Evaluating stroke rehabilitation provision in Thailand: analysis of real-world data, economic evaluation and value of implementation

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Abstract

Stroke is the second largest cause of death in Thailand and many stroke survivors suffer from disability after their stroke. The ministry of public health (MOPH) Thailand published a service plan strategy for improvement in service delivery and has endorsed new rehabilitation guidelines and policy in 2019, which recommended to provide an intensive inpatient-based rehabilitation programme to eligible stroke patients. However, there is currently limited evidence at national level regarding service provision, patients' health outcomes, as well as cost-effectiveness and value of implementation of the new rehabilitation policy.

Heath technology assessment (HTA) has received increased attention in the policy decision making process in the past decades in Thailand for assisting policy makers to enhance the allocation of resources. Economic evaluation and value of implementation of new interventions are useful tools to inform evidence-based decision making to maximise the use of cost-effective technology into real-world practice.

This study aims to assess the current situation, impact on stroke service delivery, and to evaluate the implications of the endorsement of the new policy of rehabilitation services and estimate cost-effectiveness and value of implementation of this new rehabilitation strategy. A multi-methods approach was utilised, including primary data collection in the form of a hospital survey, the analysis of routinely collected real-world data, a systematic literature review, and an economic evaluation and value of implementation analyses.

It is essential to consider a provider's capacity and service delivery in relation to the new service plan strategy. In Chapter 2, this thesis assessed the availability of stroke services and hospital facilities at different hospital levels in Thailand. In Chapter 3, national administrative stroke data, covering about 75% of the Thai population, were analysed to examine the extent to which the stroke service plan improvement affects health resource utilisation, costs, and health outcomes of stroke patients.

Chapter 2 presents results from a hospital survey of tertiary hospitals across Thailand, which are categorised into advanced-level, standard-level and mid-

level hospitals. Findings confirm that hospitals at all levels are likely to have shown improvement in service delivery, achieving the goals set by the service plan strategy in terms of setting up stroke units with essential supportive features for acute stroke treatment. However, some challenges remain in order to improve quality of care. These include establishing health information systems to record clinical measurements and health outcome measures, e.g. the Barthel index score, during the post-acute phase. This should be done to ensure continuity of care between hospitals, health regions and at national level.

Using national administrative stroke data, stroke services were evaluated in terms of resource utilisation, costs and health outcomes in Chapter 3. Resource use was measured and costs estimated using a two-part model to address issues of zero-cost observations. Parametric survival analysis was used to assess health outcomes, namely all-cause mortality and recurrent stroke events. Though the Thai MOPH attempted to enhance the quality of stroke care by improving treatment during the acute phase, treatment and services during the post-acute phase still present challenges. Findings revealed a low proportion of stroke survivors accessed rehabilitation services. But patients who received rehabilitation incurred lower mean annual medical cost and had a 15% decrease in the risk of mortality.

A systematic review of economic evaluations of rehabilitation interventions was performed in Chapter 4 to review and assess existing economic models of rehabilitation services to identify an appropriate rehabilitation model for a Thai context. The findings showed that the majority of new rehabilitation interventions/services were likely to be cost-saving or cost-effective. However, these studies were moderately heterogeneous in their economic evaluation components. Most importantly, only direct-medical costs, especially costs related to the new intervention, were considered, while costs due to lost productivity, including informal care costs, were rarely considered.

Based on results from the systematic review, an economic evaluation and value of implementation analysis of the new rehabilitation policy were performed to assess whether this initiative presents value for money for the Thai MOPH. Findings showed that inpatient rehabilitation was cost-saving from a provider perspective. It was not cost-effective when adopting a societal perspective. Only when direct non-medical costs were reduced by 20% in sensitivity analyses, the intervention was found to be cost-effective at a willingness to pay threshold of 160,000 Baht. At the current level of rehabilitation implementation, the benefits of new the rehabilitation policy is of value to The Thai MOPH which means it is worth implementing. The expected value of perfect implementation, as net monetary benefit (NMB), is approximately 23,359 Baht per person or 7.9 billion Baht over five years from a provider perspective. From a societal perspective, if non-medical costs were reduced by 25%, the rehabilitation programme would be worth implementing. Further, at the current cost of rehabilitation implementation, the actual level of implementation that would need to be achieved should be at least 69% of eligible patients over five years, so that the NMB to the Thai MOPH would be greater than the implementation costs.

Finally, healthcare intervention that have been shown to be cost-effective will be beneficial to patients and the wider healthcare system if these are offered and used in clinical practice. This thesis shows the potential of how evidence generated from real-world data can complement existing evidence from the literature to generate new knowledge to support Thai decision makers in designing the implementation strategies to ensure continuity in stroke care along the stroke care pathway.

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Author's Declaration

I declare that, except where explicit reference is made to the contribution of others, this dissertation is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution.

Signed:

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Papers and presentations

The following publications were developed as part of this thesis:

Published paper

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Abbreviations

95%CI	95% Confidence Intervals
AdjRW	Adjusted Relative Weight
AIC	Akaike's Information Criterion
BI	Barthel Index
BIC	Bayesian Information Criterion
CCI	Charlson Comorbidity Index
CEA	Cost-Effectiveness Analysis
CEAC	Cost-Effectiveness Acceptability Curve
CHEERS	Consolidated Health Economic Evaluation Reporting Standards Statement
CIS	Continue Inpatient Stay
CPI	Consumer Price Index
CSMBS	Civil Servant Medical Benefit Scheme
CT	Computerized Tomographic
CUA	Cost Utility Analysis
CVD	Cerebrovascular Disease
DALYs	Disability-Adjusted Life Years
DRG	Diagnosis-Related Group
EMS	Emergency Medical Service
EQ-5D	EuroQol Five-Dimension
ESD	Early Supported Discharge
GCS	Glasgow Coma Scale
GDP	Gross Domestic Product
GLM	Generalised Linear Model
GNI	Gross National Income
GP	General Practice
HICs	High-income countries
HIS	Hospital Information System
HMIS	Health Management Information Systems
HR	Hazard Ratio
HTA	Health Technology Assessment
ICD-10	International Classification of Diseases, Tenth Revision
ICD-9-CM	International Classification of Disease Ninth Revision - Clinical Modification
ICER	Incremental Cost–Effectiveness Ratio
ICU	Intensive Care Unit
IMC	Intermediate Care
IP	Inpatient
IQR	Interquartile Range
KPIs	Key Performance Indicators
LMICs	Low- and Middle-Income Countries
LOS	Length Of Stay
LTC	Long-Term Care
MOPH	Ministry Of Public Health

MRI	Magnetic Resonance Imaging
mRS	Modified Rankin Scale
MSU	Mobile Stroke Unit
NCDs	Non-Communicable Diseases
NEADL	Nottingham Extended Activities of Daily Living
NHB	Net Health Benefit
NHS	National Health Service
NHSO	National Health Security Office
NIHSS	National Institutes of Health Stroke Scale
NLEM	National List of Essential Medicines
NMB	Net Monetary Benefit
OLS	Ordinary Least Squares Regression
OP	Outpatient
OWSA	One-Way Sensitivity Analysis
PDX	Principal Diagnosis
PSA	Probabilistic Sensitivity Analysis
QALY	Quality-Adjusted Life Year
QOL	Quality of Life
RCC	Ratio of Cost to Charge
RCT	Randomised Controlled Trial
RFS	Recurrence-Free Survival
rt-PA	Recombinant Tissue Plasminogen Activator
RW	Relative Weight
RWD	Real-World Data
SC	Stroke Corner
SDX	Secondary Diagnosis
SFT	Stroke Fast Track
SSS	Social Security Scheme
SU	Stroke Unit
TPM	Two-Part Models
UCS	Universal Coverage Scheme
UHC	Universal Health Coverage
VHV	Village Health Volunteers
WTP	Willingness To Pay

Chapter 1 Introduction

This Chapter commences with an overview of the Thai health care system including the service delivery system, followed by a description of stroke epidemiology, management and patient pathways. Next, the current stroke service provision and challenges of service provision in Thailand will be described. These include the current routine stroke data and the usage of these data for service improvements. The final section presents the aims, objectives and thesis outline.

1.1 Thai health systems, organisation and structure of healthcare facilities

The Thai ministry of public health (MOPH) has implemented universal health coverage (UHC) in 2002 and almost 97% of Thai citizens have been covered in one of the three main health insurance schemes ever since (Table 1-1)[1-4]. Currently, the three main schemes develop their own health management information systems (HMIS) separately to collect data submitted from all hospitals under their contract[1, 2]. The Civil Servant Medical Benefit Scheme (CSMBS) is provided as a fringe benefit to government officers, pensioners, and their dependent family members. This scheme covers around 8% of the Thai population. The Social Security Scheme (SSS) serves workers in the formal private sector, but does not include their dependents. It currently covers around 14% of the Thai population. The Universal Coverage Scheme (UCS) provides to the rest of population who are not covered by either CSMBS or SSS, covering around 75% of the Thai population. It is managed by the National Health Security Office (NHSO), while their providers comprise mostly public hospitals (district hospitals and primary care contractors). Lastly, around 4% of the Thai population pay for private health insurance[1, 5].

Table 1-1 The characteristics of the health insurance schemes in Thailand

Detail	Civil Servant Medical Benefit Scheme (CSMBS)	Social Security Scheme (SSS)	Universal Coverage Scheme (UCS)
Organisation	Comptroller General’s Department (CDG)	Social Security Office	National Health Security Office
Population coverage	8%	14%	75%
Population	government officers, pensioners, dependent family members	workers in the formal private sector	the rest of Thai population
Access to service	no registration required (free to select)	registered public and private competing contractors	registered contractor provider (most are district hospitals)
provider payment	• OP: fee-for-service and directly disbursed from CGD to healthcare providers • IP: DRG with different base rates • Other high-cost interventions: fee schedule (higher rates than UCS)	• OP: Capitation • IP: Capitation + additional payments for accident and emergency and high-cost care	• OP: Capitation • IP: DRG + Global budget • Fee schedule (other high-cost interventions/special programme) • Capitation + some combination of fee schedule (health promotion and prevention)
Expenditure, 2017	384.12 USD per capita	102.24 USD per capita	94.24 USD per capita
Year - begin collected data	2004	2004	2002 but completed data started from 2013
Routine data collection	all patients who received health services in the hospital	all patients who received health services in the hospital	all patients who received health services in the hospital

* DRG: Diagnostic Related Group, ID: identifier, IP: inpatient, OP: outpatient

All health insurance organisations handle the reimbursement of medical expenses to all members under their schemes, however, NHSO takes the national responsibility in order to deliver effective health prevention and promotion for the whole population.

In terms of health services under the Thai health care systems[6-8], the Thai MOPH has classified the structure of their hospitals into five levels of care. It should be noted that more than 70% of healthcare facilities in Thailand are public providers[2, 9] mainly at primary care level. Although, there are also other public hospitals under other ministries, including university hospitals, and local government, they only contribute a small proportion[8] to the health care system. In 2018, the report on public health resource in Thailand[9] showed that there are 12,476 healthcare facilities with beds for inpatient care, of these, 1,051 (82%) and 230 (18%) places are in the public and private sectors, respectively.

Public hospitals were grouped into three main levels of care namely tertiary, secondary and primary care (Table 1-2). These can be categorised into five hospital levels comprising of advanced-level, standard-level, mid-level, first-level and primary-level hospitals.

Table 1-2 The classification of public hospitals in Thailand

Level of care	Hospital level	Referral hospital level*	Type of hospital	Number of hospitals	Number of beds	Ratio of hospital per patient	Hospital capacity
Tertiary	Advanced	High-level referral hospitals	Regional hospital	33	250 - 1,000	1:2,000,000	- deliver advance and sophisticate health technology and can have a function as the medical school. - has all major, minor medical specialties and sub – specialties. - able to support referral patients from regional/general hospitals** within the district or nearby areas.
	Standard		General hospital (node)	48	120 - 500	1:1,000,000	- a provincial general hospital and designated as the node of the provincial network. - has all major, minor medical specialties and sub - specialties in some fields (as needed). - able to support referral patients in a provincial service network***.
	Mid (M1)	Mid-level referral hospitals	General hospital (Small)	35			- a district general hospital having medical specialists in all 6 major specialties (physician, surgeon, obstetrician, paediatrician, orthopaedist and anaesthesiologist) and some minor specialties (as needed). - It is designated as a referral hospital for patients from the secondary care in their service network.
Secondary	Mid (M2)		Community Hospital (Node)	88	>120	1:200,000	- a big/node community hospitals having medical specialists in all 6 major specialties.

Level of care	Hospital level	Referral hospital level*	Type of hospital	Number of hospitals	Number of beds	Ratio of hospital per patient	Hospital capacity
							- It is designated as a referral hospital for patients from the secondary care in first-level referral hospitals.
	First (F1)	First-level referral hospital	Community Hospital (Large)	77	90 - 120	1:80,000	- a district hospital or community hospital providing the services that cover basic primary health care and secondary cares which mean that they have clinical capacity to provide admission services. - able to provide treatments from medical specialties in all or some fields.
	First (F2)		Community Hospital (Medium)	517	60 - 90	1:80,000	
	First (F3)		Community Hospital (Small)	99	10 - 60	1:30,000-50,000	
Primary	Primary (P1)	No level	Community Medical Unit	327	0	1:10,000-30,000	- the smallest size and offer basic primary care services for several type of health prevention and promotion services, but not for admission services. - close to the community, village or patient's home and the distance is usually less than 30 minutes from home to primary care unit
	Primary (P2)		Primary Care Unit	9,766	0	1:1,000-10,000	
	Primary (P3)		Health Centre	184	0	1:<1,000	

* Classification based on the service plan strategy, ** regional/general hospitals served as tertiary hospital level and mostly located in big provincial cities throughout Thailand, *** provincial service network defined as a network between provinces such as a seamless service for stroke fast track.

Tertiary care

Tertiary care comprises regional hospitals and general (standard and M1) hospitals, providing specialised care not available in secondary care. Advanced-level hospitals (regional hospitals) provide all areas of medical specialties, both major and minor, and sub-specialty fields. They can deliver advanced and sophisticated health technology and most of them serve as teaching hospitals. Standard-level hospitals (general hospitals) are provincial general hospitals and designated as the node of the provincial network. This type of hospital has medical specialists in all major specialties, all minor specialties and sub - specialties in some fields (as needed). Finally, M1-level (small general) hospitals are district general hospitals with medical specialists in all 6 major specialties (physician, surgeon, obstetrician, paediatrician, orthopaedist and anaesthesiologist) and some minor specialties that are required.

Secondary care

Secondary care comprises community hospitals (M2 and F1 to F3). These hospitals can provide services that cover primary health care services and secondary care which means they have clinical capacity to provide admission services. This hospital type has sub-categories depending on their size and capacity. M2-level and F1-level hospitals provide treatments from medical specialties in some fields (major specialty: obstetrics, orthopaedics, paediatrics, surgery, and medicine) with around 3 - 10 doctors. The differences between M2-level and F1-level is that M2-level serve as big/node community hospital having medical specialists in all 6 major specialties (physician, surgeon, obstetrician, paediatrician, orthopaedist and anaesthesiologist). F2-level (medium community) hospitals are larger with two to five doctors, no specialist, and provide services to a larger number of patients both at outpatient departments (OPD) and inpatient departments (IPD) including operating rooms. Lastly, the F3-level (small community) hospitals have one to two doctors and some services (e.g. X-Ray) and minor procedures.

Primary care

Primary hospitals offer basic primary health care services for several types of prevention and health promotion services, but do not offer inpatient services. They are close to the community, village or patients' homes and the distance is usually less than 30 minutes from home to medical service unit.

Apart from the above classification, the Thai MOPH also authorises the service plan strategy in order to improve quality of health services, increase accessibility and improve health outcomes of the Thai population since 2012 under the concept of a seamless health service network, self-contain and referral hospital cascade. The service plan strategy 2018 - 2022[6] has classified provinces in Thailand into 13 health regions (Figure 1-1). Each health region comprises 4 - 8 provinces and serves 3 - 5 million people. To monitor and evaluate the quality of care, every health region has to design their systems for enhancing the service delivery to reach the minimum standard requirement of national key performance indicators (KPIs).

