

**INFORMAL CAREGIVER BURDEN
AMONG STROKE PATIENTS IN
EAST-COAST PENINSULAR MALAYSIA:
A SHORT-TERM LONGITUDINAL STUDY**

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Dissertation submitted in partial fulfilment of the
requirement for the Doctor of Public Health
(Epidemiology)

UNIVERSITI SAINS MALAYSIA

MARCH 2023

Acknowledgement

In the name of Allah S.W.T., The Most Gracious and The Most Merciful. This dissertation would not have been possible without His guidance and blessings. I am deeply grateful to my supervisors, Associated Professor Kamarul Imran Musa and Associated Professor Mohd Ismail Ibrahim, for their guidance and constant supervision in helping me write this dissertation. My sincere thank also goes to my research team; Dato Professor Dr Jafri Malim, Dr Tengku Alina, Dr Muhammad Hafiz, Dr Sanisah, Dr Mohd Zulkifli, Professor Sanjay Kinra, Dr Suresh Kumar Kamalakannan, Dr Illiatha Papachristou Nadal, Dr Feisul Idzwan, Dr Rose Izura, Dr Daryani, Datin Dr Zariah and Pn Norsima Nazifah. Special thanks to the Ministry of Health Malaysia and the Ministry of Higher Education for allowing the research to be conducted in Ministry of Health, Malaysia and Ministry of Higher Education, Malaysia facilities. I would love to mention my family, especially my wife, Mrs Khadijah, and my children, Muhammad Ammar and Qurratul Ain, who fully supported me emotionally in this journey. Special recognition to the Department of Community Medicine, Universiti Sains Malaysia and my classmates in Doctor of Public Health, Universiti Sains Malaysia 2019/2022, especially Epidemiology Specialty, Dr Aliff Ridzwan, Dr Mohd Hazwan, Dr Mohd Nasrullah and Dr Munira, who shared their knowledge, support and help during my Doctor of Public Health course.

Declaration

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

Mohd Azmi Bin Suliman

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List of Manuscript

The following articles were drafted.

1. First Manuscript

Title: Research on Stroke Caregiver, A Bibliometric Analysis

Authors: Mohd Azmi Bin Suliman, Mohd Khairul Anwar Bin Kamdi, Tengku

Muhammad Hanis, Kamarul Imran Musa

Status: Accepted (01 March 2023)

Journal: International Journal of Environmental Research and Public Health

2. Second Manuscript

Title: A Descriptive Analysis of Burden Among Informal Caregivers of Stroke

Survivors in East-Coast Peninsular Malaysia using Zarit Burden Interview (ZBI) and Caregiver Assessment of Function and Upset (CAFU)

Authors: Mohd Azmi Bin Suliman, Chen Xin Wee, Mohd Ismail Ibrahim, Kamarul Imran Musa, Nurfaten Hamzah, Iliatha Papachristou Nadal, Feisul Idzwan Mustapha, Mohd Zulkifli Abdul Rahim, Norsima Nazifah Sidek, Jafri Malin Abdullah, Sureshkumar Kamalakannan

Status: Submitted (26 October 2022), Ongoing review

Journal: Frontiers in Neurology

3. Third Manuscript

Title: Modelling the Trend of Burden Among Informal Caregivers of Stroke

Survivors in East Coast Peninsular Malaysia

Authors: Mohd Azmi Bin Suliman, Chen Xin Wee, Mohd Ismail Ibrahim, Kamarul

Imran Musa, Nurfaten Hamzah, Iliatha Papachristou Nadal, Feisul Idzwan Mustapha,

Mohd Zulkifli Abdul Rahim, Norsima Nazifah Sidek, Jafri Malin Abdullah,

Sureshkumar Kamalakannan

Status: Draft

List of Conference

During my DrPH course, these were the conferences that were attended.

Conference 1

Conference Name: 8th International Conference on Neurology and Epidemiology

Date: 30th March & 1st April 2022

Type: Poster Presentation

Poster Title: The burden of the informal caregivers for acute stroke survivors after one-month post-discharge

Authors: Mohd Azmi Suliman, Chen Xin Wee, Norsima Nazifah Sidek, Mohd Ismail Ibrahim, Tengku Alina Tengku Ismail, Kamarul Imran Musa

Conference 2

Conference Name: 3rd International Conference on Medical Science Technology

Date: 23rd & 24th November 2022

Type: Poster Presentation

Title: Does the burden among informal caregivers of stroke survivors reduce over time?

Authors: Mohd Azmi Bin Suliman, Chen Xin Wee, Mohd Ismail Ibrahim, Iliatha Papachristou Nadal, Sureshkumar Kamalakannan

Conference 3

Conference Name: R Conference 2022

Date: 26th & 27th November 2022

Type: Invited Speaker

Title: Modelling health measurement trend with linear mixed effect model using 'lme4'

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List of Abbreviations

CAFU	Caregiver Assessment of Function and Upset
GEE	Generalized Estimating Equations
GLMMs	Generalized Linear Mixed Models
HRPZ II	Hospital Raja Permaisuri Zainab II
HSNZ	Hospital Sultanah Nur Zahirah
HUSM	Hospital Universiti Sains Malaysia
LME	Linear Mixed Effect Model
mBI	Modified Barthel Index
mRS	Modified Rankin Scale
NCDs	Non-communicable Diseases
RM ANOVA	Repeated Measure Analysis of Variance
ZBI	Zarit Burden Interview

Abstrak

Latar Belakang: Strok adalah punca utama kematian dan hilang upaya diseluruh dunia. Ramai mangsa strok memerlukan bantuan untuk menjalani aktiviti harian. Serangan strok berlaku secara tiba-tiba, dan ahli keluarga perlu segera menjalankan tugas sebagai penjaga strok tidak rasmi. Namun begitu, ramai penjaga strok berasa terbeban dan terkiln semasa menjaga pesakit strok. Kajian mengenai beban penjaga pesakit strok adalah penting dalam membantu penggubal dasar untuk menilai keutamaan dalam memberi sokongan dan penyelidikan untuk mengkaji intervensi yang menyasarkan pesakit strok dan penjaga. Kajian in bertujuan untuk mengukur perubahan tahap beban penjaga tidak rasmi di kalangan pesakit strok di kawasan Pantai Timur Malaysia.

