stroke may facilitate health behaviour change (Rosenstock, 2005; Jones *et al.*, 2010). Unfortunately, there are limited studies on stroke awareness in Malaysia, even fewer regarding the public health interventions for improving stroke risk awareness

(Sowtali *et al.*, 2016a; Albohari *et al.*, 2020). In contrast, a currently available study in Malaysia mainly targets stroke-related persons, either families and relatives or caretakers (Sowtali *et al.*, 2016a). Besides, the commonly use interventions in Malaysia were conventional health promotion and education campaigns, informative material in healthcare facilities and partly on media sources (Anuar Deen *et al.*, 2014; Sowtali *et al.*, 2016a; Yap *et al.*, 2021). Future research must always identify the most impactful population group to be specified and which interventions will increase stroke awareness and influence behaviour change the most. There are many ways to conduct stroke awareness intervention as no definite methods have been accepted as universally applicable and efficient. One of the promising ways is by using the health-app based intervention. The easily accessible and cost-effective technology positively affects general awareness of stroke and its risk factors and improves stroke and CVD prevention primarily in LMICs (Beratarrechea *et al.*, 2014; Feigin *et al.*, 2015a).

1.1.5 An Evaluation of Mobile Health Apps

The Handphone and Internet Users Survey 2020 conducted by the Malaysian Communications and Multimedia Commission (MCMC) has revealed that smartphone is the most popular device to access the internet, reaching a near saturation usage level (98.7%) in 2020 with a massive escalation in the hours spent on the internet (MCMC, 2020). Whereas in 2017, more than 325,000 mHealth apps were recently available on the Apple Store and Google Play with the global health app market is expected to reach USD236 billion by 2026, and 34% of mobile phone users had at least one health application on their mobile phone (Jake-Schoffman *et*

al., 2017; Iribarren *et al.*, 2021). However, study on usability and efficacy of the available application is still scarce.

Literature listed some methods for evaluating commercial health applications, including content analysis, usability testing, observational studies, and intervention evaluation (Kumar *et al.,* 2014; BinDhim *et al.,* 2015). Experiments or interventions are conducted to evaluate the efficacy and effectiveness of new treatments, tools and prevention programmes. Compared to the efficacy studies, the effectiveness studies (also known as pragmatic studies) examine interventions under the circumstances closer to real-world practice, with more heterogeneous patient populations, less-standardised study protocols, and delivery in routine settings (Singal *et al.*, 2014). A recent systematic review and meta-analysis provide evidence on evaluating health-based mobile apps' effectiveness (Iribarren *et al.*, 2021). Most studies in the report were parallel design or cluster randomised controlled trials (RCTs) (98.3%) which were conducted in high-income countries, including the United States, United Kingdom, Australia, Japan, Korea and Canada (Iribarren *et al.*, 2021). RCT is a 'gold standard' in evaluating the intervention and provide a valuable source of evidence in research. It is also treated as a powerful experimental tool to examine the effectiveness of intervention (Kumar *et al.*, 2014; Singal *et al.,* 2014; Jake-Schoffman *et al.*, 2017; Han and Lee, 2018) due to its capability to minimise bias through the appropriate control or comparison group (Singal *et al.*, 2014; Jake-Schoffman *et al.*, 2017). The RCT also examined whether an app improves upon a standard practice by comparing standard practice with and without the app.

However, RCT poses additional challenges due to time and resource-intensive, randomisation for treatment assignment, and/or the level of treatment adherence required (Kumar *et al.*, 2014; Jake-Schoffman *et al.*, 2017).