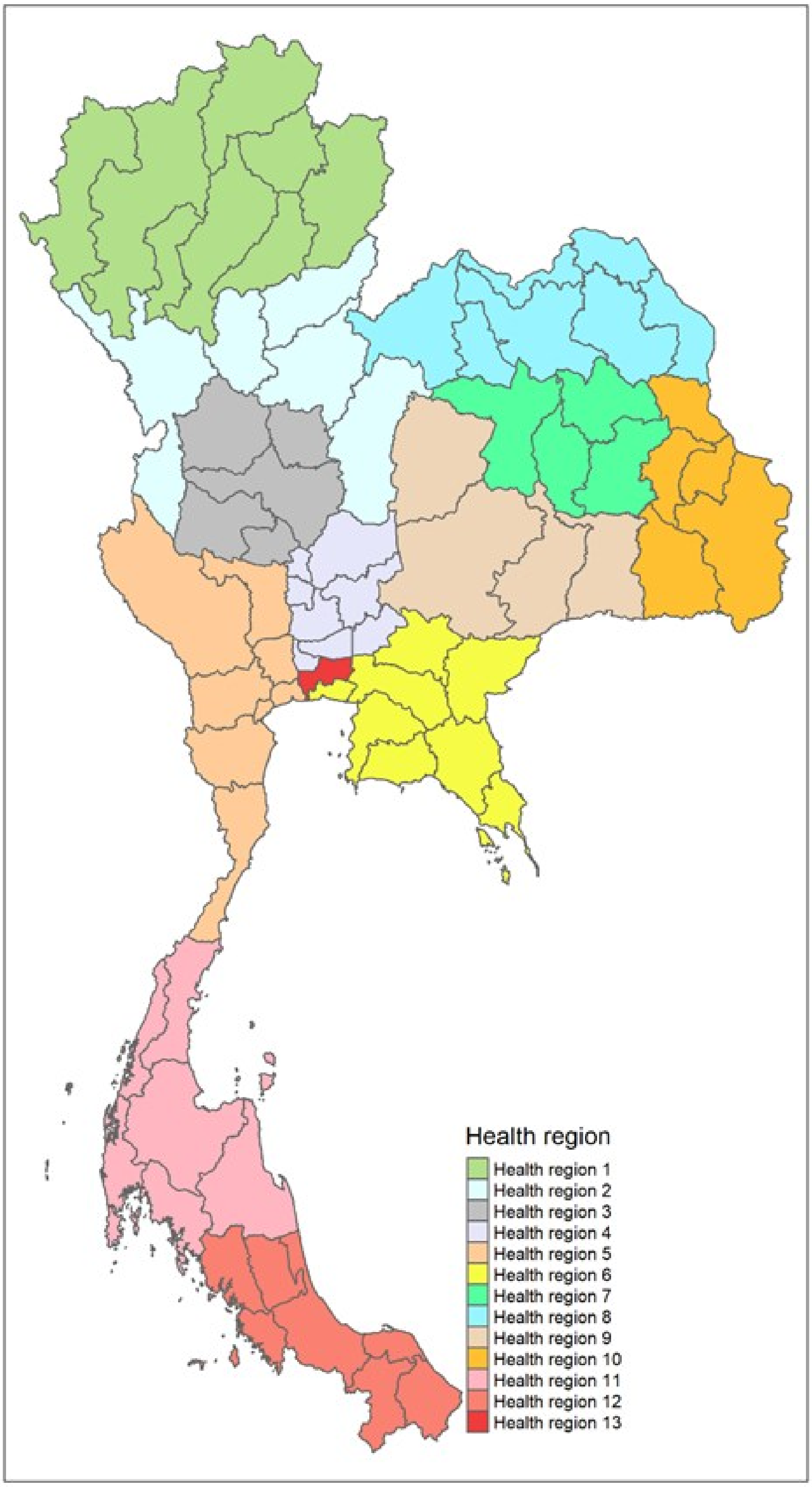


Figure 1-1 Map of health regions in Thailand

Health region13: Bangkok

1.2 Epidemiology, management and patient pathways

1.2.1 Epidemiology of stroke

Stroke is a life-threatening neurological condition which is caused by restricted supply of blood such as cerebral infarction and interrupted blood flow. Generally, stroke can be categorised into two main categories depending on its cause[10, 11]. Ischaemic strokes are caused by a clot that interrupts the blood flow to the brain. Haemorrhagic strokes are caused by a ruptured blood vessel preventing blood flow to the brain. A related condition, called a transient ischemic attack, is caused by a temporary clot, lasting from a few minutes up to one day[12]. Major risk factors for stroke comprise diabetes, hypertension, dyslipidaemia, atrial fibrillation, smoking, alcohol consumption, poor diet, stress, obesity, depression, history of cardiac disease and sedentary lifestyle[12, 13].

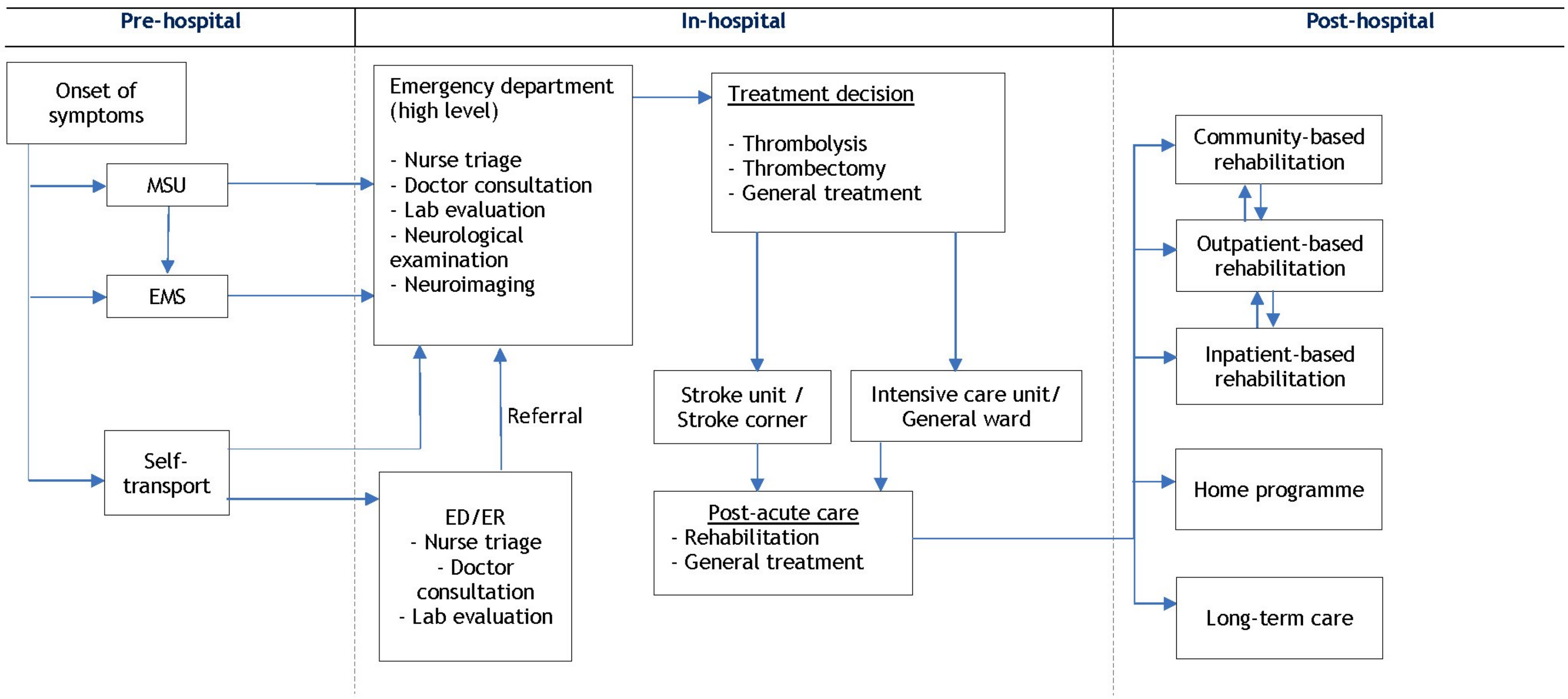
With regards to burden of stroke, stroke is a leading cause of death and disability worldwide. There were approximately 5.5 million stroke deaths and 116 million disability-adjusted life years (DALYs) lost due to stroke globally in 2016[14]. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) in 2019 reported that stroke was ranked the second leading cause of DALYs in patients aged 50 years and over[15].

Stroke is increasingly prevalent in low- and middle-income countries (LMICs) due to an increase in non-communicable diseases (NCDs) risk factors, population ageing, and life style changes[12, 16]. In Thailand, stroke is one of the biggest burdens of disease. During 2004 - 2006, the crude prevalence of stroke over the age of 45 was 1,880 per 100,000 population (1.88%, 95% confidence interval (95%CI): 1.69 - 2.07)[17] and decreased to 122 per 100,000 of population during 2009 – 2010[18]. However, there is lack of detail on incidence of stroke. It is estimated that Thailand has new cases of stroke of more than 250,000 patients annually[19].

A report of the burden of disease in the Thai population in 2014[20] concluded that stroke ranked second among the top ten causes of DALYs lost in 2014 in Thailand – for both men and women. Stroke was also the leading cause of death, for both males and females in 2014, accounting for approximately 30,000 (11.1%) and 31,000 (14.6%) deaths in males and females, respectively[20]. According to data from the strategy and planning division, MOPH, Thailand, stroke mortality rates, per 100,000 population, increased from 47.8 to 55.5 between 2017 and 2021[21].

1.2.2 Stroke management and patient pathways

Stroke management and patient pathways could be classified into three stages (Figure 1-2): pre-hospital care, in-hospital care and, post-hospital care[22-25]. Pre-hospital and in-hospital care can be considered as acute phase while post-hospital care can be considered as a post-acute phase.



EMS: Emergency medical services, MSU: Mobile stroke unit

Figure 1-2 Stroke patient pathway

Acute phase

Pre-hospital care

During pre-hospital care, the goal is timely identification of stroke symptoms and transport of patients to hospital. Hence, it is vital to be able to promptly assess patients, so that timely treatment and appropriate procedures can be initiated. Computerized Tomographic (CT) scans and Magnetic Resonance Imaging (MRI) are reliably evaluation tools to distinguish between stroke subtypes for a stroke diagnosis. Both play an important role in treatment decisions in which the former is the most commonly used, while the latter is more accurate and can be used in addition to CT scans[11]. However, it has been reported that both imaging procedures are limited in availability in most developing countries[10]. Important is timely intervention since stroke is a medical emergency and treatment with intravenous thrombolytic therapy is the proven treatment for patients following an acute ischaemic stroke and it should be prescribed within 3 - 4.5 hours of symptom onset[26].

In Thailand, emergency medical services (EMS) have been provided as a nationwide system since 2008 aiming to decrease the time it takes to transfer suspected stroke patients to hospital. However, many stroke patients travel to hospital using their own vehicle[27-29] and arrive at hospital more than 4.5 hours after symptom onset. This could be related to low awareness and health literacy of stroke detection and warning signs by stroke patients and families[27, 30, 31].

In-hospital care

Generally, hospitals can activate a stroke fast track system at emergency departments before transferring patients to general wards, intensive care units (ICU) or SUs. Emergency departments are responsible to perform a clinical evaluation which might be conducted by emergency medicine physicians or specially trained doctors or nurses. If the emergency medicine physician does not have capacity to treat the patient, they will refer patient to a higher hospital level with CT results (if they can perform this service). If patients are diagnosed with an ischaemic stroke and qualifies for thrombolytic therapy, a thrombolysis drug will be prescribed. In this case, the thrombolytic treatment can be provided by a 'drip-and-ship' model from spoke to hub hospital[32]. In addition, thrombolysis treatment at spoke hospitals can be prescribed under supervision of a hub network. Spoke hospitals can be mid-level referral hospitals depending on capacity, while hub hospitals are mostly mid-level to advanced-level hospitals[27, 33]. However, data from MOPH annual report 2018[30] showed that the door to needle time was still more than 60 minutes in many health regions.

In terms of a thrombectomy therapy, there is good evidence regarding the effectiveness of mechanical thrombectomy or endovascular treatment in appropriately selected patients with acute ischaemic stroke[34-37]. In recent years, there has also been an increasing amount of literature on the cost-effectiveness of endovascular treatment in patients with ischemic stroke receiving endovascular therapy (with or without thrombolysis) compared to those without thrombectomy. A systematic review by Wu X. et al.(2022)[38], which reviewed economic evaluation studies of endovascular treatment in patients with ischemic stroke between 2009-2019, concluded that all included 21 studies reported that endovascular treatment was cost-effective. Of these, five studies (out of 21 studies) showed thrombectomy was cost saving. Another recent systematic review by De Rubeis G et al. (2023)[39] aiming to explore the economic evaluation studies of thrombolysis and mechanical thrombectomy in patients with ischaemic stroke among the different types of health systems. Around 62% of the 35 reviewed studies showed that interventions for patients with ischemic stroke, either thrombolysis or mechanical thrombectomy, were dominant compared to conservative treatment, regardless of the country setting and type of health system. In Thailand, new guidelines for endovascular treatment in patients with acute ischemic stroke were established in 2019[40] in order to improveme acute stroke care; however, there is a limited number of hospitals that have capacity to provide this treatment.

With respect to service delivery, the NHSO reported that thrombolytic therapy for stroke patients in Thailand was 4,844 visits in fiscal year 2018, which increased from 0.05% in fiscal year 2005 to 6.58% of all ischaemic stroke patients (ICD-10: I630-I639), in fiscal year 2018. Although thrombolytic treatment has been increasingly used, utilisations remains low[41]. Moreover, there is a huge variation between health regions in terms of patterns of care and prescribing[42, 43]. Regarding health outcomes, the percentage of 30-day case fatality dropped gradually from 19.75 to 9.44 from fiscal years 2005 to 2018[41], it is still rarely monitored and the inspector general, MOPH, recommended that the 30-day mortality rate should be monitored more frequently.

Stroke units (SU) are recommended for provision of acute stroke care[26, 44]. These are comprehensive specialised services, with multidisciplinary teams and care specifically tailored to stroke patients. At hospital wards, there will be a nurse case manager who has responsibility to communicate and facilitate with the multidisciplinary team to ensure standard of care and to address any problems related to the patient status. Some hospitals do not have SUs but stroke corners - a specialised area in ICU or general ward, where healthcare staff are able to provide more intensive treatments. However, these elements of stroke care depend on the capacity of hospital infrastructure and health workforces. Recently, a network meta-analysis[44] reported that patients who received treatment in SU are more likely to be alive, independent in daily activities, and living at home at around one year after their stroke.

For the rehabilitation after the acute phase of stroke, the 'Clinical Practice Guidelines for Stroke Rehabilitation' in 2016[25] recommend that the assessment of impairments for stroke patients should be performed. If impairments are very severe and patients have a poor prognosis and functional recovery, a home program and education for stroke patients should be considered. The poor prognosis refers to the National Institutes of Health Stroke Scale (NIHSS) score at 20/42 while poor predictors for functional recovery could be a low level of consciousness, cognitive impairment, bladder and bowel incontinence, or poor sitting balance. For patients with a good prognosis, the rehabilitation programme should be offered. However, in real-world clinical practice, higher hospital levels usually refer patients back to lower hospital levels to receive continuous rehabilitation therapy or in-home rehabilitation[8, 45], while some hospitals might have inpatient rehabilitation services after acute stroke admission.

Post-acute phase

In the post-acute phase, a substantial proportion of patients experience impairment following their stroke[46]. Stroke rehabilitation interventions – a set of complex interventions that are designed to assist individuals to optimise functioning and reduce disabilities from their health condition[47] – that commences early generates better functional health outcomes for individuals with health conditions associated with disability. The golden period for rehabilitation programmes in patients with stroke is during the first three months following stroke[46, 48, 49]. It is recommended that early rehabilitation for hospitalised stroke patients should be provided by a multidisciplinary stroke care team and in organised environments[26, 46]. There is also evidence that rehabilitation units have been beneficial during the post-acute phase in terms of outcome improvements[46, 50].

If patients receive treatment at the higher-level referral hospitals, the health care professionals might refer patients to lower-level hospitals, such as mid-level hospitals which are the main contractor for patients to receive further rehabilitation services, for continuous rehabilitation.

Based on the clinical practice guidelines (CPG) for stroke rehabilitation[25, 51], the pathway to receive rehabilitation therapy can be classified into three service models which depend on the hospital policy and healthcare staff capacity. These service models comprise (1) community-based rehabilitation, (2) inpatient-based rehabilitation, and (3) outpatient-based rehabilitation. Initially, community-based rehabilitation should be considered. If not available, then the hospital-based rehabilitation should be considered. Also, inpatient-based rehabilitation should be offered if stroke patients have multiple impairments. In addition, healthcare professionals should consider hospital facilities of referral hospitals before referring stroke patients to receive continuous rehabilitation therapy. If referral hospitals are not able to provide an inpatient-based rehabilitation programme, outpatient-based rehabilitation should be offered to stroke patients.