Kaedah: Dalam penyelidikan ini, tiga artikel kajian berkaitan telah dihasilkan. Pertama, analisis bibliometrik dijalankan untuk mengukur pengeluaran akademik dan kerjasama pengarang, institusi dan negara. Penerbitan dengan tajuk yang mengandungi “stroke” dan “caregiver” telah dicari menggunakan pangkalan data *Clarivate’s Web of Science*. Kedua, analisis deskriptif dijalankan untuk mengenalpasti taburan pesakit strok, penjaga pesakit strok dan beban penjaga pesakit strok. Pesakit strok dan penjaga mereka telah dikenalpasti di tiga hospital yang terdapat di kawasan Pantai Timur Malaysia. Beban penjaga diukur menggunakan *Zarit Burden Interview* versi Bahasa Malaysia (MZBI) dan *Caregiver’s Appraisal of Functions and Upset* versi Bahasa Malaysia (Malay-CAFU), melalui panggilan telefon sebanyak empat kali dalam masa tiga bulan selepas pesakit dibenarkan keluar hospital. Ketiga, menggunakan data yang sama, analisis inferensi dijalankan menggunakan *linear mixed effect model* untuk menganggarkan perubahan beban penjaga pesakit strok, dan kesan tahap pergantungan pesakit strok ke atas perubahan beban tersebut.

Keputusan: Analisis bibliometrik yang dijalankan mendapati terdapat 678 penerbitan diterbitkan diantara 1989 sehingga 2022 dengan tajuk yang mengandungi istilah “*stroke*” dan “*caregiver*”. Kebanyakan penerbitan tersebut diterbitkan dalam bahasa Inggeris, dihasilkan di Amerika Syarikat (28.6%), Universiti of Toronto (9.5%), oleh jurnal “*Topics in Stroke Rehabilitation*” (5.8%) dan Family Bakas merupakan penulis yang paling produktif. Bagi beban penjaga strok, 85 pesakit strok dan 155 penjaga tidak rasmi telah di temuduga. Pesakit strok mempunyai secara purata dua orang penjaga, kebanyakannya wanita (58.1%). Beban penjaga didapati menurun, dengan min (SD) bagi MZBI berkurang dari 27.42 (12.73) pada minggu pertama kepada 17.77 (11.20) pada bulan ketiga, manakala IADL Malay-CAFU Upset berkurangan dari 1.14 (0.94) kepada 0.62 (0.64) dan ADL Malay-CAFU dari 1.36 (1.00) kepada 0.78 (0.65) dalam tempoh yang sama. Apabila mengambil kira kesan kelompok menggunakan *linear mixed effect model*, MZBI menunjukkan pengurangan dari minggu pertama kepada bulan ketiga [beta = -10.76 (95% CI = -11.94, -9.57)], dan Malay-CAFU di bulan ketiga [beta = -0.68 (95% CI = -0.80, -0.57)]. Beban adalah lebih tinggi di kalangan penjaga yang menjaga pesakit strok yang memerlukan lebih bantuan; namun kadar pengurangan beban tidak berbeza dengan ketara.

Kesimpulan: Kajian mengenai penjaga pesakit strok adalah meluas, namun kajian berterusan yang berkaitan adalah penting. Topik yang berkaitan termasuklah pengalaman penjaga strok, tahap dan sebab beban penjaga dan intervensi dalam menguruskan beban penjaga. Pesakit strok biasanya dijaga oleh beberapa penjaga dalam satu masa, terutamanya oleh ahli keluarga. Namun, penjaga mungkin berasa terbeban semasa memberi penjagaan, tetapi beban biasanya berkurangan dalam tempoh tiga bulan pertama. Oleh itu, penggubal dasar dan perawat perlu memulakan sokongan dan intervensi untuk pesakit dan penjaga seawal pesakit diberi diagnosis.

Abstract

Background: Stroke is a leading cause of death and disability worldwide. Many stroke survivors require assistance for basic activities of daily living (ADL) and instrumental activities of daily living (IADLs). Stroke attacks happen suddenly, and family members must act as informal caregivers swiftly. Unfortunately, many caregivers feel upset or burdened during caring for stroke survivors. Studies on caregiver burden are vital in helping policymakers prioritise support and researchers develop interventions targeting stroke survivors and caregivers. This study aims to measure the burden among informal caregivers for stroke survivors in East Coast Peninsular Malaysia.

Method: In this research, three related research articles were produced. First, a bibliometric analysis was done to measure the academic production and collaboration of the author, institutions, and countries. The publications with a title containing “stroke” and “caregiver” were searched using Clarivate’s Web of Science database. Second, a descriptive analysis was done to describe the distribution of stroke survivors, informal caregivers, and the burden of stroke caregivers. Stroke survivors and their caregivers were recruited from three East Coast Peninsular Malaysia hospitals. The caregiver burden was measured using the Malay version of Zarit Burden Interview (MZBI) and the Malay version of Caregiver Appraisal of Function and Upset (Malay-CAFU) via phone call four times within the first three months post-discharge. Third, using the same data, an inferential analysis was done using a linear mixed effect model to estimate the stroke caregiver burden trends and the effect of stroke survivors’ dependency level on the burden trajectory.

Result: In the bibliometric analysis, it was found that 678 publications dated from 1989 to 2022 with titles containing the terms “stroke” and “caregiver”. The publications were primarily published in the English language. The publications

mainly were produced in the USA (28.6%), by The University of Toronto (9.5%), in ‘Topics in Stroke Rehabilitation’ journal (5.8%), and the most productive author was Tamilyn Bakas (3.1%). For the caregiver burden, 85 stroke survivors and 155 informal caregivers were recruited. On average, the stroke survivors had two caregivers, mainly female (58.1%). In the first three months, the burden was reduced, with the mean (SD) of MZBI reduced from 27.42 (12.73) in the first week to 17.77 (11.20) in the third month, while IADL Malay-CAFU Upset reduced from 1.14 (0.94) to 0.62 (0.64) and ADL Malay-CAFU from 1.36 (1.00) to 0.78 (0.65) in the same period. When accounted for the clustering effect using a linear mixed effect model, the MZBI shows a reduction from 1-week post-discharge to 3-month [beta = -10.76 (95% CI = -11.94, -9.57)], and Malay-CAFU at 3-month [beta = -0.68 (95% CI = -0.80, -0.57)]. The burden was higher among caregivers with dependent stroke survivors; however, the rate of reduction of burden was not significantly different.