The spectrum of the health outcomes involved nutrition and physical activity (e.g., weight loss), mental health management, diabetes management, general health/well-being (e.g., quality of sleep), medication adherence, harm reduction (e.g., drug, alcohol, smoking) and management of chronic disease (Iribarren *et al.*, 2021). The involvement of the participant depended on the outcome of the study, predominantly among adults (83.1%) and adolescents (8.1%) (Iribarren *et al.*, 2021). Most studies had follow-up periods of 6 months or less (83.1%), and only 2.3% of studies had follow-up periods longer than 12 months (Iribarren *et al.*, 2021). Methodology wise, the control groups either received no intervention (58.1%), received attention control (e.g., basic version of an app, 26.2%) or were waitlisted (15.7%) (Iribarren *et al.*, 2021). As explained in the literature, a few elements could be considered in changing behaviour, including; (1) reminders or notifications (e.g., to prompt patients to take their medication at a specified time), (2) tracking activity (e.g., to encourage increased physical activity), (3) goal planning, and (4) tailored information (e.g., provide information on the consequences of continuing a behaviour) (Haase *et al.*, 2017; Lee *et al.*, 2018b; Iribarren *et al.*, 2021). The least common features were communication messaging within the app, app-based social support and gamification (Iribarren *et al.*, 2021). For example, studies were done to test weight loss apps versus standard diet counselling methods on self-monitoring and weight loss among adults. The findings showed no differences found for weight loss or reduction in blood pressure even compared to the standard care (Laing *et al.*,

2014; Wharton *et al.*, 2014). While in a study related to smoking cessation, the newly-invented app was proven to be more effective than the commercial app, 'QuitGuide' for the quit smoking and participants engagement rates (Bricker *et al.*, 2014).

All these studies were conducted using the RCTs, and they emphasised the importance of a solid and appropriate study design to develop a good evaluation study. Most related studies highlighted a substantial growth in the number of health-based apps containing behaviour change techniques (Kruse *et al.*, 2019; Iribarren *et al.*, 2021). The development significantly improves health care services and communication, particularly in LMICs with insufficient resources, but access to phones and cellular services is high even among vulnerable populations (Kruse *et al.*, 2019; Iribarren *et al.*, 2021). It will be a useful starting point in reducing the stroke and CVD burden and the bigger context of NCDs, primarily in LMICs.

1.2 Problem Statement

Recent stroke trends in Malaysia revealed a startling rise in stroke incidence among the population. The impact of the stroke burden will lead to a severe sequel on individuals and families, communities, and the countries. However, to our knowledge; (a) stroke educational campaigns, printed-based health education in health clinics and information sharing on social media platforms, knowledge and awareness of stroke risk among the Malaysian general populations are still inadequate, and (b) the currently used primary prevention strategies might not sufficiently effective on their own. Due to the reasons, new innovative and structured prevention strategies for the general population are required.

The Stroke Riskometer™ app is recently developed smart stroke prevention tool that is innovative. It not only serves as a health promotional tool in improving stroke risk awareness but more significantly can be used to assess the absolute and relative stroke risk in 5- and 10-years duration.

The availability of innovative stroke prevention tools such as Stroke Riskometer™ app gives anew opportunity to public health workers in Malaysia. They can incorporate it in the stroke control and prevention programme. Stroke Riskometer™ uses mobile platform, so it is very easily scalable. However, before Stroke Riskometer™ can be used locally it needs to be assessed in the Malaysian population. Its effectiveness on the stroke awareness and reduction in stroke probability should be measured.

The use of the mobile app in the Malaysian clinical practice is still not optimal. In addition, many mobile apps do not go intensive clinical trials and do not involve expert opinions during their developments. Failure to use properly developed tool will compromise the control and prevention programme. Stroke Riskometer™ packaged in SIPS have been developed by experienced stroke scientists. There have been publications that support Stroke Riskometer™.

1.3 Study Rationale

The study provided the opportunity to evaluate the effectiveness of Structured Intervention Program for Stroke (SIPS) – Stroke Riskometer™ app, informational leaflets and reminder system – to improve stroke and CVD awareness and to reduce stroke probability. Even though, studies from other countries are available for similar category of mobile apps, but this study enables us to show the findings specific to the population residing in Kelantan, Malaysia.

Secondly, this study quantitatively measured the change in stroke awareness and stroke probability as a result of using SIPS. The change from baseline until six weeks is available for stroke awareness. The change of stroke probability is available at baseline and six week. Amount of change between baseline to 2^{nd}–4^{th} week and baseline to sixth week can also be measured. In addition to that, the change will add findings that reflect the response to SIPS in the Kelantan population useful for public health workers in the northeast of Malaysia.