It has been suggested that, although the Thai MOPH has published the rehabilitation guidelines in 2016[25], these were not well implemented by health care professionals. A possible explanation includes a lack of adequate resources and infrastructure in provincial and rural areas and limited stroke rehabilitation services in several regions[33, 52]. Furthermore, some hospitals referred stroke patients from the hospital directly to their home without further liaising with community hospitals for further follow up, reducing the chances for patients to access rehabilitation services[30, 31, 45].

Until 2019, a new rehabilitation policy and guideline named **"intermediate care (IMC)"** guidelines for stroke, traumatic brain injury and spinal cord injury patients[51] was endorsed (Figure 1-3) to increase service provision. The guidelines recommend that patients should receive rehabilitation therapy in the post-acute phase of stroke and the Barthel Index (BI) should be used for measurement of activities of daily living. The national KPIs to follow up the improvements in service provision[43] were set and focus on mid-level and first-level hospitals. The service plan strategy stipulates that all mid-level hospitals should establish rehabilitation units to reduce over-crowding of stroke care in advanced-level and standard-level referral hospitals and to increase capacity and accessibility of rehabilitation in rural areas[8, 45, 53]. In 2021, the IMC policy has been listed in the service plan strategy and substituted the stroke service plan accordingly.

The three settings to provide rehabilitation remain unchanged; however, new criteria and recommendations for providing rehabilitation services were added to the guidelines. Each form of rehabilitation service is different in terms of intensity, frequency and place of delivery.

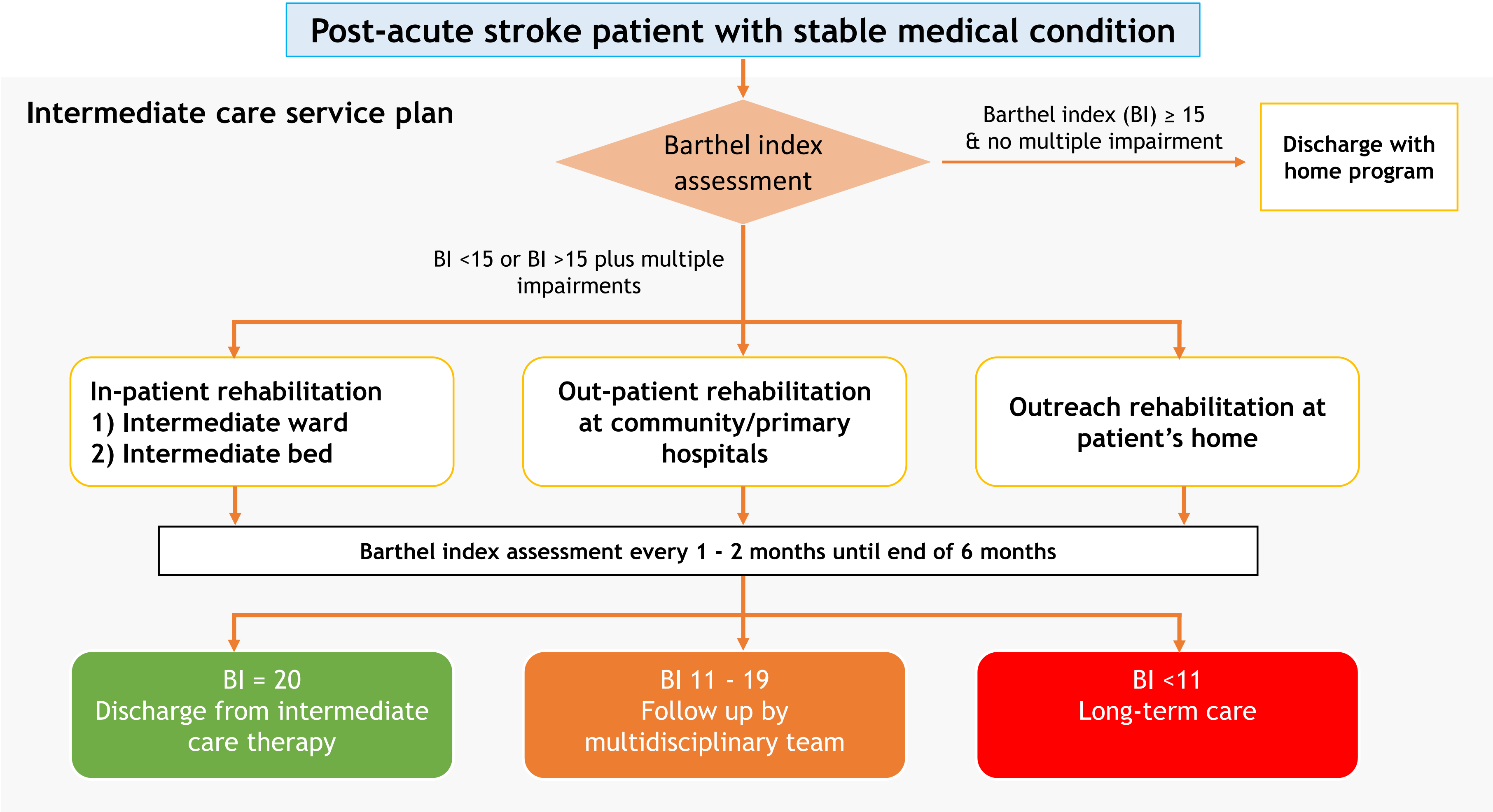


Figure 1-3 Intermediate care service plan for stroke patient
(Adapted from the intermediate care guideline, 2019)[51]

The Thai MOPH set priority on the inpatient-based rehabilitation programme. Inpatient-based rehabilitation contains two modes of services. The first mode of service is an intermediate ward which refers to an 'intensive inpatient-based rehabilitation' programme. This service requires community hospitals to provide at least six beds for rehabilitation services, including multidisciplinary teams such as physical medicine and rehabilitation (PM&R) or internal medicine, family medicine, or general practice. In addition, the IMC guidelines recommend that the service should include nurse training in stroke or a 4-month rehabilitation training course, physiotherapists and occupational therapist (if available). The second mode of service, 'intermediate beds', refers to a 'less-intensive inpatient-based rehabilitation' programme. The requirements comprise at least two beds specifically for this service and the service should include family medicine or general practice, nurse training in a five-day rehabilitation training course, and physiotherapists. In terms of intensity, patients who receive intensive inpatient-based rehabilitation will be offered rehabilitation therapy at least three hours per day for five days per week (or ≥15 hours per week). Patients who receive less intensive inpatient-based rehabilitation will be offered rehabilitation therapy at least one hour per day for three days a week (or ≥3 hours per week).

In terms of an outpatient-based rehabilitation programme, patients will be offered rehabilitation therapy as an outpatient with an intensity of 45 minutes per visit for 1-3 visits per week within 6 months following the incident stroke (or at least 24 visits).

Lastly, an outreach rehabilitation programme which is provided by a multidisciplinary team and staff from health promoting hospitals in patients' catchment area. Patients should receive rehabilitation therapy for at least 60 minutes per visit with at least two visits per month within six months following the incident stroke (or at least 12 visits). The type and number of healthcare workforce in multidisciplinary teams may vary depending on hospital capacity. However, to select these rehabilitation services, the decision and agreement between doctor, patient and carer should be made including a consideration of referral hospital capacity.

The completion of a rehabilitation programme is defined as discharge. This is normally when patients' BI score reaches 20 or the patient has been followed up for at least 6 months even if their BI score does not reach 20. The BI score measures mobility and ability to function in daily live[51, 54]. A BI of 20 stands for independence and patients can be discharged from rehabilitation therapy; a BI of 11 to 19 stands for mild to moderate dependence and patient follow up through a multidisciplinary team should be performed; and a BI of 0 to 10 stands for severe to total dependence and long-term care (LTC) services should be offered to patients.

In terms of monitoring and evaluation of rehabilitation service delivery, the Thai MOPH has set main outcome measure indicators for hospital services in fiscal year 2021[43] which include: (i) at least 80% of mid-level and first-level hospitals should provide inpatient rehabilitation (intermediate bed/ward), (ii) at least 40% of provinces in each health region should provide intensive inpatient rehabilitation (intermediate ward) in mid-level and first-level hospitals, and (iii) at least 65% of survivors (stroke, traumatic brain injury and spinal cord injury patients), who have a BI score <15 or a BI score >15 with multiple impairments, should receive rehabilitation therapy and should be followed up for six months or until a BI score of 20 is reached. However, no long-term health outcomes, such as quality of life are currently being monitored.

1.3 Current stroke service provision and challenges

Current stroke service provision

As mentioned in the previous section, aiming to reduce the burden of stroke and the improvement of stroke service delivery is listed in the service plan strategy 2018 – 2022[6], which have set the national KPIs of stroke service delivery based on hospital level. This service plan strategy aims to increase service capacity and improve health outcomes by expanding stroke fast track systems and there are different plans for different levels of hospitals under MOPH. For example, setting up stroke fast track systems and SUs in advanced-level and standard-level hospitals while setting up a rehabilitation unit in mid-level referral hospitals.

The MOPH service plan also considers the national stroke mortality rate (International Classification of Diseases - Tenth Revision (ICD-10): I60-I69), ischaemic stroke mortality rate (ICD-10: I63) and haemorrhagic stroke mortality rate (ICD-10: I60-I62) for monitoring and evaluation of their service delivery. The overall stroke mortality rate[55] defines the percentage of stroke patients who have died during their hospital stay per total number of stroke patients discharged from hospital. The MOPH service plan report for fiscal year 2020[55] showed that the national stroke mortality rate, ischaemic stroke mortality rate and haemorrhagic stroke mortality rate were 7.9%, 3.8% and 21.9%, respectively[56].

Although, ischaemic stroke and haemorrhagic stroke death rates were lower than the national KPIs (5% and 25%, respectively), the stroke mortality rates did not reach the national target in several health regions (Figure 1-4). Also, what can be observed from Figure 1-5 is the high rate of overall stroke mortality against the national goal (<7%) in some health regions.

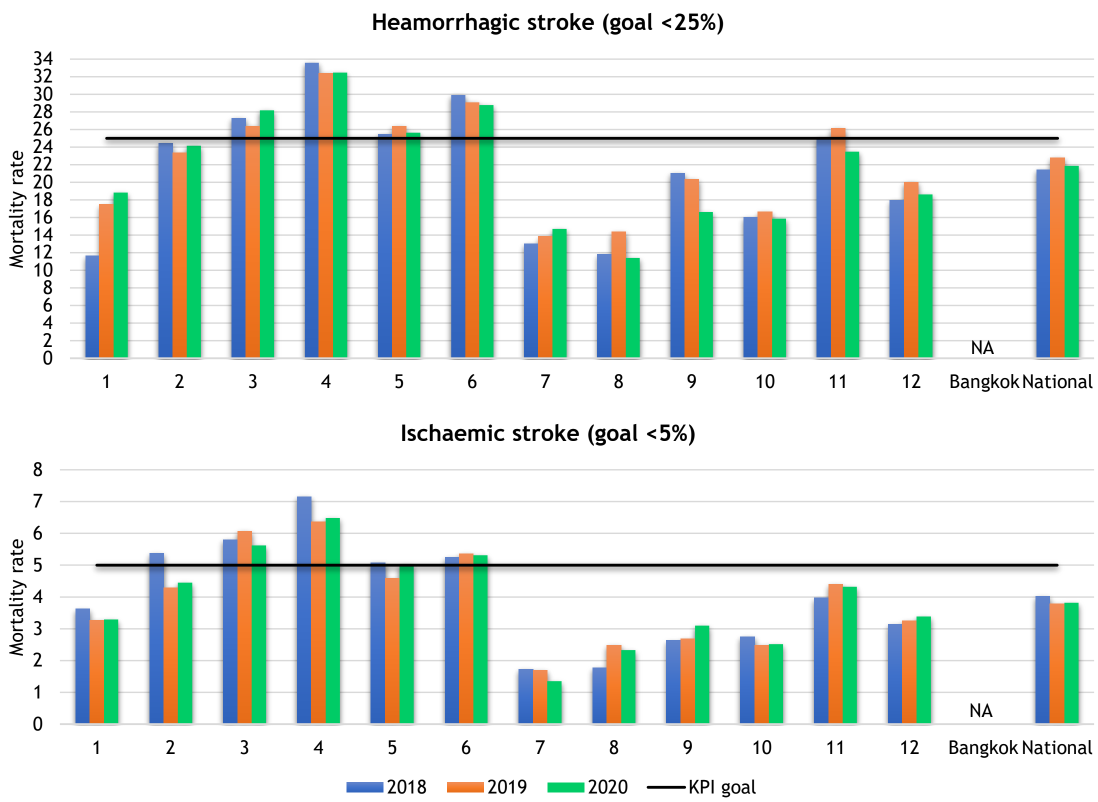


Figure 1-4 The ischaemic stroke and haemorrhagic stroke mortality rate

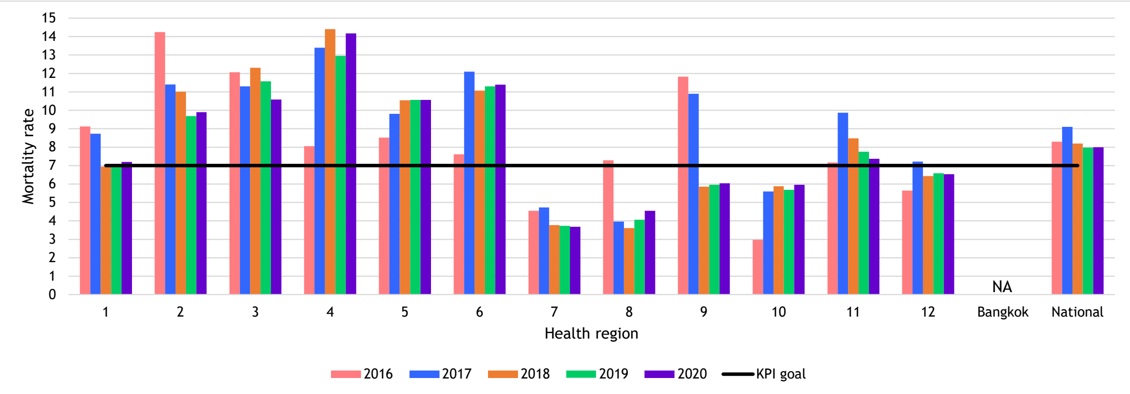


Figure 1-5 The stroke mortality rate in Thailand between 2016 and 2020

<u>Challenges for stroke services</u>

Thus far, challenges in the provision of stroke services in Thailand remain. Previous studies[19, 27, 45, 57-59] have suggested that the stroke care provision in Thai settings should be improved, especially SUs and thrombolysis treatment as these elements are the standard of stroke care[55]. On the one hand, it can be seen from the mortality rates that remain high. On the other hand, health providers also experience many obstacles while providing stroke care services. For instance, as mentioned above, a low health literacy and awareness could lead to long transfer times from a stroke scene to hospital. A global observational study across countries, including Thailand, (the INTERSTROKE study)[60] emphasised that poorer access to investigations, treatments, and services was found in LMICs compared to high-income countries (HICs). Although, there were several Thai studies describing the improvement in stroke services reported at provincial or hospital level, only few were conducted in large-scale population-representative samples or at national level[31, 33, 52, 61, 62].

Despite a substantial improvement of endovascular treatment, there is limited research undertaken in Thailand. Endovascular procedures can only be partially reimbursed by health care purchasers and the price for mechanical devices was noticeably high[63]. Though, some public and private hospitals are able to provide thrombectomy, the majority of hospitals is located in the Bangkok area and there are insufficient health care specialists, such as neurointerventionist, in many hospitals[27, 63].

Despite the fact that a remarkable development of stroke treatment has been managed, many stroke survivors can also experience disabilities or difficulties with activities of daily living[46, 64]. Rehabilitation therapy is one of the essential parts of standard patient care[50]. As previously stated, several challenges remain in the provision of rehabilitation in Thailand. For example, inadequacy of patient awareness in terms of the importance of rehabilitation therapy which leads to a loss of opportunity to access rehabilitation therapy[30, 31, 45], lack of health care resources and infrastructure[33, 52], lack of unified data capture contributing to discontinuity in stroke rehabilitation services between hospitals[30, 31]. As a results, patients may not receive a seamless service and lose the opportunity to access rehabilitation services in the post-acute phase. A Thai study conducted in 2015 suggested that access and availability of rehabilitation services remained low, with only 13% of patients accessing inpatient rehabilitation services[45]. This could be due to either patients and family awareness or a shortage of rehabilitation personnel[45, 54]. There was also a geographical imbalance in accessibility of rehabilitation services, attributable to disparities across supply-side service capacities[8].