Conclusion: The studies on stroke caregivers were extensive; however, ongoing studies on the field are essential. Areas of interest in the field include the experience of stroke caregivers, the level and the determinant of burden and the interventions in managing the burden. Many stroke survivors were taken care of by several informal caregivers, especially family members. However, the caregivers may feel burdened while giving care; however, the burden is usually reduced in the first three months post-stroke. Therefore, policymakers and healthcare providers should initiate support and interventions for caregivers and stroke survivors as early as at the time of diagnosis.

Chapter 1 Introduction

1.1. Overview of Stroke

Stroke is a collective term representing cerebrovascular disease in which vascular circulation is lost to the central nervous system. Stroke may cause various disabilities, including sensory-motor, cognitive-perpetual, psychological and behavioural. Stroke is common worldwide, with significant mortality and morbidity (GBD 2019 Diseases and Injuries Collaborators, 2020). With advancements in medical treatment and health management, more stroke patients survive with lower morbidity. However, stroke survivors may need to adapt to changes post-stroke, especially if they develop residual disability (Sarıkaya, Ferro and Arnold, 2015). In reducing stroke morbidity and mortality, various preventive action needs to be taken at all levels of prevention and held responsible by multiple stakeholders (Pandian *et al.*, 2018).

In ensuring good quality of life among stroke survivors, it is essential to have good acute medical treatment, but stroke survivors may also require prolonged medical attention and rehabilitation to improve their post-stroke condition (McCurley *et al.*, 2019). Furthermore, stroke rehabilitation can range from hospital-based to home-based rehabilitation programs. Thus management of post-stroke care requires multidisciplinary involvement (Abdul Aziz *et al.*, 2014).

1.2. Stroke Caregiver

Stroke episodes can be sudden, and many stroke patients and their relatives are unprepared. Therefore, not only do stroke survivors need to adapt to their condition, as they may develop a residual disability, but their relatives also need to adapt to the new norm, taking over some of the responsibilities previously held by the stroke

survivor and taking care of the stroke survivors (Wagachchige Muthucumarana, Samarasinghe and Elgán, 2018).

While caring for loved ones can be gratifying, caring for those with morbidity can strain the caregivers too. The burden of care is not only due to physical support but also financial, emotional and spiritual support, in addition to adapting to the new lifestyle. Many caregivers also feel missing out due to their commitment to caring for stroke survivors (Gertrude *et al.*, 2019). In addition, the burden of caring may lead caregivers to anxiety, stress and depression. Even worse, caregivers are often neglected by the health practitioner and left out of rehabilitation programs (Loh *et al.*, 2017; Bierhals, Low and Paskulin, 2019; Ugur and Erci, 2019).

1.3. Problem Statement & Study Rationale

1.3.1. Problem Statement

Every year, more stroke patients survive attacks and were discharged with less mortality and morbidity (Chen *et al.*, 2019). However, stroke patients may develop significant residual disability. These disabilities increase the survivors' dependence on caregivers, especially their family members. Therefore, with the increased number of stroke survivors, stroke caregivers were expected to increase too (Caro, Costa and Da Cruz, 2018).

Research on stroke care and stroke caregiver is extensive; however, local culture and social values often influence local community perception, which may lead to different perceptions of stroke caregivers in specific populations (Camak, 2015).

Currently, studies on the local perception of stroke caregiver burden are scarce, and most were cross-sectional studies (Abdul Hadi *et al.*, 2016; Rahman *et al.*, 2018).

We currently lack research that tries to quantify the dynamics of the burden of stroke caregivers in the long term.

1.3.2. Justification

Most stroke rehabilitation programs require the involvement of those around the stroke survivors, especially family members and carers. First, this study tries to understand the current academic environment and trends regarding the studies of stroke caregivers. Understanding the current trends of stroke caregivers' studies can help guide us to focus on the area that requires priority.

Next, this study also explores the unique information regarding stroke survivors, their caregivers and the dynamic of stroke caregiver burden. In addition, the information provided will be helpful to healthcare workers involved in the stroke rehabilitation program, such as the domiciliary care team, to plan the stroke survivors' home care programme.

This study also aims to establish the relationship between stroke survivors' dependence level and caregiver burden. With this information, a clinician can tailor their discharge plan to optimise the stroke survivors' outcome and long-term care at home.

The longitudinal study also provided a more accurate picture of the caregiver burden, especially in measuring the dynamics of the burden. The longitudinal study is also valuable for inferring cause-and-effect relationships rather than merely measuring association relationships.

1.4. Objective

The objectives of this study are listed according to each research paper.

1.4.1. Objectives for Research Paper 1

General Objective: To explore the research pattern related to stroke caregivers.

Specific Objectives:

1. To identify influential authors related to stroke caregivers.
2. To identify journals that were most represented in studies related to stroke caregivers.
3. To visualize collaboration patterns between countries, authors, and institutions related to stroke caregivers' studies.
4. To identify top keywords or hotspots related to stroke caregivers' studies.

1.4.2. Objectives for Research Paper 2

General Objective: To measure the burden of caring for stroke survivors among their caregivers in East Coast Peninsular Malaysia.

Specific Objectives:

1. To describe the characteristic of stroke survivors and their informal caregivers in East Coast Peninsular Malaysia
2. To describe the burden of caregiving in a short-term period, from discharge to three months post-discharge.
3. To measure the stroke informal caregivers' burden, based on the stroke survivor's dependence levels and the caregivers' gender, from discharge to three months post-discharge.

1.4.3. Objectives for Research Paper 3

General Objective: To estimate the trend of caregiver burden among informal caregivers of stroke survivors in East Coast Peninsular Malaysia.

Specific Objectives:

1. To estimate the trend of burden (ZBI and CAFU-U) of caring among stroke caregivers from baseline up to 3-month post-discharge in east-coast peninsular Malaysia.
2. To model the effect of survivor's dependence level with the trend of ZBI and CAFU-U.