This study will provide findings that is useful if there is planning to scale up the SIPS to larger geographical areas and larger population. The stakeholders such as the Ministry of Health Malaysia can take advantage of SIPS and incorporate it in their current stroke control and prevention programme. Lastly, the finding from the study will help to spur more mobile-based apps which has been shown elsewhere to be effective at facilitating the control and prevention of stroke and others NCD.

1.4 Research Questions

1. Is the Malay Version of Attitudes and Beliefs about Cardiovascular Disease (ABCD-*M*) risk questionnaire a valid and reliable tool to assess the awareness for stroke and CVD risk among the adult population in Kelantan?

2. Would the Structured Intervention Programme for Stroke (SIPS) – Stroke Riskometer™ app, informational leaflets, and reminder system change stroke awareness among the adult population in Kelantan?

3. Would the Structured Intervention Programme for Stroke (SIPS) – Stroke Riskometer™ app, informational leaflets and reminder system change the stroke risk probability among the adult population in Kelantan?

1.5 Objectives

1.5.1 General Objective

To study the effectiveness of the Structured Intervention Programme for Stroke (SIPS) – Stroke Riskometer™ app, informational leaflets and reminder system in improving the stroke risk awareness and reducing stroke risk among the adult population in Kelantan, Malaysia.

1.5.2 Specific Objectives

1. To translate and validate the ABCD risk questionnaire into the Malay language in assessing stroke awareness among the adult population in Kelantan, Malaysia.

2. To compare the change in the stroke awareness (ABCD-*M* scores) between the control and the intervention group at three different time points (baseline, 2nd–4th week and sixth week).

3. To compare the change of 5- and 10-years stroke risk probability between the control and the intervention group at different time points (baseline and sixth weeks).

1.6 Research Hypothesis

1. There is a significant difference of ABCD-*M* scores between the intervention and control group over follow up time (from baseline to 2nd–4th week and sixth week).

2. There is a significant difference in 5- and 10-years stroke risk probability between the intervention and control group over follow up time (from baseline to sixth week).

1.7 Phases of Study

This study consists of two phases. The first phase was a translation and validation of the Attitudes and Beliefs about Cardiovascular Disease (ABCD) risk questionnaire. It was to fulfil the first objective, which was to translate and validate the ABCD risk questionnaire. The second phase of this study was a parallel-group of the cluster randomized-controlled trial (RCT) with a 1:1 allocation ratio. It was to cover the second and third of study objectives which were to evaluate the effectiveness of the Stroke Riskometer™ app as part of the Structured Intervention Programme for Stroke (SIPS) in improving stroke awareness and reducing stroke risk among the adult population in Malaysia.

Further discussion on the methodology used in both phases is elaborated extensively in Chapters 4, 5 and 6. Finally, the flowchart of the study is summarised in Figure 1.1.