According to recent IMC guidelines, there is very limited national evidence assessing the performance of the new rehabilitation policy. Chuenklin et al[65] investigated the early phase of the IMC policy in 17 hospitals across all regions of Thailand during 2019-2020. Their evidence showed that medical expenses reimbursed from NHSO was only at 74% of medical costs in advanced-level and standard-level hospitals, and at 64% in community hospitals. This was due to reimbursement being based on the DRG approach covering only acute treatment but not IMC rehabilitation. Another study[66], from the same team of researchers, analysed the IMC policy process reporting that this policy was successful in some provinces. Their suggestions included further research on rehabilitation service costs, for both short and long-term care, improvement of the inter-hospital linkage recording system and data sharing of BI scores of patients. Moreover, only one study examined the cost-effectiveness of the new rehabilitation policy but considered only a short-time period[62]. To date there has not been any research to evaluate the cost-effectiveness and value of implementation of this new policy considering long-term health outcomes of patients.

1.4 Health information systems and stroke data

Stroke health information systems also play an important role in stroke care especially at the national level. As described in the previous section, the MOPH service plan allows each health region to develop their own system to achieve the national goal. Therefore, hospitals under each health region are also able to design their own systems to deliver their services. Their responsibilities include the design of data collection for the national report and reimbursement. Data collection includes information on recombinant tissue plasminogen activator (rt-PA) prescribing, CT-scan examination results and patients' demographic information. However, currently, there is no formal national stroke registry in Thailand. Therefore, the most important system is a hospital information system (HIS). All hospitals have to deliver standard services to meet national benchmarks, so that they have to develop their tracking system for collecting and reporting data. Some might have their own stroke registry as well as programmes which could be developed by their hospital information technology staff or using paid programmes; some might not develop the registry and only use the HIS for checking the medical history of patients, collecting, managing and reporting the data to MOPH. For reimbursement, as a result of fragmented health insurance schemes, hospitals have to upload their data to different health insurance systems[8, 67], based on the patient's scheme. Despite the achievement of universal health coverage since 2002, a centralised information system has not been developed or integrated from these three main health insurance schemes[67-70].

Besides, these HISs have not been linked among hospitals, so that hospitals cannot retrieve electronic patient records from other hospitals. Also, sharing of hospital information databases among hospitals remains limited[2, 67]. As such, researchers try to maximise the value of routine data collected in the NHSO database, covering most of the Thai population from all provinces, which can bring about an increase of research generalisability. There have been several studies in Thailand using national databases, especially the NHSO database, in the past decade[18, 57-59, 71-83]. These studies analysed the current situation of health care services to identify gaps and provide suggestions and recommendations for the development of the health service systems. There are relatively few studies in the area of stroke services using national data[18, 57-59, 71-

[74, 84]. These researchers investigated stroke prevalence, mortality and treatments from routine data. By way of illustration, Limwattananon, et al[57, 58] reported differences in stroke care and outcomes, e.g. 30-day case fatality, and across health insurance schemes. More recently, Vongmongkol, et al[59] assessed trend, cost and 30-day case fatality of using rt-PA. However, several studies reported that there are lots of limitations to using the NHSO data to understand stroke burden and management in Thailand. In particular, stroke severity data is not included in this NHSO database.

1.5 Aims and objectives

This thesis addresses the gaps in evidence identified above and evaluates the cost-effectiveness and the value of implementation of the new rehabilitation policy in the Thai context. The overarching aim of this thesis is to evaluate the implications of (i) the endorsement of the new policy of rehabilitation services "intermediate care (IMC)" for stroke patients, and (ii) the value of implementation of this new strategy on rehabilitation provision. The following research questions are investigated:

Research question 1: What are the characteristics of stroke services provided, and hospital facilities available across different hospital levels in Thailand?

Research question 2: To what extent does the stroke service plan improvement affect health resource utilisation, cost and health outcomes of stroke patients and does it differ across stroke subtypes?

Research question 3: What is the existing evidence in terms of economic evaluation of stroke rehabilitations services? How can this evidence be used to inform an evaluation of the new rehabilitation guidelines in Thailand?

Research question 4: Is adopting the new rehabilitation service policy cost-effective and what is the potential value of implementation of the new rehabilitation service policy for future eligible stroke cohorts?

The evidence generated by this thesis will help inform policy decision makers or researchers for further potential improvements of rehabilitation services policy in Thailand.

1.6 Thesis outline

This thesis contains three main empirical sections, and the remainder of the thesis is structured as follows.

Chapter 1 presented an overview of health systems, current stroke and rehabilitation care and management and challenges in stroke and rehabilitation services in Thailand. Chapter 2 presents a survey study that collected data on stroke service provision from a provider perspective. Chapter 3 presents an analysis of resource utilisation, costs, and health outcomes for stroke patients. Key results from the systematic literature review on economic evaluations of stroke rehabilitation will be presented in Chapter 4. This will serve as the basis for constructing an appropriate economic model to assess cost-effectiveness and value of implementation of the new rehabilitation service policy in Thailand, which will be presented in Chapter 5. The thesis will conclude with Chapter 6, summarising the key findings and discussing key contributions to knowledge as well as limitations and policy implications. Finally, recommendations for future research are presented.

Chapter 2 Current healthcare service provision of stroke in Thailand

2.1 Background and rationale

As mentioned in the previous chapter, all health regions have been tasked to develop their service delivery to achieve the KPIs set out by the Thai service plan strategy 2018-2022[6] and hospitals under each health region are able to design their own network systems to deliver their services. In 2018, the strategy stipulated that stroke units (SU) should be the standard of care and should be available in all advanced-level, and in 80% of standard-level referral hospitals within each health region[30]. All mid-level referral hospitals should establish rehabilitation units to reduce over-crowding of stroke care in advanced-level and standard-level referral hospitals and to increase capacity and accessibility of rehabilitation services in rural areas[8, 53]. Following regular reviews, this was updated in 2019, and the service plan strategy stipulated that all advanced-level and standard-level referral hospitals should set up SU while for mid-level referral hospitals this would be based on their performance (Table 2-1)[85].

Table 2-1 National key performance indicators set by service plan

Level of care	Hospital level	No. of hospitals[1]	Stroke unit (SU) based-on service plan and goals within 5 years					
			2017[2]	2018	2019	2020	2021	2022
Tertiary care	advanced-level referral hospitals	33	26	+7	-	-	-	-
	standard-level referral hospitals	48	26	+5	+5	+5	+5	+2
	mid-level[2] referral hospitals	36	-	-	Setting up SU if hospitals have capacity.			

[1]data at year 2017; [2]current number of hospitals providing stroke unit

Challenges in the provision of stroke services

In spite of the efforts of hospitals, there are variations of health services between hospital levels and health regions in Thailand[41]. This can be seen from the variation in mortality rates between health regions during 2017-2020 in

Chapter 1 which could be caused by a difference in clinical practice between health regions. This is also supported by previously published Thai studies describing the improvement in stroke services at a provincial or hospital level[31, 33, 52, 61, 62]. Furthermore, the Thai MOPH allows each health region to design their service delivery system - the hub-and-spoke model – independently[6, 32, 86]; thus, a referral for rehabilitation services during the post-acute phase, could contribute to regional differences and inconsistencies of rehabilitation provision. Khiaocharoen et al[45], evaluated the development of new rehabilitation services among 4 health regions (5 provinces, 24 hospitals) and their service network. The authors reported that all health regions set up and implemented the new system according to context within each province and differences were found in terms of the number of patients who received rehabilitation services. In addition, some patients were lost to follow up while being transferred to other healthcare settings.

There is currently no evidence or literature that examines the available health care facilities, supporting facilities for SU/SC, including health care workforce, and current clinical practice for the provision of stroke care at each hospital level following the endorsement of the service plan strategy. It is imperative to investigate the current stroke service information and how health providers respond to the Thai MOPH to improve: (i) inputs e.g. hospital infrastructure, (ii) processes e.g. pattern of services, and (iii) outcomes e.g. clinical or health outcomes. Therefore, this chapter aims to characterise stroke services and hospital facilities by investigating differences in facilities across different hospital levels in Thailand. Findings from this chapter will provide insight into differences in services available towards stroke care provision that have been developed to respond to the MOPH monitoring and evaluation across different hospital levels in Thailand.

2.2 Methodology

2.2.1 Questionnaire Development

Questionnaire content

The service level data of each hospital were collected using a developed questionnaire (Appendix 1) which was adapted from the INTERSTROKE study[60] - an international observational study designed to compare the patterns of care available and their association with patient outcomes in high-income countries, upper-middle-income countries and lower-middle-income or low-income countries - before translating the developed questionnaires to Thai language. Adaptations were made to reflect the Thai context. The full questionnaire can be found in Appendix 2. To summarise its content, the questionnaire comprised the following six parts:

1) Hospital characteristics

This part collected information on hospital characteristics. For example, hospital level, beds, number of staff, stroke registry and stroke fast track networks.

2) Healthcare service funding

This part focused on sources of funding in providing stroke services.

3) Stroke unit characteristics

This part collected information on characteristics of SU such as beds in SU, type and the number of staff providing care, proportion of stroke patients, other supported features for SU and rehabilitation services after acute care.

4) Other facilities and services

Other facilities and services in supporting stroke services. For instance, written guidance of each hospital, type of clinical assessment scores, investigations and medications provided.

5) Post-stroke care

This part focused on services after patient discharge from hospital such as type of rehabilitation provided, type of staff, number of stroke patients receiving this service, and the availability of intermediate care and long-term care services.

6) Suggestions and feedback for stroke service delivery improvement

This part was opened for the respondents to provide suggestions for services improvement.

Ethical consideration

Ethical approval (Appendix 2) was sought and granted by the Ethical Review Committee of the Institute for Development of Human Research Protection, MOPH (No.IHRP722/2562). All research was performed in accordance with the declaration of Helsinki ethical principles. Ethical approval was granted for public hospitals under the Thai MOPH (12 health regions). The questionnaire and related documents such as informed consent, definition, research summary, ethical approval certificate, were translated into Thai language.

Pilot test and revision

Before circulating the questionnaire, it was reviewed by two non-academic healthcare staff from hospitals (neurologists) and one academic staff member. After revision, a pilot questionnaire was sent to four secondary hospitals. Finally, the questionnaire was revised based on their comments.

2.2.2 Study sites and participants

Study sites

Questionnaires were distributed to 119 public hospitals in the 12 health regions under the MOPH service plan strategy. These do not include hospitals within Bangkok (health region 13) and other university hospitals (one questionnaire per hospital). Hospitals are classified into: (1) 34 advanced-level, (2) 49 standard-level and (3) 36 mid-level hospitals. Data anonymisation was used for those hospitals under the 12 health regions; therefore, the hospital code and hospital name were not present to protect identifiable information of hospitals within regions.

Participants

Questionnaires were sent to health professionals whose main responsibilities are related to stroke service provision in their hospital. Therefore, all types of physicians, nurses and other healthcare staff can complete this questionnaire. Additionally, participants provided written informed consent before answering the questionnaire.

2.2.3 Data collection procedures

The questionnaire was distributed via post, online and e-mail (pdf file) to all hospitals between November-December 2019. All hospitals received the questionnaire via post with a link to the online-questionnaire. Telephone calls were offered if clarification was required by respondents. The timeline of the data collection procedure is shown in Table 2-2. After distributing the self-reported questionnaire (day 0), respondents were contacted by e-mail or telephone within 7-14 days to confirm whether the questionnaire and related documents were received. This was repeated after four weeks. Following this, reminder e-mails were sent and telephone calls were performed every two weeks. The survey was closed at month seven. Data were collected for the fiscal year 2018 (1 October 2017-30 September 2018). A 10% random sample of responses was checked by one of the Ph.D. supervisory team (CG). All data were checked for consistency and a telephone call was made to the respondent if there were errors or if confirmation or clarification were needed. Data were entered or exported into the Microsoft Excel spreadsheets before being transferred to R programme for analysis.

Table 2-2 Data collection timeline

Period	Date	Detail
Day 0	1-Nov-2019	Distribution of the self-reported questionnaire to all hospitals by post and online questionnaire channels
Day 7-14	15-Nov-2019	- Telephone call to confirm whether questionnaire was registered into the hospital systems and whether the participants received questionnaire - Distribution of self-reported questionnaire by E-mail to coordinator/respondents who had received permission from their hospital directors
Day 30	30-Nov-2019	Telephone call to confirm whether the participants received questionnaire and had completed it
Day 31-60	30-Dec-2019	- Data collection and data confirmation - A follow-up email was sent and a telephone call for reminding and stimulating the respondents
Every 2 weeks		- Data collection and data confirmation - A follow-up email was sent and a telephone call for reminding and stimulating the respondents
Month 5th	30-Mar-2020	Data collection (extending due to Coronavirus-19 outbreak) and data confirmation
Month 6th	30-Apr-2020	- Data collection - Data management and analysis
Month 7th	31-May-2020	- Study was closed - Data management and analysis

2.2.4 Statistical analysis

Data were analysed by comparing service availability, healthcare staffing, stroke service characteristics (such as accessibility of SU, SU characteristics and resources - manpower, money, material) and add-on features (such as post-discharge rehabilitation). Comparisons were made between hospital levels. All analyses were undertaken using R programme (version 3.6). Descriptive statistics, such as percentage, median and inter-quartile range (IQR) were used to compare the difference of services provided.

2.3 Results

Responses were received from 38 hospitals (response rate 32%). The majority was returned by post (66%, N=25), followed by online questionnaires (24%, N=9) and email (11%, N=4). Respondents who provided the information were nurses (98%, N=37) and physicians (2%, N=1). Eight (21%) of these were advanced-level, 19 (50%) standard-level and 11 (29%) mid-level hospitals, representing all health regions except regions 7. The highest proportion of respondents (18%) came from health regions 5 and 11 (Figure 2-1 and Figure 2-2).