1.5. Thesis Structure

This thesis focuses on using current and established epidemiological and statistical methods to develop a model of the dynamic of burden among informal caregivers of stroke survivors over three months. The information provided in this study would help improve the overall understanding of the trend of stroke caregiver burden, specifically in Kelantan, where data on stroke caregivers are scarce.

First, the current knowledge on stroke caregiver burden was explored quantitatively with bibliometric analysis, in which the number of publications produced in the field by authors, journals, institutions and countries was calculated. Highly reoccurrence keywords were also explored to find hotspots in the field (Paper 1).

Then, stroke survivors and their informal caregivers were recruited from three different hospitals in east-coast peninsular Malaysia – including Hospital Universiti Sains Malaysia, Hospital Raja Permaisuri Zainab II and Hospital Sultanah Nur Zahirah. Their demographic information was collected on baseline (prior discharge),

and the stroke caregiver burden was measured at four different times, from one-week post-discharge (as baseline) to three months post-discharge. Here, descriptive analysis was used to understand the current population distribution and the caregiver burden, the demographic information, and the level of caregiver burden (Paper 2).

Lastly, a linear mixed effect modelling was applied to the same data to model the trend of caregiver burden and the effect of the survivor's dependence level on stroke caregiver burden (Paper 3).

Chapter 2 Literature Review

2.1. Stroke Overview

A stroke is characterized by a neurological deficit attributed to an acute focal injury of the central nervous system. The deficits may include cerebral infarction, intracerebral haemorrhage, and subarachnoid haemorrhage. Typical stroke symptoms include sudden unilateral weakness, numbness, visual loss, altered speech and non-orthostatic vertigo.

Stroke significantly contributes to disability and death worldwide (GBD 2019 Diseases and Injuries Collaborators, 2020). Even though stroke has an acute onset, it should be seen as a chronic disease with an increased risk of death. Stroke also shares risk factors with other non-communicable diseases (NCDs), and many stroke patients have multiple NCDs comorbidities (Sarikaya, Ferro and Arnold, 2015).

A multidisciplinary team should manage an acute stroke attack, with appropriate medical treatment focusing on restoring vascular circulation to the affected brain area, followed by long-term stroke care. In addition to having multiple NCDs comorbidities, many stroke survivors carry lifelong physical, emotional, cognitive, and economic burdens. Furthermore, physical disability requires stroke survivors to adjust their daily activities, and adjusting to new norms may also lead to stress, anxiety, and depression. Thus, various measures must be taken to prevent recurrent stroke episodes, control current disability and symptoms, and improve quality of life, with rehabilitation (McCurley *et al.*, 2019).

Stroke, as with other NCDs, is preventable and treatable. Therefore, health education should aim to increase public awareness, especially rapid identification of stroke symptoms. FAST test, an acronym for Face, Arm, Speech and Time, is a simple

test that can be done by the public, allowing the public to act fast, improving the stroke patient's survival and reducing the chance of lifelong disability (Wolters *et al.*, 2018).

Stroke incidence was worldwide, affecting everyone, directly or indirectly, especially stroke survivors' family members and carers. In addition, among stroke survivors, the next of kin often suffer emotionally, economically and socially from the stigma associated with stroke, associated NCDs and the disability (Rigby, Gubitza and Phillips, 2009).

2.2. Post-stroke Care

In Malaysia, more stroke patients are discharged with lower morbidity and mortality (Chen *et al.*, 2019). However, stroke survivors may experience residual disability, and post-stroke care should focus on rehabilitation services, aiming to increase the stroke survivors' independence and ability. Stroke rehabilitation requires a multidisciplinary team approach involving the stroke survivors, family members, physicians, nurses, therapists and social workers. A multidisciplinary team approach is vital because rehabilitation concerns the prevention of complications and covers various aspects of the survivor's life, including physical and emotional health and integration into the community (Teasell *et al.*, 2012).

In Malaysia, when the stroke survivors are discharged from the hospital, their medical care and rehabilitation will be continued in various sites, including primary care – both public and private health care, hospital-based rehabilitation services, community-based rehabilitation services or nursing home. However, the lack of an integrative care pathway, from acute medical care to long-term post-stroke care, affects stroke survivors to access personalized care that best suits them. In addition, many stroke survivors feel there was a lack of written information during the transfer

of care after discharge from the hospital and information regarding rehabilitation therapy services (Abdul Aziz *et al.*, 2014).

Even in short periods, some stroke survivors may significantly improve in the first three months. However, the improvement may vary over more extended periods. Highly motivated stroke survivors and those with good motor function were good predictors for improvement, whereas stroke survivors with poor motor function had a high risk of withdrawal from rehabilitation programs (Vahlberg *et al.*, 2017).

2.3. Informal Caregiver for Stroke Survivors

There are various reasons for those taking care of their loved ones with comorbidities. Common reasons include love and attachment toward the stroke survivor and giving something back. The caregiver felt it was natural for them to take responsibility without expecting payment. They also hope their loved one improves and enjoy their life. Some caregivers also feel that caring for their loved ones gives them new insight into the life (Moral-Fernández *et al.*, 2018).

The caregiver is often unprepared, balancing their routine life with taking care of the stroke survivors. Many caregivers complained that their routines were significantly changed adversely. In addition to their routine life, with many already having responsibilities, they also need to cover some responsibilities that the stroke survivors previously undertook and take care of the stroke survivors themselves. As a result, some of them feel isolated and miss social activities such as family gatherings. Those of lower social economic status would be more affected, as their resources were become more restricted with the burden of caring for the stroke survivors. The lifestyle and buying power changes affect their quality of life (Wagachchige Muthucumarana,

Samarasinghe and Elgán, 2018). A short longitudinal study by Bierhals, Low and Paskulin (2019) found that the quality of life among caregivers worsens over time.

Caring for stroke survivors may also have a psychological impact. For example, it was reported that anxiety dan depression was common among stroke caregivers, with 21.4% having anxiety symptoms and 40.2% having depressive symptoms (Loh *et al.*, 2017). In addition, it was also reported that anxiety, depression and burden of care were correlated, with some studies reporting medium-to-large effect sizes (Hu *et al.*, 2018; Oni *et al.*, 2019).