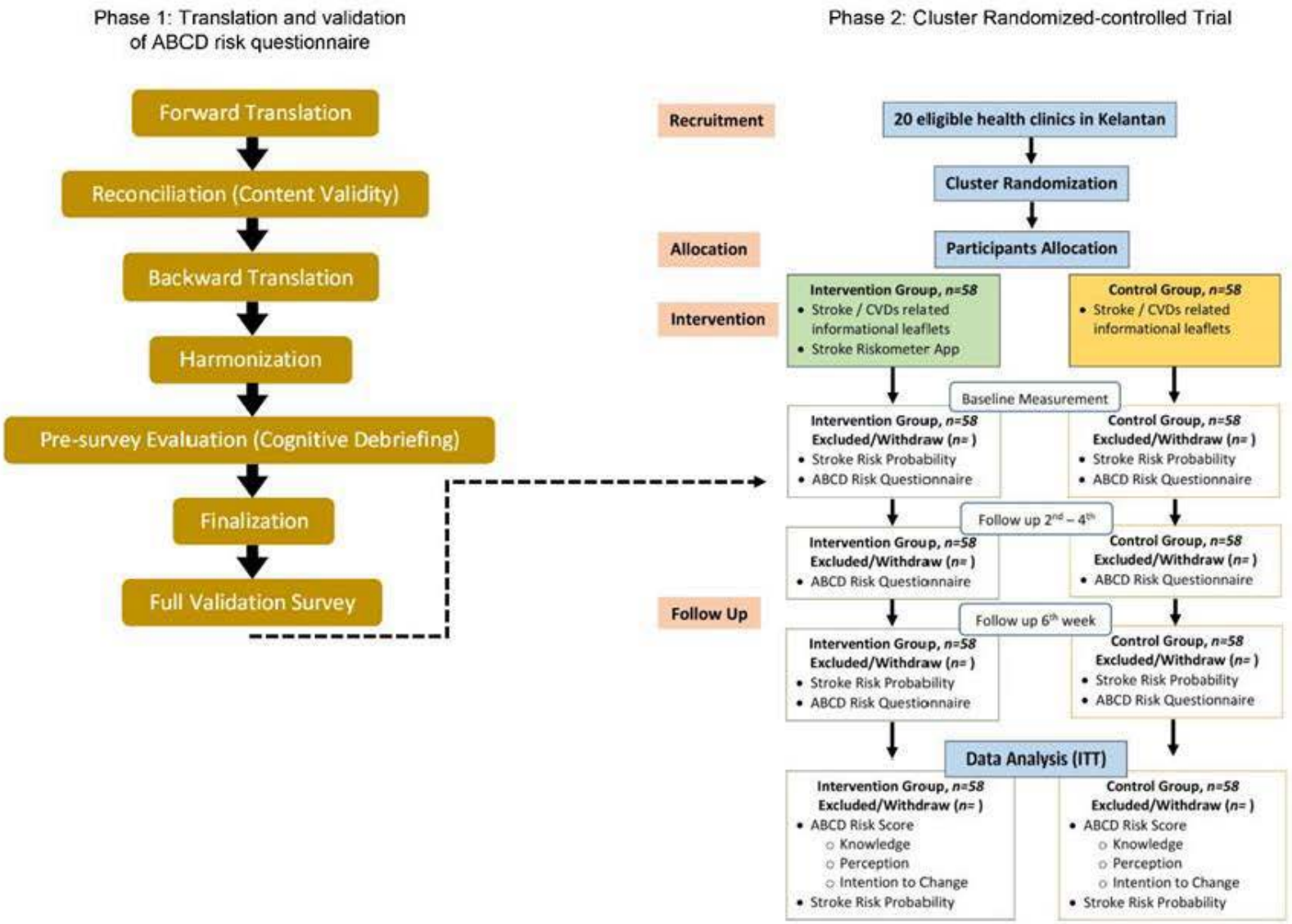

Figure 1.1 Overall flowchart of the study

1.8 Study Setting

1.8.1 Duration

Overall, the study was conducted over twenty-seven months, from October 2019 till December 2021. The first phase of the study was conducted from January 2020 to May 2020, while the trial phase was followed simultaneously from June 2020 to February 2021.

1.8.2 Area

This study was conducted in Kelantan, located in the northeastern corner of Peninsular Malaysia, with an area of 15,040 square kilometres (DOSM, 2020a). Narathiwat Province of Thailand borders it to the north, Terengganu to the south-east, Perak to the west and Pahang to the south. The third-largest state in Malaysia is divided into ten districts/*jajahans*, including Kota Bharu, Pasir Mas, Tumpat, Pasir Puteh, Bachok, Kuala Krai, Machang, Tanah Merah, Jeli, and Gua Musang with an estimated 1.9 million population in 2019 (DOSM, 2020a). Of the total population, 95.7% are Malay, followed by other ethnic groups such as Chinese, Indian, and others. While the age distribution reported 63.7% of the population is between 15–64 years old, 29.8% is between 0–14 years old, and 6.5% of the population is aged 65 years and above (DOSM, 2020a). Kelantan had a GDP per capita of RM13,593 in 2017, significantly lower than any other state in Malaysia and has a mainly agricultural economy dominated by rice, rubber and tobacco. Total 682,000 are in the labour force comprising skilled workers (19.1%), semi-skilled workers (67.8%) and low skilled workers (13.1%).

The first phase of the study involved four districts, namely Bachok, Machang, Tanah Merah and Pasir Puteh. While the second phase of the study involved another three districts, included Kota Bharu, Pasir Mas, and Tumpat. The districts were selected using purposive sampling as they contribute more than 60% of the adult population in Kelantan (DOSM, 2020a). The study area and data collection centres are illustrated in Figure 1.2.