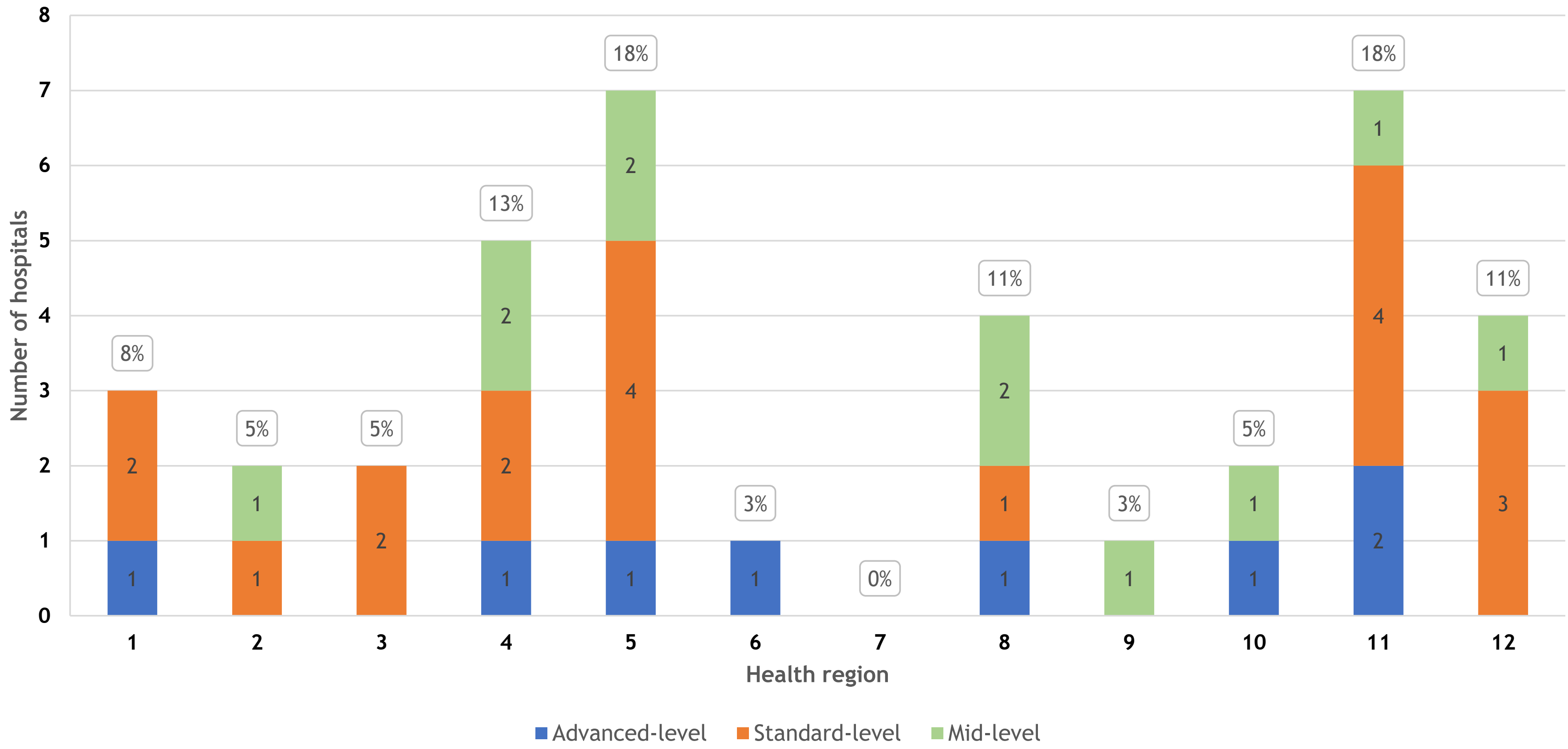


Figure 2-1 Number of questionnaires received and proportion of questionnaires

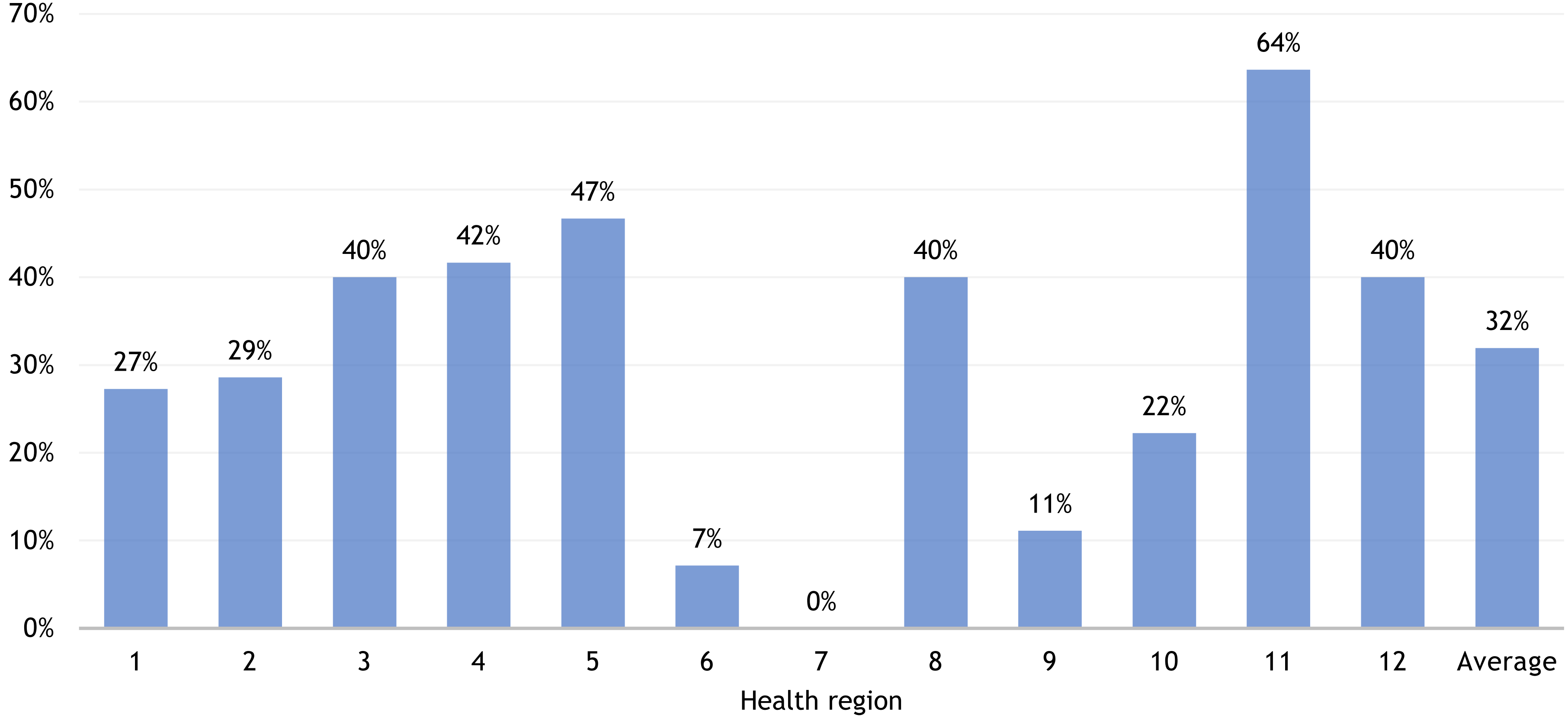


Figure 2-2 Response rate, by health region

2.3.1 Hospital characteristics

Hospital characteristics comprised general questions about their organisation to explore their overview and operation systems, namely the number of hospital beds, the number of physicians in hospital, the number of stroke patient admissions and transfers, the number of stroke patients admitted at any one time, departments providing stroke acute care, the proportion of stroke patients who were looked after by a specialist doctor with training in stroke, stroke registry, stroke fast track (SFT) network and referral system with other hospitals.

In terms of the number of hospital beds (Table 2-3), advanced-level hospitals had the highest number of beds (median: 705; IQR: 608 - 773), followed by standard-level (median: 400; IQR: 319 - 508) and mid-level hospitals (median: 252; IQR: 216 - 290). Regarding the number of dedicated beds for stroke patients, advanced-level hospitals had the highest number of beds (median: 8, IQR: 8-12) while mid-level hospitals had the lowest number of beds (median: 4, IQR: 4-7). However, the number of beds were similar across health regions at each hospital level.

Table 2-3 The number of hospital beds

	Advance-level (n=8)		standard-level (n=19)		mid-level (n=11)	
	Median (IQR)	min-max	Median (IQR)	min-max	Median (IQR)	min-max
Number of beds						
Total beds	705 (608 - 773)	600 - 1,022	400 (319-508)	319 - 540	252 (216 - 290)	208 - 320
Stroke beds	8 (8-12)	6 – 23	6 (4-8)	4 - 20	4 (4-7)	4 - 8
Health regions						
1	8	-	6	4 - 8	-	-
2	-	-	20	-	8	-
3	-	-	7	4 - 10	-	-
4	6	-	4	4 - 5	4	4 - 4
5	8	-	7	4 - 10	4	-
6	23	-	-	-	-	-
8	16	-	8	-	4	1 - 8
9	-	-	-	-	4	-
10	8	-	-	-	8	-
11	8	6 – 10	4	4 - 9	4	-
12	-	-	6	4 - 8	4	-
Average	8 (8 - 12)	-	6 (4 - 8)	-	4 (4 - 7)	-

The number and type of health care staff are presented in Table 2-4. The median number of physicians in advanced-level (median 167; IQR: 116 - 189) was more than double that of standard-level (median 61; IQR: 43 - 73) and more than triple that of mid-level hospitals (median 38; IQR: 24 - 42). The most noticeable difference was the type of physician and this number represents the number of staff in hospitals which might not have a role in stroke service delivery. Overall, the main type of physicians at all three hospital levels were similar, comprising general practice (GP), internal medicine and surgeon. In advanced-level hospitals, the main group of doctors consisted of internal medicine with 20 doctors (IQR: 7 - 28), followed by surgeons with 11 staff (IQR: 10 - 20) and GPs with 7 staff (IQR: 2 - 16). The same type of physician was found in standard-level referral hospitals, but the number of healthcare staff was approximately half of those in advanced-level hospitals. In mid-level hospitals, a difference in the type of physician was observed. The highest number of doctors was GP at 6 persons (IQR: 1 - 10) followed by internal medicine at 5 persons (IQR: 4 - 6) and surgeon at 3 persons (IQR: 3 - 4) and family medicine at 3 persons (IQR: 2 - 4).

Interestingly, neurologists were available only at advanced-level (100%) and standard-level hospitals (around 50%), and not at mid-level referral hospitals. Rehabilitation physicians were available in all advanced-level and standard-level, and in 50% of mid-level referral hospitals.

Table 2-4 The number and type of doctors

	advanced-level (unit: person)			standard-level (unit: person)			mid-level (unit: person)		
	Median (IQR)	**min-max**	**N**	**Median (IQR)**	**min-max**	**N**	**Median (IQR)**	**min-max**	**N**
General practice	7 (2 - 16)	1 - 41	7	3 (2 - 17)	1 - 41	12	6 (1 - 10)	1 - 11	6
Internal medicine	20 (7 - 28)	4 - 34	8	9 (6 - 14)	2 - 16	19	5 (4 - 6)	3 - 6	11
Neurologist	2 (2 - 3)	1 - 9	8	1 (1 - 2)	1 - 3	8	-	-	-
Surgeon	11 (10 - 20)	6 - 29	7	5 (4 - 8)	1 - 13	19	3 (3 - 4)	2 - 6	11
Neurosurgeon	3 (2 - 3)	1 - 5	8	2 (1 - 2)	1 - 3	13	1 (1 - 1)	1	2
Emergency medicine	5 (3 - 6)	2 - 8	7	2 (1 - 4)	1 - 6	15	2 (1 - 2)	1 - 4	8
Radiologist	5 (4 - 6)	2 - 9	7	2 (1 - 4)	1 - 5	19	2 (1 - 2)	1 - 3	9
Rehabilitation physician	4 (2 - 4)	1 - 5	8	1 (1 - 2)	1 - 4	17	1 (1 - 1)	1	5
Family medicine	3 (3 - 5)	2 - 8	7	2 (1 - 3)	1 - 7	16	3 (2 - 4)	1 - 8	9

N: number of hospitals

The main department providing acute-phase stroke care comprised internal medicine (97%), nursing (89%) and pharmacy (87%), respectively (Table 2-5). In addition, the proportion of departments providing stroke acute care across health regions was similar, except in one advanced-level hospital, reporting that only nurses provided care during acute illness. Furthermore, two advanced-level and two standard-level hospitals had no neurologist involved in acute stroke care. In terms of stroke registry, overall, advanced-level hospitals had the highest number of hospitals having their own stroke registry at 75% followed by standard-level at 53% and mid-level hospitals at 27%.

Table 2-5 The departments providing acute stroke care

Departments	advanced-level (N=8)	standard-level (N=19)	mid-level (N=11)	Total (N=38)
internal medicine	88%	100%	100%	97%
nursing	100%	95%	73%	89%
pharmacy	88%	95%	73%	87%
rehabilitation	88%	84%	45%	74%
surgery	88%	84%	36%	71%
general practice/ family medicine	75%	58%	18%	50%
neurology	63%	37%	9%	34%
radiology	50%	16%	18%	24%
emergency	25%	11%	0%	11%
social medicine	13%	5%	0%	5%

Admission and referral systems

Next, the stroke fast track networks and referral systems are considered (Table 2-6). Most advanced-level hospitals were a hub for standard-level and mid-level hospitals.

Table 2-6 The proportion of stroke fast track network and referral system

type of network	advanced-level (N=8)	standard-level (N=19)	mid-level (N=11)
stroke fast track (SFT) network			
SFT - N (%)	2* (25%)	13* (68%)	9* (82%)
SFT hub - N (%)	5 (63%)	4 (21%)	0
referral systems			
refer - N (%)	3 (37%)	16 (84%)	11 (100%)
referral hub - N (%)	5 (63%)	3 (16%)	0

N: Number of hospitals; *Missing data

Overall, the highest total number of stroke patient admissions per year was found in advanced-level at 1,659 patients (IQR: 1,098 - 1,949) followed by 749 patients (IQR: 535 - 1,218) in standard-level and 468 patients (304 - 512) in mid-level hospitals (Table 2-7). When considering stroke subtypes, the highest number of stroke patient admissions was observed for patients with ischemic stroke at all hospital levels followed by patients with haemorrhage stroke. While the lowest number of admissions was for patients with unspecified stroke. Moreover, the number of admissions for patients with ischemic stroke at advanced-level hospitals was nearly 2.4 times higher than the number observed in standard-level and mid-level referral hospitals. Whereas the number of admissions for haemorrhage stroke in advanced-level was 2.5 times higher than the number observed in standard-level and almost 8.7 times higher than mid-level referral hospitals.

In addition, most stroke patients who were transferred from advanced-level and standard-level hospitals to other hospitals were those with haemorrhagic stroke. In contrast, in mid-level hospitals patients with ischemic stroke were those who were transferred more frequently. Considering health regions, seven hospitals reported that they had no stroke patients who were referred to other hospitals (Appendix 3).

With regards to the proportion of stroke patients who are looked after by specialist doctors with training in stroke, these were similar at all hospital levels (advanced-level: median 80, IQR: 58-100; standard-level: median 80, IQR: 50-90; mid-level: median 100, IQR: 57-100). Nevertheless, 10 hospitals reported 0% as they did not have a specialist. These included three standard-level hospitals in three health regions and seven mid-level hospitals (two hospitals from health region 4, 5 and 8 each, and one from 12).

Table 2-7 Number of stroke patient admissions and transfers to other hospitals

	Advanced-level			Standard-level			Mid-level		
	Median (IQR)	**percent**	**N**	**Median (IQR)**	**percent**	**N**	**Median (IQR)**	**percent**	**N**
number of stroke patient admission per year									
Ischemic	984 (589 - 1,310)	63%	8	438 (362 - 606)	62%	19	408 (234 - 428)	78%	11
Haemorrhagic	538 (419 - 630)	33%	8	215 (124 - 286)	25%	19	62 (35 - 103)	19%	11
Unspecified	77 (44 - 114)	4%	8	123 (27 - 184)	13%	19	8 (4 - 12)	3%	11
Total	1,659 (1,098 - 1,949)	100%	8	749 (535 - 1,218)	100%	19	468 (304 - 512)	100%	11
number of stroke patients who was transferred to other hospitals per year									
Ischemic	63 (33 - 102)	42%	3	6 (5 - 14)	47%	16	25 (10 - 39)	75%	11
Haemorrhagic	84 (74 - 94)	51%	3	15 (8 - 24)	29%	16	12 (3 - 22)	18%	11
Unspecified	12 (7 - 16)	7%	3	9 (6 - 13)	24%	16	2 (2 - 10)	7%	11
Total	122 (44 - 192)	100%	3	22 (17 - 40)	100%	16	39 (20 - 53)	100%	11

2.3.2 Healthcare service funding

In this section, the respondents were asked about sources of funding for stroke services (government, private and other funding) including the proportion of each source for each service namely medical services, medicine (e.g. rt-PA drug), investigation (e.g. CT scanning, MRI, laboratory test), rehabilitation services, material and equipment, education programme and any other services. Generally, the proportion and sources of funding for stroke services did not differ between hospitals (N=34), as almost all hospitals reported that nearly 100% of funding of all services came from government.

The only exception was the education programme for their healthcare staff and/or patients and their families as one standard-level referral hospitals reported that 50% of funding for education programmes came from government and the remaining 50% were funded privately. While two standard-level referral hospitals reported that 90% of funding came from government with the remaining 10% coming from private funding.

In addition, the respondents were also asked for the list of items that patients have to pay for out-of-pocket (N=37). These items comprised medical services, investigations (e.g. CT scanning, MRI), medicines, therapy (e.g. physiotherapy), medical equipment, and other items. Almost all hospitals reported that all items were free-of-charge. However, one hospital reported that they had a new hospital policy to charge their patients for MRI scans, in case the patients needed to be examined, because this service was provided by an outsourcing company. Additionally, the other items that patients had to pay for out-of-pocket were acupuncture services (only one standard-level hospitals reported) and non-essential drugs (only one mid-level hospitals reported).

2.3.3 Stroke unit services

Capacity for providing a stroke unit (SU) or stroke corner (SC)

Overall, 87% (33 hospitals) provided SU services (Table 2-8). Of these, all advanced-level and standard-level hospitals provided this service (one standard-level hospital was able to provide both SU and SC services). In contrast, only 55% of mid-level hospitals (six hospitals) had sufficient capacity for SU services while 36% (four hospitals) had SC. Only one mid-level hospitals reported not to have either SU or SC. According to the number of stroke beds in SU or SC, the median number of beds were eight beds (IQR: 8 - 13), six beds (IQR: 4 - 8) and five beds (IQR: 4 - 8) in advanced-level, standard-level and mid-level hospitals, respectively.