2.4. Stroke Caregiver Burden

Unfortunately, caring for stroke survivors may also negatively impact the caregivers. Providing continuous care to the stroke survivors, often with a disability, can be stressful for the caregivers. Some stroke survivors may even develop not only physical disabilities but also disability in terms of behavioural, communication and cognitive. Caregivers are often caught off guard and unprepared to carry the responsibility of providing care. Most adult caregivers, especially the survivors' spouses, may also have to deal with their health and care for the stroke survivors (Camak, 2015).

In Malaysia, Abdul Hadi *et al.* (2016) found that the caregiver burden among stroke caregivers in Kelantan was moderate. The authors' measured burden using Zarit Burden Interview found that the mean (SD) of burden was 25.42 (6.45). The burden was similar to other studies worldwide (Imarhiagbe *et al.*, 2017; Caro, Costa and Da Cruz, 2018; Hu *et al.*, 2018). However, changes or trends in the burden over time differed among different populations. For example, in the Netherlands, it was found

that most caregiver burden remains stagnant within one year, while a study in China found that the caregiver burden improves within six months (Zhu and Jiang, 2018).

In Malaysia, most stroke survivors are taken care of by informal caregivers. These informal caregivers were mostly female, most of whom were the stroke survivors' daughters (Abdul Hadi *et al.*, 2016). Achilike *et al.* (2020) found that higher caregiver burdens were reported among female caregivers than male caregivers. In addition, higher socioeconomic status among caregivers reported lower caregiver burden (Abdul Hadi *et al.*, 2016).

The caregivers' psychological status was also associated with the caregiver burden. For example, one study reported that depression and burden among caregivers had reciprocated relationship, in which depression symptoms can be predictors for high caregiver burden and vice-verse – the high burden is a risk for depression among caregivers (Achilike *et al.*, 2020).

Apart from the caregiver, stroke survivors can also be predictors of high caregiver burden. For example, a study by Abdul Hadi *et al.* (2016) reported that bed-bound stroke survivors had a higher caregiver burden, which concurs with the study by Zhu and Jiang (2018) and Achilike *et al.* (2020), which found a higher caregiver burden taking care of stroke survivors with poor functional level. In addition, stroke survivors with depressive symptoms were known to be associated with a higher caregiver burden (Zhu and Jiang, 2018).

While the intervention for stroke survivors was abundant, the intervention for stroke caregivers was limited. In post-stroke care, any interventions that cater to stroke survivors and the caregivers, such as home education for stroke survivors, will reduce the caregiver burden (Ugur and Erci, 2019).

2.5. Modelling the Effect of Caregiver Burden

2.5.1. Current Knowledge

Caregiver burden, or the perception of caregivers' burden toward caregiving, may adversely affect the caregiver's emotional, social, financial, physical and spiritual functioning. Since the burden is not a physical material, unlike body weight (or mass), but a concept of perception (like pain), it can be quantified using psychometric assessment tools. Various tools used to measure the perception of caregiver burden, and each tool may measure different dimensions – such as physical, economical, psychological and quality of life affected by caregiving activities, were available, such as Zarit Burden Interview (ZBI) (Zarit, 2018), Caregiver Burden Scale (CBS) (Elmstahl, Malmberg and Annerstedt, 1996) and Caregiver Burden Inventory (CBI) (Novak and Guest, 1989). These tools were a set of questionnaires, with scores for each response corresponding to the level of burden perceived by the caregivers.

The level of burden can be described with a descriptive statistic such as mean and median score - depending on the data distribution. Many authors also categorised the score and described it with count and percentage. When measuring the burden level, researchers commonly conduct cross-sectional studies and find the determinant of the burden using correlation tests and regression tests (Abdul Hadi *et al.*, 2016; Achilike *et al.*, 2020).

However, like other health measurements, caregiver burdens were dynamic (i.e., not static). The cross-sectional study, however, cannot estimate caregiver burden changes. In addition, some of the caregiver burden predictors may also be time-dependent. Since the caregiver burden may change over time, the burden measurement is correlated.

2.5.2. Generalized Linear Mixed Models (GLMMs)

Some research data were presented in a multilevel structure, where individual levels might be nested or clustered into higher organizational levels. While modelling for an individual might be adequate to explain most of the relationship, we might want to consider the variation at the cluster level; thus, multilevel modelling was usually used (Bingenheimer and Raudenbush, 2004). For example, a study by Reeves et al. (2010) measures the quality of acute stroke care for stroke patients in different hospitals. Likewise, the caregiver burden can be measured, in which the caregivers were nested to their care recipients – the stroke survivors. At the time of writing, most studies related to stroke caregivers were done either on the caregiver themselves (Zhu and Jiang, 2018; Achilike *et al.*, 2020) or one caregiver and one care recipient dyad relationship (Pont *et al.*, 2020). None of the studies considers that stroke survivors may have more than a single caregiver, which can be clustered among the care recipient.

A generalized linear mixed model allows researchers to model fixed and random effects. The fixed effect is the explanatory variable in standard linear regression, for example, the effect of gender on the caregiver burden. Meanwhile, the random effect can be understood by the grouping factor that we tried to control. For example, when caregivers were nested with the care recipient, the care recipient (or the stroke survivors) is the grouping factor. While we were primarily interested in the fixed effects, the adjustment needs to be done for the random effect if we suspect the variance in the data was affected by the nested structure. GLMMs also allow researchers to model each random effect with random intercepts, random slopes or both (Gueorguieva and Krystal, 2004).

2.5.3. Correlated Data in Longitudinal Studies

In longitudinal studies, for each participant, data will be collected several times. Therefore, the data was not independent for each measurement and was considered nested to the participants. The structure of longitudinal data is another form of a multilevel structure.

For longitudinal studies, various statistical tests were used to measure the relationship, including dependent t-test, repeated measure analysis of variance (RM ANOVA), generalized linear mixed models (GLMMs), generalized estimating equations (GEEs), growth latent model and time series models. The distinctive feature of longitudinal studies is that the data were correlated, in which each measurement for every individual was dependent on the measurement prior to it, specific to the individual. The measurements can also be considered nested to the participants, akin to a multilevel structure.(Burke *et al.*, 2018; Bierhals, Low and Paskulin, 2019; Connors *et al.*, 2020).