1.8.3 Population

Generally, this study has referred to the adult (aged ≥18 years) population in Kelantan, Malaysia. In phase 1, the target population was the adult population in Kelantan who attended the government health clinics (HCs). At the same time, the source population/sampling pool was referred to the adult population in Kelantan who attended the government HCs during the study periods. The respondents were among the attendee list of selected government HCs in Bachok, Machang, Tanah Merah and Pasir Puteh, who fulfil the study criteria. The HCs were KK Labok, KK Selising, KK Cherang Ruku, KK Batu Gajah, KK Tanah Merah, KK Bachok and KK Gunong.

Meanwhile, in phase 2, the target population was the adult (aged 18–70 years) Kelantan who attended the government HCs and the private general practitioner (GP) clinics in Kelantan. This phase's source population/sampling pool was referred to the adult population in Kelantan who attended selected government and/or private GP clinics within the study periods.

The participants were selected among the attendee list of selected government and/or private GP clinics in Kelantan that fulfils the study criteria. It could be registered for a specific reason or accompanying anyone in the clinics. Twenty HCs (nine government and 11 private GP) from Kota Bharu, Pasir Mas, and Tumpat have been selected and received an official invitation letter and descriptive materials related to this study. Most of the selected HCs (among government) were frequently visited clinics with family medicine specialists (FMSs) and equipped with complete in-house medical facilities such as medical laboratory tests, plain x-rays and pharmacy. At the same time, another 11 private GP clinics were selected based on patient attendance, types of facilities, and services.