Table 2-8 The number of beds in stroke unit or stroke corner

HR	advanced-level			standard-level						mid-level					
	stroke unit (SU)			SU			stroke corner (SC)			SU			SC		
	median	min-max	N	median	min-max	N	median	min-max	N	median	min-max	N	median	min-max	N
1	8	-	1	6	4 - 8	2	-	-	-	-	-	-	-	-	-
2	-	-	-	20	-	1	-	-	-	8	-	1	-	-	-
3	-	-	-	7	4 - 10	2	-	-	-	-	-	-	-	-	-
4	6	-	1	4	4 - 5	2	-	-	-	6	-	1	4	-	1
5	8	-	1	7*	4 - 10	4	2*	-	1	4	-	1	-	-	-
6	23	-	1	-	-		-	-	-	-	-	-	-	-	-
8	40	-	1	8	-	1	-	-	-	8	-	1	8	-	1
9	-	-	-	-	-		-	-	-	4	-	1	-	-	-
10	8	-	1	-	-		-	-	-	-	-	-	8	-	1
11	8	6 - 10	2	4	4 - 9	4	-	-	-	-	-	-	4	-	1
12	-	-	-	6	4 - 8	3	-	-	-	4	-	1	-	-	-
Median (IQR)	**8 (8 - 13)**		**8**	**6 (4 - 8)**		**19**	**2 (-)**		**1**	**5 (4 - 8)**		**6**	**4 (4 - 8)**		**4**

*Both stroke unit and stroke corner in the same hospital

In terms of essential features between stroke treatments given and services available in SU/SC (Table 2-9), 76% (28 hospitals) reported that their hospital was able to provide all of these features for supporting services in SU/SC. The results suggested that all 37 hospitals (100%) were able to provide information and education for patients/caregivers and 36 hospitals (97%) had staff and multidisciplinary teams with main responsibility in managing stroke patients. However, only 90% were able to provide a special education programme for their staff with the lowest percentage observed in advanced-level hospitals.

Table 2-9 Features of the stroke units

Features	advanced-level (N=8)	standard-level (N=19)	mid-level (N=10)	total (N=37)
1) Information and education for stroke patients/carers	100%	100%	100%	100%
2) Staff whose work is mainly managing stroke patients	100%	100%	90%	97%
3) Multidisciplinary team	100%	100%	90%	97%
4) Discrete ward area	100%	89%	100%	96%
5) Written standard protocols	100%	95%	90%	95%
6) Special education programmes for staff	75%	95%	100%	90%

It should be noted that, although multidisciplinary teams have been widely implemented, the frequency with which those teams met was not on a regular basis to plan patient management. It was found that 57% of hospitals (21 hospitals) had a meeting less than once a week, especially in mid-level (9 hospitals) and standard- level (9 hospitals). The frequency ranged from every two weeks up to six months.

The Thai MOPH also recommends the health care providers should apply for stroke centre certification. Results suggest that a higher proportion of advanced-level (75%, 6 out of 8 hospitals) and standard-level (79%, 15 out of 19 hospitals) had a stroke centre certification compared to mid-level hospitals that provided SU (20%, 2 out of 6 hospitals). None of the four mid-level hospitals that provided SC received stroke centre certification.

In terms of health care workforce, type and number of staff who are involved in providing care for stroke patients in SU/SC differ among health regions and hospital levels (Table 2-10). All advanced-level hospitals reported that most of the staff who are usually involved in providing care in SU/SC comprised neurologists, neurosurgeons, rehabilitation physicians, nurses, physiotherapists and occupational therapists. In standard-level hospitals; though the results slightly varied across hospitals, the main type of staff was similar to advanced-level referral hospitals and comprised internal medicine, rehabilitation physicians, nurses, physiotherapists, and pharmacists. However, these types of staff differed from the former group in terms of the number of staff involved. However, there were no neurologists who provided care in mid-level hospitals, the most common type of staff comprised internal medicines, nurses, physiotherapists and social workers. The number of staff involved was also remarkably less than at other hospital levels.

To summarise, the results showed that there was a lack of neurologists in mid-level hospital while nurses, physiotherapists and internal medicine practitioners were the main type of staff in all hospital levels and mostly worked in SU/SC as a full-time.

Table 2-10 Type and number of staff providing care for stroke patients in stroke unit/stroke corner

Type of staff	Detail	advanced-level (N=6)			standard-level (N=17)			mid-level (N=10)		
		All	full-time	part-time	All	full-time	part-time	All	full-time	part-time
internal medicine	Median (IQR)	4 (3-8)	4 (3-8)	-	2 (1-5)	4 (1-6)	1 (1-1)	4 (2-5)	2 (1-4)	5 (5-6)
	min-max	1-12	1-12	-	1-7	1-7	1-2	1-7	1-5	4-6
	N	**3**	**3**	**-**	**14**	**9**	**6**	**10**	**8**	**3**
neurology	Median (IQR)	2 (1-3)	1 (1-3)	2	1	1	1	-	-	-
	min-max	1-3	1-3	-	1	1	1	-	-	-
	N	**6**	**5**	**1**	**5**	**3**	**2**	**-**	**-**	**-**
neurosurgery	Median (IQR)	3 (2-3)	2 (1-2)	3 (3-3)	1 (1-1)	2 (1-2)	1 (1-2)	1	-	1
	min-max	1-4	1-2	3-4	1-2	1-2	1-2	-	-	-
	N	**6**	**2**	**4**	**8**	**3**	**5**	**1**	**-**	**1**
radiology	Median (IQR)	5 (3 - 7)	1	7 (6-7)	2 (1-2)	2 (1-2)	2 (1-2)	2 (1-2)	2 (1-2)	2
	min-max	1-8	-	5-8	1-3	1-2	1-3	1-2	1-2	-
	N	**3**	**1**	**2**	**8**	**5**	**3**	**7**	**5**	**2**
rehabilitation physician	Median (IQR)	2 (1-3)	1 (1-3)	1 (1-2)	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-1)	1
	min-max	1-5	1-5	1-2	1-2	1-1	1-1	1-1	1-1	-
	N	**5**	**3**	**3**	**13**	**7**	**6**	**4**	**3**	**1**
nurse	Median (IQR)	13 (9-17)	10 (7-15)	13 (8-17)	8 (5-11)	8 (4-11)	8 (6-14)	8 (7-12)	8 (7-12)	2

Type of staff	Detail	advanced-level (N=6)			standard-level (N=17)			mid-level (N=10)		
		All	**full-time**	**part-time**	**All**	**full-time**	**part-time**	**All**	**full-time**	**part-time**
	min-max	7-22	7-18	3-22	2-20	2-15	4-19	3-18	1-18	-
	N	**6**	**5**	**2**	**16**	**14**	**3**	**9**	**9**	**1**
physiotherapist	Median (IQR)	1 (1-2)	1 (1-1)	2	1 (1-3)	1 (1-3)	2 (1-3)	4 (2-5)	3 (2-4)	5 (3-6)
	min-max	1-2	1-2	-	1-7	1-7	1-7	1-6	1-6	1-6
	N	**6**	**5**	**1**	**14**	**7**	**8**	**10**	**8**	**3**
Social worker	Median (IQR)	1	1	1	1	1	1	1	1	1
	min-max	1	1	-	1-2	1	1-2	1-2	1-2	1
	N	**4**	**3**	**1**	**11**	**2**	**9**	**9**	**6**	**3**

Proportion of stroke patients admitted to SU/SC

With regards to ensuring accessibility to high quality acute care, the proportion of stroke patients admitted to SU or SC was evaluated (Table 2-11). On average, the median percentage was 59 (IQR: 49 - 77), 68 (IQR 55-80) and 82 (IQR: 76 - 90) in advanced-level, standard-level and mid-level hospitals, respectively. Based on these data, there was a higher number of patients admitted to SU/SC in mid-level than in advanced-level or standard-level hospitals. However, there were wide variations between health regions in advanced-level hospitals as half of them reported that the proportion of admissions was less than or equal to 50%, while there were only four standard-level and one mid-level hospital reporting the same issue.

Table 2-11 Proportion of patients admitted to stroke unit or stroke corner

HR	advanced-level			standard-level			mid-level		
	median	min-max	N	median	min-max	N	median	min-max	N
1	50	-	1	76	60 - 91	2			
2				46	-	1	85	-	1
3				59	51 - 66	2			
4	45	-	1	49	38 - 60	2	72	65 - 80	2
5	28*	-	1	78	44 - 81	4	27	-	1
6	70	-	1						
8	98	-	1	80	-	1	80	-	1
9							90	-	1
10	100	-	1				90	-	1
11	59	50 - 68	2	75	59 - 100	4			
12		-		80	27 - 88	3	95	-	1
Median (IQR)	59 (49 - 77)		8	68 (55 - 80)		19	82 (76 - 90)		8

*SU has just been set up a few months ago before the survey; thus, the proportion of stroke patients admitted to SU was less than 30% of total stroke patients.

Rehabilitation in hospital after initial acute treatment

Respondents were asked in which department patients usually received continuing rehabilitation after initial acute treatment (N=38). Overall, all advanced-level and standard-level hospitals reported that they provided rehabilitation at SU/SC. In advanced-level hospitals (N=8), some stroke patients received rehabilitation in SU or SC and some in general medical wards. In addition, five respondents reported that their patients were also referred to a lower-level hospital and one hospital added that they also referred their patients to their network hospitals that provided IMC services for further rehabilitation services.

In standard-level hospitals (N=19), the results were similar to advanced-level hospitals with stroke patients receiving rehabilitation services in either SU/SC or general medical wards (N=13). It should be noted that only one hospital referred their patients to receive rehabilitation services at higher-level hospitals, while most hospitals (79%, N=15) referred their patients to lower-level hospitals. In other words, there were four out of 19 hospitals (21%) that did not refer patients to other hospitals, but they provided rehabilitation services within their hospitals. Five mid-level hospitals were able to provide rehabilitation services both in their SU or SC and general medical wards, while three hospitals provided these services only at general medical wards. Only one out of 11 hospitals, referred their patients to receive continuing rehabilitation therapy to either higher-level or lower-level hospitals, while two hospitals referred to only lower-level hospitals.

In summary, from all 38 hospitals, there were 100% providing rehabilitation services in their SU/SC in advanced-level and standard-level, whereas there was only 73% (N=8) of all mid-level hospitals. Moreover, most mid-level hospitals (73%) provided rehabilitation services in general medical wards followed by standard-level and advanced-level hospitals at 68% and 50%, respectively. In terms of referring patients to another hospital, most standard-level (79%, N=15) referred their patients to lower-level hospitals followed by advanced-level and mid-level hospitals at 63% (N=5) and 27% (N=3), respectively. The results are summarised in Table 2-12.

Table 2-12 The places providing rehabilitation in hospital after initial acute treatment

	advance-level (N=8)	standard-level (N=19)	mid-level (N=11)
stroke unit - N(%)	8 (100)	19 (100)	8 (73)
general medical ward - N(%)	4 (50)	13 (68)	8 (73)
transfer higher-level hospital - N(%)	-	1 (5)	1 (9)
transfer lower-level hospital - N(%)	5 (63)	15 (79)	3 (27)
others	• Hospitals having intermediate care • Physiotherapy department	• Physiotherapy department	• Physiotherapy department

<u>Staff who educate patients or family members/care givers in rehabilitation</u>

Table 2-13 reports the healthcare staff delivering care for patients who required rehabilitation at the time of discharge from hospital (N=38). The key staff groups included physiotherapists, nurses and occupational therapists in advanced-level referral hospitals. While the key staff groups in standard-level were physiotherapists and nurses, similar to advanced-level referral hospitals. Additionally, village health volunteers (VHV) were more involved at this hospital level. There was a marked increase in the proportion of VHV at mid-level compared to advanced-level and standard-level hospitals.

The respondents were also asked about providing rehabilitation education for patients or family members/caregivers before hospital discharge. All hospitals reported that their healthcare staff provided this education. Overall, the main healthcare staff involved were physiotherapists and nurses followed by doctors and occupational therapists. Regarding doctors, there were 63% of all advanced-level hospitals providing this service, whereas the proportion increased to 74% in standard-level but only 55% in mid-level hospitals. In contrast, it was found that the occupational therapists providing the services accounted for 75%, 53% and 18% in advanced-level, standard-level and mid-level hospitals, respectively. Furthermore, few hospitals reported that other departments were also involved, including the social medicine department, social work department, continuity of care department, pharmacy department and nutrition department.

Table 2-13 Staff type delivering rehabilitation and education

	advance-level (N=8)	standard-level (N=19)	mid-level (N=11)
staff who delivered care when patients required an ongoing rehabilitation - N (%)			
doctor	4 (50)	9 (47)	6 (55)
nurse	7 (88)	16 (84)	8 (73)
physiotherapist	8 (100)	18 (95)	11 (100)
occupational therapist	6 (75)	9 (47)	2 (18)
speech therapist	1 (13)	3 (16)	-
psychologist	2 (25)	5 (26)	2 (18)
village health volunteer	5 (63)	11 (58)	8 (73)
staff who usually educates patients or care givers in rehabilitation - N (%)			
doctor	5 (63)	14 (74)	6 (55)
nurse	8 (100)	19 (100)	10 (91)
physiotherapist	8 (100)	19 (100)	10 (91)
occupational therapist	6 (75)	10 (53)	2 (18)
speech therapist	4 (50)	-	-
psychologist	-	1 (5)	2 (18)
village health volunteer	-	1 (5)	1 (9)

2.3.4 Other healthcare facilities and services to support the stroke service provision

Written guidance for stroke management

Written guidance for stroke management can be found in all hospitals. Although, the topics in their guidance varied greatly, it covered several aspects and represented the comprehensive management and interventions during the acute phase of stroke. For example, swallowing impairment assessment, prevention of complications, prevention of falls, prevention of bed sores, activities of daily living assessment, the Modified Rankin Scale (mRS) assessment, the National Institutes of Health Stroke Scale (NIHSS) assessment, stress and mental support, nutrition, early mobilisation and discharge plan. Moreover, almost all hospitals can provide their guidance if requested, except for one hospital.

Clinical assessment scores for evaluating stroke patients

When enquiring about the type of clinical assessment that was used for evaluating stroke patients (Table 2-14), overall, the Glasgow coma scale (GCS) and the BI scores were mostly used while a malnutrition assessment was the one that was used least in all hospitals.

In advanced-level hospitals, all of these clinical assessments were recorded at both admission and discharge. However, only the GCS, BI scores and swallowing problems were measured at admission in all standard-level and mid-level hospitals. However, not all hospitals repeated these measurements when patients were discharged. For those, who measured scores at discharge, this was mostly done using the GSC and BI scores at standard-level hospitals. Mid-level hospitals seemed to mainly use BI scores only at discharge. It should be noted that there are differences in terms of systems for a data recording at each hospital level. These included: writing in chart of inpatient record, recorded in their health information systems, or recorded in electronic files (MS Excel, Google drive).

Table 2-14 Clinical assessment at admission or discharge from hospital

type of assessment	advanced-level (N=8)		standard-level (N=18)		mid-level (N=11)	
	admission	discharge	admission	discharge	admission	discharge
Glasgow coma scales	100%	100%	100%	89%	100%	82%
Barthel Index	100%	100%	100%	89%	100%	91%
modified Rankin Score	100%	100%	72%	78%	82%	82%
National Institutes of Health Stroke Scale	100%	100%	94%	67%	82%	73%
Swallowing impairment	100%	100%	100%	61%	100%	82%
Level of consciousness	100%	100%	94%	78%	91%	82%
Malnutrition	50%	50%	78%	50%	73%	36%

Investigations and medications provided in acute-phase of stoke care

The percentage of investigations performed within 24 hours after patient admission (Table 2-15) showed that, overall, approximately 58% (N=22) of all hospitals provided only two services namely Electrocardiogram (ECG) monitor and CT scan. Three services, namely ECG, CT brain and MRI/magnetic resonance angiography (MRA) were provided in 10 hospitals (26%). All services (ECG, CT scan, MRI and carotid doppler ultrasound) were provided in five hospitals (13%). The proportion of patients receiving MRI scans was low with a wide variation between hospital levels. Unfortunately, four hospitals reported that they provided the service but did not collected data (one advanced-level and three standard-level hospitals). Lastly, 24 hospitals (67%) did not perform the carotid doppler ultrasound service while three hospitals did not collect any data on this service (two in advanced-level and one in standard-level hospitals).