2.5.4. Repeated Measure Analysis of Variance as Alternative

RM ANOVA was more widely used due to being more straightforward to interpret than GLMMs (Gueorguieva and Krystal, 2004; Park, Cho and Ki, 2009). While both RM ANOVA and GLMMs can measure within-subject and between-subject variation, there are various reasons why GLMMs are preferable in some situations. One of the limitations of RM ANOVA is missing data. RM ANOVA requires complete data set; however, missing data is common and expected, particularly in longitudinal studies (Abdullah *et al.*, 2021). There are various ways to handle missing data, such as data deletion. List-wise deletion, in which the subject with missing data is removed, will reduce the number of samples, reducing the

statistical test's power. Another standard option to handle missing data is by data imputation, in which new data is calculated to fill in the missing data. Unfortunately, data imputation can be very complex. First, authors need to ascertain the nature of the missing data – whether it is missing completely at random (MCAR), missing at random (MAR) or missing not at random (MNAR). There are also various ways to do data imputations, such as mean imputation, regression imputation, interpolation and extrapolation imputation, or multiple imputations (Austin *et al.*, 2021).

In RM ANOVA, the time component is treated as categorical. For longitudinal studies, the time gap between each data collection may or may not be consistent. For example, a study by Pucciarelli *et al.* (2018) collected data at four different times with consistent time gaps, which were at baseline, 3-month, 6-month, 9-month and 12-month, while the study by Olai, Borgquist and Svärdsudd (2015) collect data at three different times with varying gap, which were at baseline, 3-months and 1-year. When treated time as categorical, the statistical software may be unable to recognize the importance of varying time gaps between the time data was collected (Maurissen and Vidmar, 2017).

2.6. Conceptual Framework

Based on the literature review, the conceptual framework for this study can be visualised in Figure 2.1.

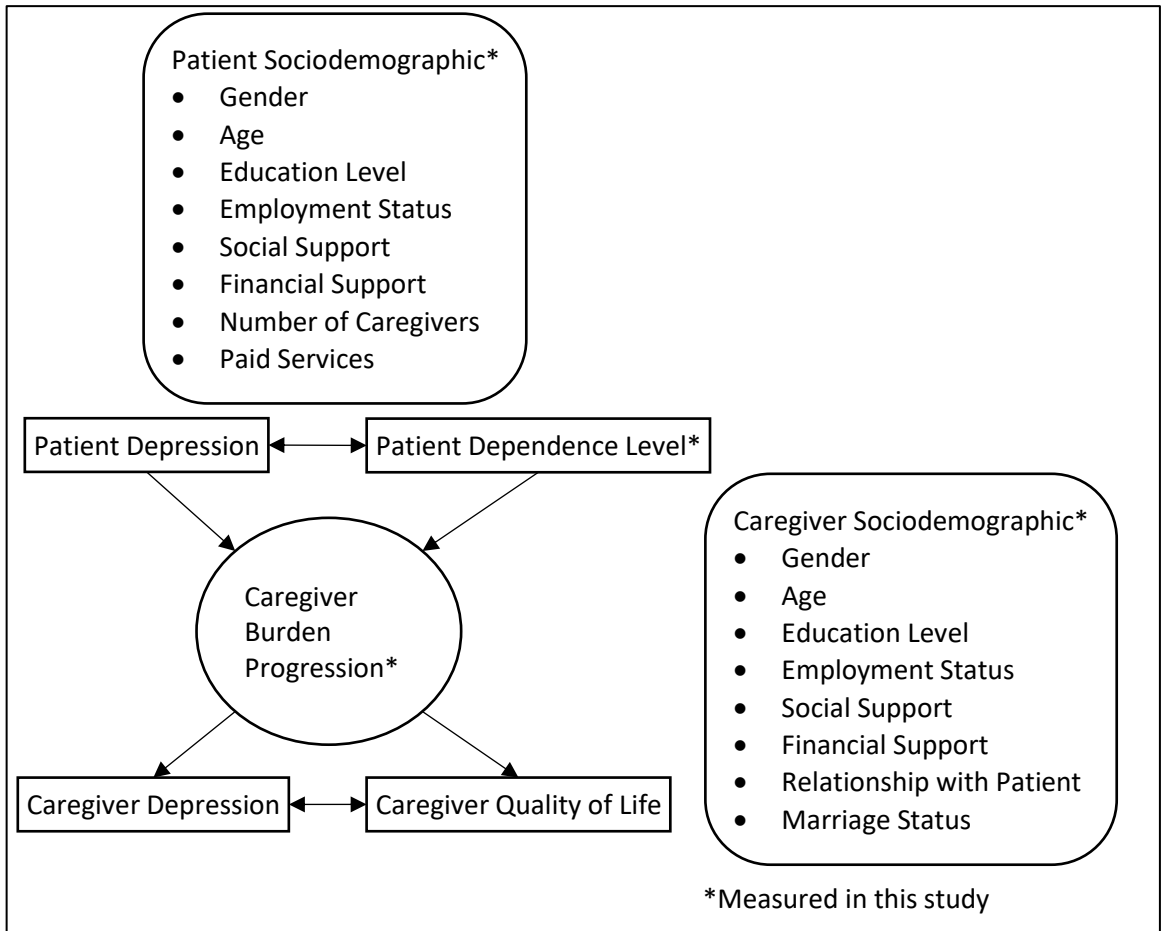


Figure 2.1: Conceptual Framework

Chapter 3 Methodology

3.1. Research Design and Settings

This study consists of a short-term longitudinal study conducted in Kelantan and Terengganu. The two states were in the east coast region of peninsular Malaysia.

Kelantan is the most northeast state of peninsular Malaysia, bordered by Thailand in the north, the South China Sea and Terengganu in the east, Pahang in the south and Perak in the west. There were eight government hospitals and one university hospital in Kelantan. The state hospital, Hospital Raja Permaisuri Zainab II, and the university hospital, Hospital Universiti Sains Malaysia, are located at Kota Bharu, the capital city of Kelantan. The Malay ethnic constitutes the majority of Kelantan's population – about 94%, with other minority ethnicities including Siamese, Chinese, Indian and Orang Asli.