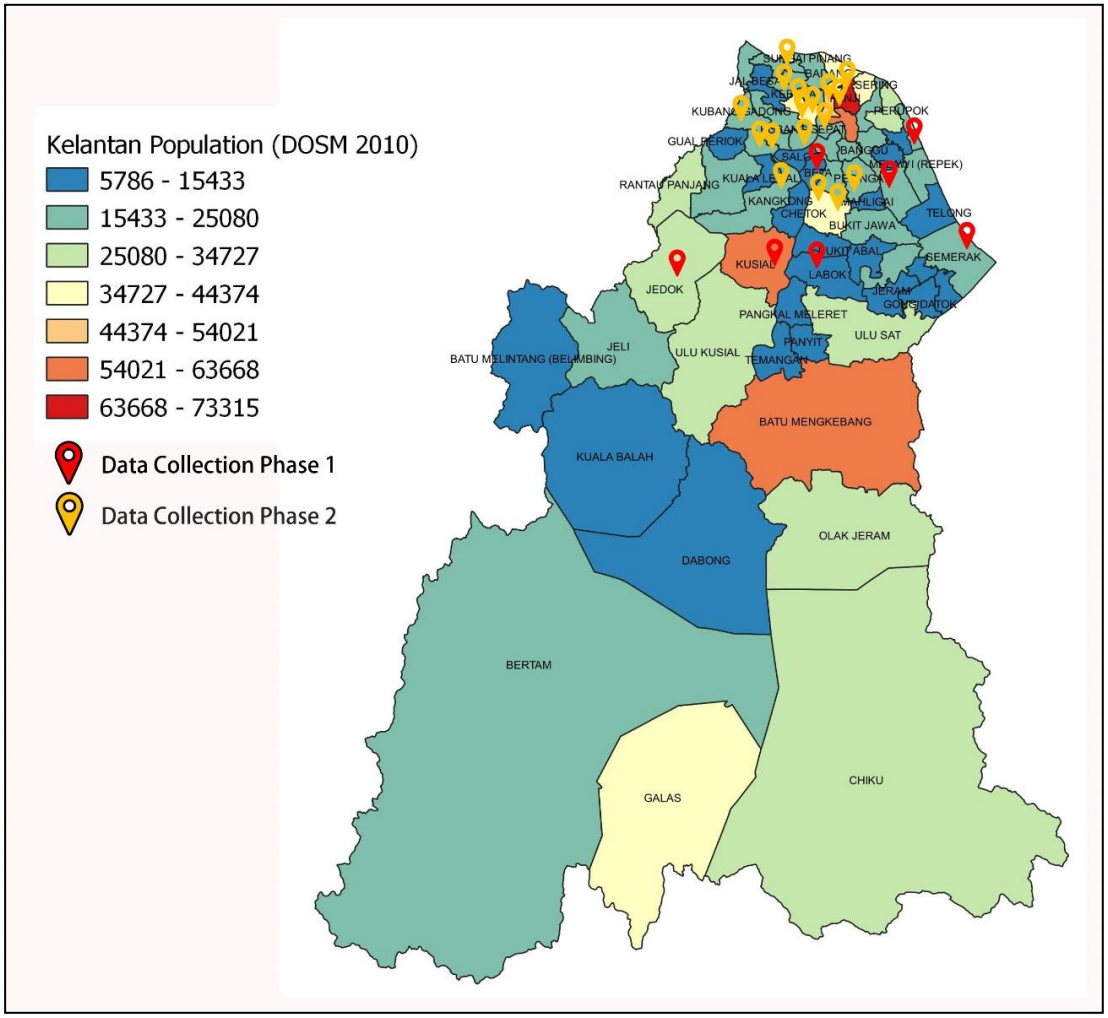

Figure 1.2 Study area and data collection centres

CHAPTER 2: LITERATURE REVIEW

2.1 Role of Personalised Risk Communication in Preventing Stroke

The unexpectedly high frequencies of modifiable risk factors that lead to stroke incidences indicate a need for aggressive primary and secondary prevention strategies. The primary prevention focuses on identifying the stroke risk in asymptomatic individuals and managing the known risk factors (Putaala *et al.*, 2012; Kim *et al.*, 2015b; Smajlović, 2015). Alternatively, personalised medicine is a growing field where a range of diagnostic tests, such as genetic screening and other risk stratification tools, including chronic diseases risk assessment are applied. The practice will enable the treating physician to develop evidence-based and individually tailored care plans (Kim *et al.*, 2015a). In the case of chronic diseases such as stroke and CVD, the personalised risk assessment summarises the recommended assessment pathway, interventions, treatment targets, and follow-up (Kim *et al.*, 2015b). Many studies concluded the importance of risk assessment for the young and middle-aged populations (Powers *et al.*, 2011; Wang *et al.*, 2016; Lee *et al.*, 2018a; Feigin *et al.*, 2021). Not only as a tool to predict the risk but also to differentiate those with high-risk and low- and moderate-risk and strengthen the motivation towards the behavioural changes (Wang *et al.*, 2016; Feigin *et al.*, 2017; Lee *et al.*, 2018a).

Besides, it is a personalised warning and lifestyle correction message about the stroke risk factors primarily among the younger age population (Powers *et al.*, 2011).

For example, for those at high risk, the warning message will motivate lifestyle modifications while having intensive treatment involving medications in order to have optimum effects (Powers *et al.*, 2011; Kim *et al.*, 2015b). Notably, over time, combined effects of modifiable (e.g., smoking and diabetes) and non-modifiable (e.g., age and sex) risk factors will escalate the absolute risk of getting stroke even when the initial risk is low. Here is the most significant advantage of doing continuous risk assessment. Moreover, knowledge and awareness are essential to strengthen the motivation of health management and induce changes in health behaviours (Flynn *et al.*, 2013; Lee *et al.*, 2018a). Personalised risk communication improved disease knowledge, perceived risk and decision quality, making them more aware of the information and assessment (Powers *et al.*, 2011; Flynn *et al.*, 2013). The Global Burden Disease study emphasised the importance of individual stroke risk assessment as a potential value of the measure for the primary prevention of stroke throughout a person's lifespan (O'Donnell *et al.*, 2016). Knowing that can suggest the strategy to reduce the burden of stroke and CVD and NCDs for both younger and older adults (Powers *et al.*, 2011; Collaborators, 2018; Feigin *et al.*, 2021).

Despite the greater role of personalised risk assessment in reducing the chronic diseases burden, it may be limited depending on the individual's level of autonomy (Kim *et al.*, 2015b). For example, those who are cognitively impaired may not express their preferences and values, and therefore would be unable to participate in the effort actively. In these instances, it would require more significant input from the family or carer.