Table 2-15 Proportion of investigations within 24 hours after admission

Interventions	advanced-level	N	standard-level	N	mid-level	N
electrocardiogram monitor						
median (IQR)	100 (100 - 100)	8	98 (52 - 100)	18	100 (98 - 100)	8
min-max	61 - 100		25 - 100		69 - 100	
computerized tomography						
median (IQR)	100 (100 - 100)	8	100 (100 - 100)	19	100 (100 - 100)	11
min-max	99 - 100		6 - 100		80 - 100	
magnetic resonance imaging						
median (IQR)	20 (4 - 82)	6	2 (2 - 4)	3	1 (1 - 6)	3
min-max	1 - 100		1 - 5		1 - 10	
carotid doppler ultrasound						
median (IQR)	30 (20 - 40)	2	10 (6 - 36)	3	5 (3 - 52)	4
min-max	10-50		2 - 62		1 - 98	

Endovascular therapy

Unlike the above interventions, only one standard-level hospital in health region 11 was able to perform thrombectomy during the acute stroke phase.

Medications and investigations

In terms of medications provided for stroke patients (Table 2-16), the proportion of hospitals prescribing thrombolytic drugs, such as rt-PA, was less than 10%. Two mid-level hospitals reported that they did not provide rt-PA drugs. In contrast, prescribing of antiplatelets, such as aspirin, was at nearly 100% at all hospital levels. When considering anticoagulant drugs, i.e. warfarin, data varied greatly not only between health regions but also between hospital levels and the percentage was relatively low.

Table 2-16 Percentage of stroke patients who received medications and investigations

Interventions	advanced-level	N	standard-level	N	mid-level	N
recombinant tissue plasminogen activator drug (N=34)						
median (IQR)	8 (7 - 13)	8	9 (6 - 12)	18	7 (5 - 13)	8
min-max	2 - 60		3 - 33		0.3 - 21	
antiplatelets (N=23)						
median (IQR)	80 (75 - 86)	4	98 (84 - 94)	12	87 (70 - 92)	7
min-max	64 – 97		71 – 98		10 – 96	
anticoagulants (N=21)						
median (IQR)	5 (3 - 18)	5	5 (3 - 7)	12	44 (1 - 88)	4
min-max	2 - 20		2 - 80		1 - 88	

2.3.5 Post-stroke care services

Rehabilitation unit and type of rehabilitation services

There was considerable variation in the proportion of stroke patients receiving rehabilitation. This was found for all types of services available and was not only observed between health regions but also between different hospital levels, and within hospital levels (Table 2-17).

Overall, rehabilitation units were provided in most hospitals (advanced-level: 7 (88%), standard-level: 13 (68%), mid-level: 9 (82%) hospitals). Surprisingly, none of the hospitals in health region 1 has a rehabilitation unit. Turning to the type of rehabilitation services provided (N=35), it was found that there were 34% of all hospitals being able to provide all types of rehabilitation services while inpatient rehabilitation (89%, 31 from 35 hospitals) was the most frequent type of rehabilitation service provided, followed by inpatient plus outpatient rehabilitation (77%, 27 from 35 hospitals), home-based rehabilitation (74%, 26 from 35 hospitals), only outpatient rehabilitation (66%, 23 from 35 hospitals) and only community-based rehabilitation (51%, 18 from 35 hospitals).

In advanced-level hospitals, inpatient rehabilitation was the most common rehabilitation therapy, while the least frequent type of service was community-based rehabilitation. In standard-level hospitals, inpatient rehabilitation still predominated this service, and in contrast to advanced-level hospitals, a higher percentage of providing home-based rehabilitation was detected. In mid-level hospitals, the most common type of rehabilitation provided deemed to be different from both hospital levels, as home-based rehabilitation was provided most at this hospital level. What stands out in the table is the difference in the proportion of stroke patients receiving community-based and outpatient-based rehabilitation, which was greater than at other hospital levels. Inpatient-based plus outpatient-based rehabilitation was found to be the services that highest percentage of stroke patients received across hospital levels.

Table 2-17 Type of rehabilitation services and percentage of stroke patients receiving this service

	advanced-level	N=8	standard-level	N=19	mid-level	N=11
inpatient rehabilitation						
median (IQR)	100 (84 - 100)	7	97 (88 - 100)	15	98 (95 - 100)	9
min-max	72 - 100		40 - 100		92 - 100	
inpatient followed by outpatient rehabilitation (N=27)						
median (IQR)	83 (73 - 98)	6	50 (30 - 97)	13	93 (75 - 96)	8
min-max	30 - 100		5 - 100		20 - 100	
only outpatient rehabilitation						
median (IQR)	20 (20 - 60)	5	48 (9 - 79)	12	91 (30 - 97)	6
min-max	15 - 100		5 - 100		9 - 100	
only home-based rehabilitation						
median (IQR)	16 (10 - 72)	5	50 (13 - 92)	12	100 (85 - 100)	9
min-max	6 - 74		5 - 100		55 - 100	
only community-based rehabilitation						
median (IQR)	26 (15 - 36)	3	20 (9 - 92)	9	92 (59 - 100)	6
min-max	3 - 46		5 - 100		10 - 100	

Another aspect of rehabilitation is a home health care service. The most common type of healthcare staff who provided home health care services for stroke patients (Table 2-18) comprised physiotherapists, nurses, VHVs and social medicine practitioners. No neurologists or neurology training fellows in stroke provided home health care services at any hospital level. In advanced-level hospitals, all hospitals reported that the physiotherapists, VHVs and social medicine practitioners were the main healthcare staff who provided home health care, while there were nurses, physiotherapists, VHVs and social medicine practitioners in most standard-level and mid-level hospitals.

Table 2-18 Type of staff who provided home health care services

type of staff - N (%)	**advanced-level (N=8)**	**standard-level (N=19)**	**mid-level (N=11)**
physiotherapist	8 (100)	16 (84)	8 (73)
VHV	8 (100)	14 (74)	8 (73)
social medicine	8 (100)	14 (74)	6 (55)
family medicine	5 (63)	12 (63)	8 (73)
nurse	5 (63)	17 (89)	10 (91)
general practice/internal medicine	4 (50)	4 (21)	2 (18)
nutritionist	4 (50)	3 (16)	4 (36)
rehabilitation physician	3 (38)	8 (42)	3 (27)
pharmacist	2 (25)	9 (47)	6 (55)
Thai traditional medicine	1 (13)	4 (21)	4 (36)

<u>Intermediate care service and long-term care services</u>

Intermediate care (IMC) and long-term care (LTC) services were assessed (Table 2-19). Overall, IMC and LTC were provided at around 87% and 70% of all hospitals. Four hospitals (one advanced-level and mid-level, two standard-level hospitals) provided neither IMC nor LTC services.

Table 2-19 Proportion of intermediate care service (IMC) and long-term care (LTC) services

	advanced-level		**standard-level**		**mid-level**	
	IMC (N=8)	LTC (N=8)	IMC (N=19)	LTC (N=16)	IMC (N=11)	LTC (N=9)
Total - N (%)	7 (88)	7 (88)	18 (95)	12 (75)	8 (73)	4 (44)

2.3.6 Suggestions for stroke service improvement

In the final part of the survey, respondents were asked for comments on stroke service delivery improvements and the results showed a variety of perspectives expressed. In advanced-level hospitals, these suggestions comprised: a clear policy and direction in order to respond to the MOPH policy, government funding to support human resource development, and an efficient system of health data records and linkage between hospitals along with monitoring and data analysis teams. Staff from standard-level and mid-level hospitals, commented on the need for materials and facilities to be able to care for patients at their own home and the need for a budget and manpower to be able to provide appropriate care post-discharge. Moreover, staff at some mid-level hospitals reported they would require ongoing teaching support from the higher-level hospitals to improve patient care in SUs.

2.4 Discussion

2.4.1 Summary of main findings

This chapter offers novel insights into current practices of stroke care at different hospital levels in Thailand. The findings were discussed and used to address gaps in or barriers to achieve the provision of stroke and improve stroke implementation and ultimately patient care.

The descriptive results of hospital characteristics showed that the number of dedicated beds for stroke patients were similar between health regions in all hospital levels. However, the available specialties were different between hospital levels, especially neurologists were available in advanced-level and standard-level hospitals due to the scarcity of neurologists. A deficiency in number of neurologists was mostly found in the provincial levels. The service plan strategy sets out that, at SU, at least one neurologist and/or neurosurgeon and/or internal medicine practitioner should be available as a minimum standard requirement. The availability of these specialists therefore very much determines whether standard-level referral hospitals are able to provide SUs. The scarcity of neurologists in this study is in line with the MOPH report about the national public health resource[9] which indicated the total number of neurology specialists of the whole country was only 421 persons or equal to around 15% when compared to internal medicine. Moreover, approximately 50% of neurologists practice in the Bangkok area[9] with the remaining neurologists ranging from 3 to 27 per health region which could contribute to the shortage of professionals in rural areas[27, 53]. Therefore, well-trained non-neurologists have played a key role in thrombolytic treatments[27]. Nurses were the main group providing stroke care at all hospital levels. The service plan strategy recommends that at least four nurses should be available at SUs as a minimum standard requirement, and results from our survey confirmed an adequate number of nursing staff.

In view of departments providing stroke acute care, nursing was the main group in advanced-level hospitals, whereas internal medicine was reported in all standard-level and mid-level hospitals. In addition, the proportion of stroke patients who are looked after by specialist doctors with training in stroke are almost identical across all hospital levels. It is possible that, higher-level hospitals had skilled stroke nurses, who have undertaken special training and qualifications, particularly, in stroke management[6, 27]. However, patients still received care from physicians training in stroke.

In terms of stroke patient admission, the main type of patients had ischemic strokes, while patients, who were most frequently referred were those with haemorrhagic stroke. It is possible that patients were transferred because of a lack in capacity for haemorrhagic stroke treatment or lack of neurosurgeons in their hospitals[6, 56]. Furthermore, many patients were transferred from advanced-level hospitals. This result may be explained by the fact that patients might need to receive specialist care during the acute phase, such as surgery for haemorrhagic stroke. Patients are referred back to their registered hospitals when they are clinically stable.

When considering the SU services and other facilities supporting stroke services, our findings highlight that all advanced-level and standard-level hospitals had a SU, thus achieving the goal set by the service plan strategy (100% at advanced-level and standard-level hospitals). Some mid-level referral hospitals were also able to set up SU/SC. Despite some hospitals with SU being eligible to apply for stroke centre certification, not all had this certification. The stroke centre certification assessment was recommended by the Department of Medical Services, MOPH, Thailand. They recommended that hospitals should improve SU and should obtain certification to provide standard of stroke care for acute stroke patients and hospitals should be accredited or re-accredited every 3 years [87]. On the other hand, the service plan policy also allow health care providers to setup SC if they had any limitations on the health care capacities.

Additionally, the type and number of staff involved in providing care in SU/SC differed between hospital levels. One possible explanation could be the limited number of staff based at these hospitals and the scarcity of specialists in standard-level hospitals[27]. This is consistent with previous studies[88, 89] indicating that mid-level hospitals not only had fewer health professionals than advanced-level or standard-level hospitals but also that there was maldistribution of healthcare workers. Apart from that, approximately 76% of all hospitals had capacity to provide all other essential features supporting SU/SC; however, the only activity that all hospitals conducted was providing information and education for stroke patients/caregivers. This may be because healthcare providers would like to ensure that the patients receive sufficient information about stroke and prevention prior to discharge. Although, the percentage of access to SU was almost 70%, the percentage of stroke patients admitted to SU/SC was low compared to some developed countries[90, 91]. It has been suggested by the INTERSTROKE study[60] that the LMICs - including Thailand -, were less likely to have sufficient capacity to look after most hospitalised stroke patients and to provide all six quality characteristics of SU[92], namely discrete ward, health care staff which specialises in stroke care, multidisciplinary team, protocols, education and training for staff, information for patients and carers. In contrast to previous studies[60, 93], findings from this thesis showed that most hospitals had sufficient capacity to look after over 50% of stroke patients (A-level: 59%, standard-level: 68%, mid-level: 82%). Nevertheless, these results are still lower than in some developed countries[90, 91], for instance, there is around 82% in Scotland. Finding from this study also showed that 95% of all hospitals can provide all six-key components (Table 2-9).

In terms of the proportion of medications provided to stroke patients, standard-level hospitals had greater provision of thrombolysis compared to advanced-level hospitals. It seems possible that stroke service delivery was improved due to the improvement of stroke fast track and thrombolytic treatment in mid-level and standard-level hospitals. Thrombolysis treatment can be provided at mid-level hospitals by non-neurologist, such as internists or emergency physicians, under the supervision of a neurologist from advanced-level or standard-level hospitals[94]. It should be noted that there could be regional differences ranging from 5%-22%. These results are supported by a Thai study using national stroke data[94] which showed that the percentage of acute ischemic stroke patients who were treated with thrombolysis varied widely across the country. Although, there is no agreed benchmark for thrombolysis rates, the utilization rate remains low compared to other countries, especially developed countries[95-97]. Possible explanations include the onset of symptoms had been more than 4.5 hours[27, 52], or patients may have had some contraindications or poor prognosis, which could affect the rate of thrombolysis initiation. Furthermore, this study supports evidence from the INTERSTROKE study[60] that CT scans and antiplatelet drugs given were nearly 100%, while provision of MRI scans, carotid doppler ultrasound and thrombolytic therapy was extremely low.

The proportion and type of rehabilitation therapy post-acute stroke differed between hospital levels. Advanced-level and standard-level hospitals focused mainly on inpatient-based rehabilitation, while most home-based and community-based rehabilitation were provided by mid-level hospitals. Indeed, these findings reflect the real-world service delivery in Thailand with the higher-level hospitals having the capacity to provide specialised care, while lower-level hospitals having fewer resources offering basic care including home health care services[8, 53]. One interesting finding relates to the clinical assessment scores. Not all hospitals evaluated patients at discharge as suggested in IMC guidelines[51]. They recommend to measure the need for rehabilitation as well as the follow up processes using the BI scores. This will affect health outcome assessments in the post-acute period.

The main type of staff providing home health care services for stroke patients were physiotherapists, nurses, VHVs and social medicine practitioners. Thailand has introduced VHVs[8, 53] based in the community and VHVs play an important role in supporting healthcare providers such as follow-up care and acting as a link between providers and community resources. A previous study indicated that well-trained VHVs could help improve quality of life for stroke survivors [88]. However, VHVs seem to be unique to a Thai context and no international comparison can be made here.

Taken together, although, national stroke mortality rates in fiscal year 2019 and 2020 decreased in some health regions, it remained constant at 8% (2019: 7.97% and 2020: 7.99%), not reaching the national target of less than 7% per year[98]. The results from this study show that these hospitals have restructured trying to improve their service delivery under the concept of the seamless health service network, self-contain and referral hospital cascade. All advanced-level and standard-level hospitals are able to set up SU and are achieving the goal set by the service plan strategy including health care facilities, workforce, all essential supportive features. However, some challenges still remain to ensure improvements in terms of quality of care. These included the stroke centre certification, health information systems, in particular the monitoring systems for clinical measurements and health outcome assessments in the recovery phase, e.g. the BI scores, for a continuing of care inter-hospitals both between health regions and national levels. Also, there is still a need for service delivery improvements in mid-level hospitals. All aspects mentioned above need to be complemented with costs and effectiveness of the new rehabilitation implementation policy to ensure that stroke rehabilitation truly implements, with the standard of cares, into a routine clinical practice. These are very important to policy makers to pay attention to the improvement stroke care at mid-level hospitals in Thailand.

2.4.2 Strengths and limitations

This is the first study to provide a detailed picture of healthcare facilities and services available to stroke patients in Thailand. Indeed, the Thai MOPH published the annual service plan reports providing information of stroke service delivery of each health region, the report did not compare between hospital levels while the level of information provided was an aggregated data. This study offers novel insights into stroke care to investigate differences in the practice of stroke care between hospital levels in Thailand. The questionnaire was adapted from the INTERSTROKE study[60], allowing to draw comparisons. The findings in this chapter seem consistent with the INTERSTROKE study but should be interpreted with caution.