Terengganu is bounded by Kelantan in the northwest, the South China Sea in the east and Pahang in the southwest. Kuala Terengganu is the capital city of Terengganu state. There are six government hospitals and one university hospital in Terengganu. The state hospital, Hospital Sultanah Nur Zahirah, is located at Kuala Terengganu. Like Kelantan, 95% of the Terengganu population is Malay ethnic, with other minority ethnicities including Chinese, Indian and Orang Asli.

The study was conducted between January 2021 to December 2021.

3.2. Study Population and Sampling Method

3.2.1. Study Population

Our reference population consisted of stroke caregivers in East Coast Peninsular Malaysia, whereas our target population consisted of stroke caregivers currently taking care of stroke survivors in Kelantan and Terengganu. The source

population or the sampling pool were the informal caregivers of stroke survivors recently admitted to Hospital Universiti Sains Malaysia (HUSM), Hospital Raja Permaisuri Zainab II (HRPZ II) and Hospital Sultanah Nur Zahirah (HSNZ). The sampling frame was among informal caregivers of stroke survivors admitted during the study period (January – December 2021).

3.2.2. Subject Criteria

Stroke Survivors

1. Inclusion Criteria: We included all stroke survivors recently admitted to HUSM, HRPZ II or HSNZ for acute stroke attack, age 18 or older.
2. Exclusion criteria: We exclude the stroke survivors who reported that they have any paid assistance, such as nurses or maids.

Informal Caregivers

1. Inclusion Criteria: We included all informal caregivers taking care of stroke survivors during the study, age 18 or older.
2. Exclusion criteria: We exclude the informal caregivers that may have a cognitive problem (based on the assessor's subjective assessment) that may have a problem responding to our questionnaires.

3.2.3. Sampling Method

All eligible caregivers were invited to participate in the study.

The treating physician identified stroke patients admitted to Hospital USM, HRPZ II and HSNZ during the study duration. Subsequently, a trained research assistant approached the stroke survivors and their caregivers and invited them to

participate in this study. If the stroke survivors have several caregivers, they may need those caregivers to be invited to the study. Prior written and informed consent was obtained from every participant.

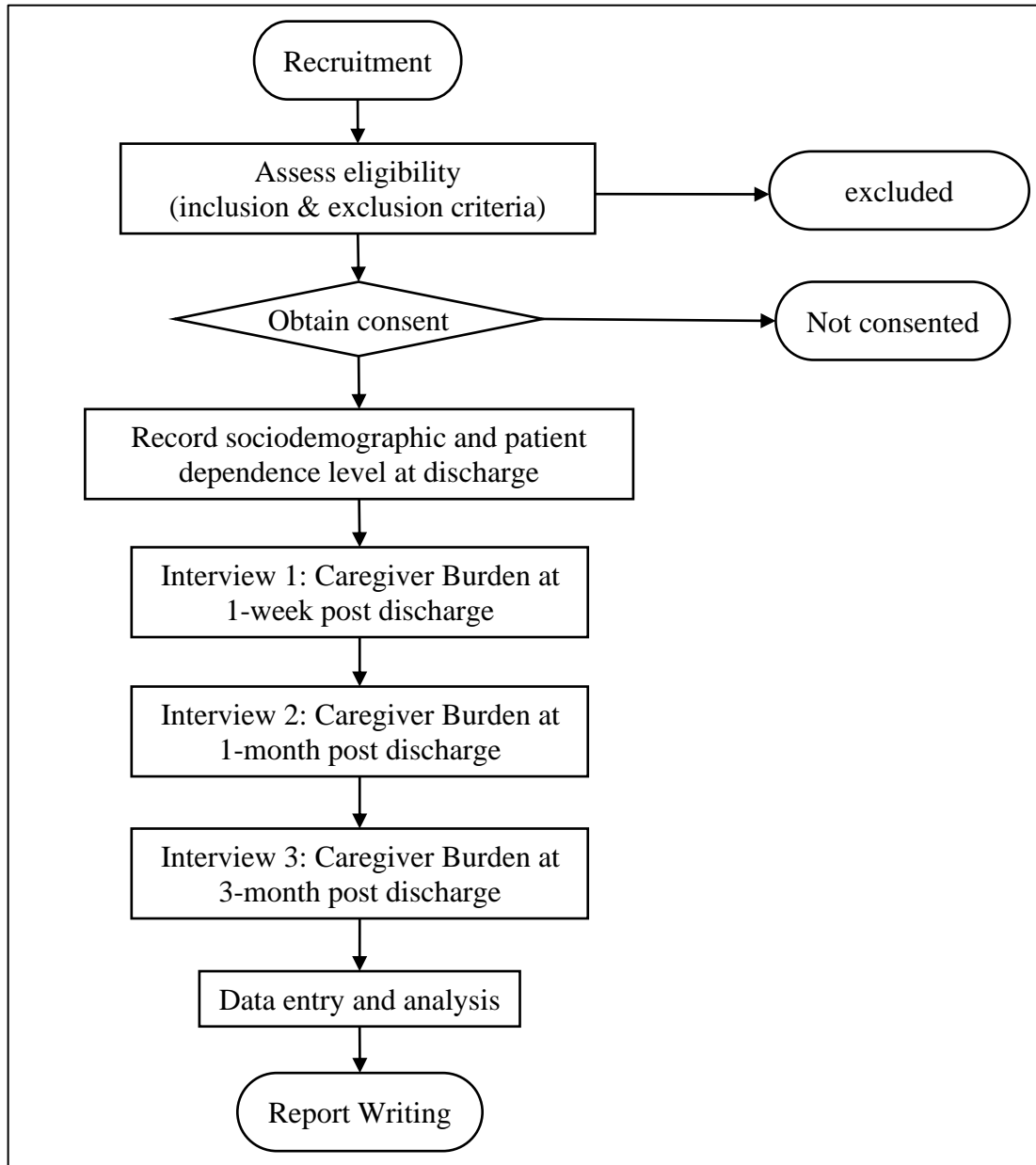


Figure 3.1: Subject Recruitment and Study Flowchart

3.3. Research Tools and Data Collection

3.3.1. Study Proforma

Study proforma was used to collect demographic information on stroke survivors and caregivers.

3.3.2. Modified Rankin Scale – Malay Version

Modified Rankin Scale (MRS) – Malay version was used to collect stroke survivors' functional levels. mRS has been widely used in clinical and research settings in measuring the patient's functional level, especially in stroke settings. mRS had seven levels, ranging from no symptoms (score 0) to death (score 6) (Ganesh *et al.*, 2018), with many studies opting to categorize the score into independence (mRS = 0-2), dependence (mRS = 3-5) and death (mRS = 6) (Balu, 2009; Cioncoloni *et al.*, 2012). While initially used by trained individuals (researchers or health practitioners) to assess stroke patients by direct observation, mRS scores can also be used via phone interviews (Chen *et al.*, 2019). The study found that despite the reported observed agreement between three raters of 65.9%, the mRS – Malay version was reliable when administered via phone interview, with high ICC (0.958) and kappa (0.872). In this study, the mRS was collected at baseline. The mRS score was collected in numerical value, and participants were categorized into two groups, which were then grouped into independent stroke survivors (mRS = 0-2) or dependent stroke survivors (mRS = 3-5).

3.3.3. Modified Barthel Index – Malay Version

Modified Barthel Index (mBI) – Malay version was used to collect the level of activity of daily living of the stroke survivors. mBI had ten questions, with a possible total score from 0 (require full assistance) to 100 (fully independent). The stroke survivors received numerical scores based on whether they could perform the specific task independently or require assistance. Some studies categorized the score; however, there was no standardization of the cut-off point (Oveisgharan *et al.*, 2006; Prasad *et al.*, 2018). mBI has been used in research settings and clinical practice settings. While initially used by trained individuals (researchers or health practitioners) to assess stroke survivors by direct observation, mBI can also be conducted via phone interview (Prasad *et al.*, 2018). mBI – Malay version was reliable when conducted via phone interview, with a reported ICC of 0.996 (Chen *et al.*, 2019). In this study, mBI was collected at baseline, in numerical value. Due to the lack of cut-off point agreement, the score was not categorized for this study.

3.3.4. Malay version of Zarit Burden Interview

The Malay version of the Zarit Burden Interview (MZBI) was used to measure the caregiver burden. This tool measures the subjective burden or the appraisal of the impact of providing care on the caregiver's life. It was commonly used to assess the caregiver's burden during the care of a patient with impairment, including stroke survivors, the elderly and dementia (Zarit, 2018). MZBI had 22 questions, each being scored with a score ranging from 0 (never) to 4 (nearly always), making total scores possible ranging from 0 to 88. Examples of questions asked in ZBI include “did the patient ask for more help than needed”, “not having enough time for the caregiver yourself”, “feel angry around the patient”, and “negative effect on other relationships”.

Higher scores indicate more significant caregiver distress or burden. ZBI allow for missing response up to 6 (out of a total of 22 questions) answer missing. The total score can be prorated for missing responses by using the average score for the individual. ZBI can be used either by a self-administered or administered by an interviewer (Smith, George and Ferriera, 2018) or via phone interview (Lin, Ku and Pakpour, 2017; Damien *et al.*, 2020). While some studies suggest different dimensions, the original author mentioned that the score could be reported by total or global score (Zarit, 2018). MZBI had good reliability with high internal consistency (Cronbach $\alpha = 0.898$), had a good significant correlation with the Malay version of the Centre for Epidemiologic Studies Depression scale – MCES-D, with Spearman ρ of 0.58 and a high significant correlation with the English version of ZBI, with Spearman ρ of 0.84 (Shim, Ng and Drahman, 2018). For this study, MZBI were collected via phone interview at 1-week, 1-month, 2-month and 3-months.

3.3.5. Caregiver Appraisal of Function and Upset

Caregiver Assessment of Function and Upset – Malay version (Malay-CAFU) was used to measure the stroke survivor's functional level and the caregiver's reaction to caregiving. While MZBI focuses on the impact of providing care on the caregiver's life, Malay-CAFU focuses on how much the caregiver feels upset or burdened in helping the stroke survivors do their daily activities. Malay-CAFU had 15 items, eight for the instrumental activities of daily living (IADLs) subscale and seven for the basic activities of daily living (ADLs) subscale. Items in IADLs include telephone, shopping, meal preparation, housework, laundry, travel, medicine, and finance, while ADLs include bathing, dressing the upper body, dressing the lower body, toileting,

grooming, eating, and getting in and out of bed. Each item in Malay-CAFU had two dimensions, measuring the survivors' dependence level and the caregivers' upset level.

The questions were asked in the same manner for both dimensions. For the functional dimension, the question was “Does the care recipient require assistance for using [the items]?” and if the caregiver answered “yes”, the caregiver needed to quantify the level of assistance required. For the upset dimension, the caregiver needs to answer the question, “how much this assistance is bothering or upsetting you?”. Both dimensions were scored with a Likert scale, with the dependence dimension scored from 0 (total assistance) to 7 (complete independence), and the upset level was scored from 0 (not bothered or no upset at all) to 4 (extremely upset). The score can be reported by the subscale – IADLs, ADL or total, for each dimension – functional level and upset level (Gitlin *et al.*, 2005). The original English version of CAFU had good validity and reliability, with exploratory factor analysis showing a scree test suggesting two factors model and confirmatory factor analysis showing good fitness. The tool had a significant correlation with CES-D; however, the correlation was poor with Spearman's ρ between 0.07 and 0.32 (Gitlin *et al.*, 2005). The Malay-CAFU had good reliability and internal consistency (Hamzah *et al.*, 2023).

3.3.6. Data Collection Method

For this study, data was collected using REDCap electronic data capture tool, which was also used to manage and store data. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export

procedures for seamless data downloads to common statistical packages, and (4) procedures for data integration and interoperability with external sources.

The study proforma and research tools (mRS, mBI, MZBI and Malay-CAFU) were constructed in REDCap, in which a trained research assistant recorded all the data during the interview in the system. For each interview session, the time to complete the questionnaire was about one hour.