Some limitations arise due to the nature of the survey method. First, despite a low response rate, this study was able to include representatives of almost all geographical areas in Thailand. Second, the questionnaires were sent to the key managerial health professionals who work or have main responsibility related to stroke service provision in their hospital. The consent form needed to provide a name and surname of the respondent to ensure completion by a stroke nurse who worked with the MOPH service plan policy. However, despite these efforts, there is no mechanism to establish whether respondents were actually the same person as stated in the consent form. This could contribute to a small proportion of implausible figures i.e. the percentage of patients who received anticoagulants which is likely to be unrealistic at 100%. Thus, this value was excluded from the analysis. Additionally, the data collection period coincided with the COVID-19 pandemic, which will have affected the ability of staff to respond to our service, given the important role in responding to the increased demand on healthcare services during this time. As there is no standard agreement for an acceptable minimum response rate, to maximise future response rates, further studies could use monetary incentives or gift certificates along with a registered mail or shorter questionnaires[99]. Moreover, the appearance of an interviewer could help increase response rates[100]. Third, endovascular thrombectomy was performed only in one standard-level hospital, and not in any of the advanced-level hospitals; thus this should be interpreted with caution. Fourth, this study does not cover all hospital types such as Bangkok area and university hospitals which mostly serve as excellence centres. These hospitals had to be excluded as their differing procedures for ethics approval would have meant numerous separate application to individual hospitals, which was not possible due to study timelines and budget. This study therefore focuses on public hospitals in 12 health regions throughout Thailand. This will have led to limitations in terms of comparability between health regions. Another limitation arises due to a lack of information on secondary prevention medication. Lastly, the investigation of a care map and information of IMC was not performed since the questionnaire was developed and circulated before the new IMC guideline and new rehabilitation policy have been endorsed in 2019[51].

2.5 Conclusion

The survey was designed to explore the practice of stroke care and facility utilisation on provision of stroke care in Thailand. The findings highlight that hospitals at all levels are likely to have shown adequate quality of stroke service delivery, achieving the goals set by the service plan strategy in terms of setting up SUs with essential supportive features. The higher-level of care, such as advanced-level hospitals, has a comprehensive infrastructure and allocation of adequate medical resources together with a greater number of human resources compared to standard-level and mid-level hospitals. Although, mid-level hospitals have potential to provide stoke service delivery similar to standard-level or advanced-level hospitals, improvements still need to be made in areas of health care workforce. Data linkage and health record systems for clinical or health outcomes in order to follow-up and monitor health outcomes of patients should be developed between hospitals and at national levels.

Moving forward, the findings in this chapter also suggest that the stroke organisational survey should be reviewed and updated regularly in the MOPH annual reports and audit systems. The use of patient-level data could help to improve information that is fed back to health facilities. Developing a system of national health data records and linkage between hospitals would be valuable for collecting data on clinical assessments and continuous stroke care between hospitals. Moreover, the national data should not be a fragmented database, rather, it should be in co-operation between heath schemes and MOPH. Finally, further research should be undertaken to investigate the implementation of new rehabilitation programme both cost measurements and health outcome improvement thanks to the initiative of new rehabilitation therapy for stroke patients. Further, the limited capacity of service delivery should encourage policy makers to improve stroke care at mid-level hospitals in Thailand.

Chapter 3 Stroke resource utilisation and all-cause mortality in Thailand

3.1 Background and rationale

Chapter 2 discussed that setting up a stroke unit (SU), as a national goal that was set out in the service plan strategy 2018-2022, was achieved fully (100%) in advanced-level and standard-level hospitals including key essential supportive components. However, capacity in hospitals was found to be limited and stroke service delivery needs to be improved especially at mid-level hospitals. These results disclosed information on healthcare provider aspects. However, it is also important to examine the extent to which the stroke service provision as provided in healthcare facilities could impact health outcomes of stroke patients – as a demand side factor. These also include factors such as resource utilisation and cost.

As introduced in Chapter 1, a number of studies in Thailand have used the NHSO database, as real-world evidence, in the past decade to monitor and support policy decisions in terms of the impact of health service provision or health outcomes of certain interventions/diseases in Thailand. These data are useful to assess the impact of stroke service delivery on stroke patients' health outcomes. However, there are relatively few research studies in the area of stroke service delivery using the NHSO database. Limwattananon et al.[57] analysed 30-day all-causes mortality rates and survival rates of patients with first stroke during fiscal years 2007 to 2012. Butsing et al.[73] identified post-stroke survival times from 2004 – 2013. Vongmongkol et al.[59] investigated the trend, cost and 30-day case fatality of using rt-PA as a thrombolytic treatment for ischaemic stroke patients between fiscal years 2011 and 2014. These prior studies are either outdated or focussed only on one type of stroke. As detailed in Chapter 1 the Thai MOPH aims at improving the stoke service delivery in Thailand and have published their service plan strategy 2018 – 2022[6]. Policymakers have not only set the national KPIs of stroke service delivery based on stroke subtypes and hospital level, but also planned to increase the service capacities and improve health outcomes by expanding stroke fast track systems (SU in advanced-level and standard-level hospitals, rehabilitation in mid-level hospitals).

In terms of health outcomes of patients, MOPH and NHSO have focused and reported the thrombolytic rate, percentage of deaths and 30-day case fatality for haemorrhagic and ischaemic stroke, but long-term survival of both subtypes is rarely monitored. Despite some recent research reporting results from their stroke services[32, 101, 102], these studies have reported short-term outcomes and were conducted in one local hospital or small hospitals, and may not be representative at a national level. Therefore, current national stroke information is needed to track how healthcare providers responded to the Thai MOPH to improve their service provisions and how the policy impacts health outcomes of Thai stroke patients.

The aim of this chapter is to examine the capabilities of providers in terms of evaluating resource use and cost for stroke patients as well as assessing the influence of stroke on health outcomes with a particular view on how these might be affected by the service plan strategy and whether the associations varied by stroke subtypes using the NHSO database. This evaluation will enable an assessment of the burden of stroke such as mortality, recurrent stroke and the effectiveness of the health service delivery with respect to health care utilisation. It is hypothesised that lower rates or mortality and recurrent stroke are desirable. Evidence generated in this chapter could ultimately provide additional information to inform policymakers in terms of further improvement in the continuum of stroke care policy in Thailand.

The remainder of this chapter is structured as follows: the methodology section will describe (a) the processes carried out to check data quality, cleaning and preparing NHSO data for analysis, and (b) the statistical methods to quantify resource utilisation and evaluate health outcomes of stroke patients. This will be followed by presenting results, a discussion of the main findings and conclusions.

3.2 Methods

3.2.1 Data source

This study employed national stroke data from the NHSO information systems which contains the reimbursement database (claims database) of medical records from contracted health service providers[8]. The NHSO information system has been developed since 2002[68, 69], data restructuring and improvements have been performed continually and their systems have been stable since 2009[2, 103]. After NHSO had implemented the stroke fast track programme in 2008 under which the costs for thrombolytic treatment can be reimbursed to all contracted hospitals[8, 12, 59], a new independent database for stroke patients was developed through the "disease management programme", a vertical programme focused on one specific disease area with special short- and medium-term objectives[104], after achieving their objectives, NHSO stopped using this standalone programme and integrated stroke patient data into the main claims database. Accordingly, the comprehensive stroke-related data sets are a reliable source of information from 2015 onwards[105].

NHSO data covers most of the Thai population, records all hospitalised events, as well as discharges from health care institutions including contracted private hospitals. Hence, this data represents 75% of the Thai population including stroke patients. To improve and ensure data quality, a selection of patient records are chosen for regular audit under the NHSO auditing system[106].

3.2.2 Ethics

In order to gain access to the NHSO database, researchers must submit a formal letter to the NHSO secretary-general including an application form for permission to use the data in their management information system. Further, a research proposal, ethical approval, criteria for retrieving the data and a variable request form are required. The application is then reviewed by the NHSO secretary-general, and upon approval a relevant department is assigned to co-ordinate the work with the researcher. A non-disclosure agreement has to be signed between the researcher and the NHSO secretary-general before the requested data are extracted and made available to the researcher. As the requested data did not contain any personally identifiable information and fully anonymised, this study was exempt from ethics reviews.

3.2.3 Criteria for retrieving a cohort of stroke patients

The following criteria for identifying a cohort of stroke patients from the NHSO database were adopted to ensure that all stroke patients and their healthcare utilisation data are included.

(1) All patients were selected, who had either a principal (PDX) or secondary diagnosis (SDX) of stroke using the ICD-10 coding system[107] between year 2015 and 2020. The Thai ICD-10 code was modified and extended from the International Classification of Diseases by WHO. ICD-10 for stroke were I60 - I69, I60 - I62 (haemorrhagic stroke), I63 (ischaemic stroke) and I64 - I69 (unspecified stroke).

(2) Patient characteristics, routine outpatient attendances and inpatient admission records, diagnosis, procedure carried out and mortality records were consequently retrieved for the identified stroke cohort. Therefore, the patient cohort can be tracked starting from their first outpatient visit or inpatient admission until death or study end.

Eligibility criteria for stroke patients in this study consisted of (a) patient age at least 18 years, (b) identification of patients' incident stroke by using the years 2015 and 2016 as a look back period to avoid double-counting stroke incident events.

3.2.4 NHSO stroke data set information

The NHSO stroke data contained individual level data of stroke patients from the year 2015 to 2020. Data can be grouped into 5 parts: (1) patient information containing personal characteristics, (2) inpatient admission data, (3) outpatient visits, (4) procedure data, and (5) hospital bills or claims data. Detailed information regarding the variables used in the analysis is presented in Table 3-1. In order to ensure that the incident stroke event was captured, a two-year look-back period was applied (calendar year 2015 and 2016). This study focuses on an adult population and hence includes stroke patients aged 18 years and above.

Table 3-1 Variables in NHSO data

Patient information	Outpatient visit	Inpatient admission	Health service intervention	Bills
• Encrypted person identifier (PID) • Encrypted transaction identification number (TID) • Death age • Date of death • Sex • Type of service	• PID • TID • Hospital code • Service date • Principal diagnosis code (PDX) • Secondary diagnosis code (SDX) • Age at the time of outpatient visit	• PID • TID • Hospital code • Admission date • Discharge date • PDX • SDX • Discharge type • Discharge status • Age at the time of inpatient admission	• PID • TID • Hospital code • Procedure code	• PID • TID • Diagnosis Related Group (DRG) • Relative weight (RW) • Adjusted RW (AdjRW) • Total amount of hospital charge • Total out of pocket payment • Reimbursement payment

Patient information

Each individual is given an encrypted unique PID, as the main and unique linkage-key in the NHSO databases. Sex, date of death and type of service (outpatient or inpatient) are also recorded. This information enables the records of individuals to be linked with other electronic medical records. However, to protect the privacy and confidentiality of an individual, their hospital number (HN) which is a unique identifier for each patient assigned by a hospital and date of birth is not provided. The NHSO data has also been linked to the citizenship database to retrieve date of death from the Bureau of registration administration, Ministry of Interior which is responsible for birth and death registration[2].

Inpatient admissions

This data set contains all inpatient records of individuals, including admission date, discharge date, encrypted transaction identification number (TID) – used for tracking bills, age when utilising inpatient care, discharge status and discharge type.

In terms of diagnosis, this data set contains one PDX, and up to twelve SDX for each admission. Both PDX and SDX codes were recorded using ICD-10. The ranking of SDX codes does not affect the reimbursement rate but all SDXs have an impact on the diagnosis-related groups (DRGs) when a reimbursement rate is calculated by NHSO. DRG information are provided in more detail to measure cost of treatment in cost analysis sub-section under 3.2.6 Statistical analysis section.

Outpatient visits

This data set contains all routine outpatient visits and record the date of service use, an encrypted transaction identification number, age when utilising outpatient services, PDX and SDX.

Health service interventions

This data set provides information on medical procedures, operations, diagnosis, physical therapy or interventions, such as surgery, radiology, and pathology, of each inpatient admission or outpatient visit. This included a code for thrombolytic therapy. These health service intervention codes were recorded using the International Statistical Classification of Disease Ninth Revision - Clinical Modification (ICD-9-CM) coding system[108]. The ICD-9-CM is different from ICD-10 due to the fact that none of ICD-10 and ICD-9 provided codes for classification of these health service interventions. As a result, an adaptation of ICD, the clinical modifications (CM) of ICD were developed[109] and in Thai MOPH still used the ICD-9-CM version. The health service intervention codes can be recorded with a maximum of 15 codes per outpatient visit or inpatient admission.

Hospital bills or claims

The NHSO did not provide information on unit costs for services. The provided data set contains the DRG code, relative weight (RW) and adjusted relative weight (AdjRW) of each inpatient admission. Additionally, both outpatient visit and inpatient admission records contain the total amount of hospital charges, any out-of-pocket payments by patients and reimbursement payments by NHSO. The AdjRW can be used to calculate a cost together with information on charges.

3.2.5 Data management

Comprehensive data cleaning and manipulation were carried out. The following paragraph describes data cleaning and manipulation steps.

Prior to the assessment of data consistency, data cleaning and data validation, data were examined to ensure that all variables were delivered as requested. Then, frequency of patients per year, missing values and the uniqueness of records were examined. Consistency of data was assessed through a series of steps.

- Identify duplicates (two or more rows have the same values in all variables for the same patient)
- Record missing values of age, sex and diagnosis.
- Assessment of consistency of values such as date of death and sex in the same patient.
- Person-level inconsistencies were flagged for exclusion from further data analysis. Thus, records for patients with a date of death before date of admission, or those for whom the admission date was later than the discharge date were removed. Inconsistencies across data sets were corrected if plausible. For instance, typographical errors, improperly formatted.

3.2.6 Statistical analysis

The analysis in this section consists of 3 main parts: (1) service utilisation analysis, (2) cost analysis and (3) time to event analysis. R programme version 4.1 was used for all analyses except for the two-part models (TPM) which were estimated using Stata version 16 (StataCorp LP College Station, TX)[110]. Statistical significance was set at $p<0.05$ for all comparisons.

Service utilisation and baseline characteristics

Descriptive analysis of service utilisation and baseline characteristics at the time of incident stroke diagnosis was carried out by stroke subtype for either incident inpatient admission or outpatient visit for events recorded as either PDX or SDX. The outcome was volume of use such as visits or admissions per person per year, average length of stay (LOS), frequency of recurrent stroke. Some variables were modified to enhance explanatory power, for example, creating age groups from age (continuous variable), SDXs were converted to comorbidity grouping using the Charlson Comorbidity Index (CCI)[111]. For zero LOS, a value of one was added to all LOS values to reflect positive resource use.

Cost analysis

This section presents methods for converting charges as recorded in the NHSO data set to costs for each patient. Following on from this, the second part of this section then presents the methods to estimate annual costs using a regression analysis framework.

Cost measurement from claims data

Traditionally, Thailand has used DRG, as a case-based provider payment (or reimbursement rate) for inpatient care from NHSO since 2002 under the concept that patients in the same DRG will have the same LOS and the same level of hospital resource use. DRGs are derived from PDX, SDXs, procedure, age, sex, body weight at admission, discharge type, admission date, admission time, discharge date, discharge time, number of days of a temporarily leave the hospital and LOS[112]. The fixed base rate or reimbursement rate from NHSO was 8,050 Baht per AdjRW and 8,250 Baht per AdjRW in fiscal year 2019 and 2020, respectively[113, 114].

With regard to DRG calculation, first, RW is assigned to each DRG. RW refers to the average resource use for IP treatments according to the DRG and it compares between the average resource use for patients of a specific DRG and the average resource use of all patients in all DRGs[113, 115]. Thus, it reflects the severity of illness and the cost of care and higher reimbursement. For insurance, the higher the RW, the more resources are required for treatment. Therefore, individual hospitals have different compensation per DRG relative weight. Second, an AdjRW is calculated by adjusting RW with average LOS[1] based on the concept that LOS is one of the factors reflecting the severity of illnesses, efficiency of inpatient treatment, and cost of treatments[113, 116]. Finally, the NHSO reimbursement rate is calculated by multiplying AdjRW with a base rate per AdjRW of a disease.

However, the base rate from NHSO does not reflect the treatment cost. Therefore, instead of using the NHSO reimbursement rate as described above, the cost analysis in this thesis uses unit costs for outpatient visits and unit costs per AdjRW from a costing study entitled **"The unit cost per disease phase 1 year 3 report"**[112] which examine costs from 23 hospitals across all hospital levels in Thailand based on the provider perspective for the fiscal year 2019 by using the standard costing method and micro-costing approaches. The NHSO stroke data set had additional hospital types to those recorded in the costing study. Here, the number of hospital beds was used to assign a hospital type.

To conclude, the cost analysis in this thesis was carried out by using the unit cost per outpatient visit and the unit cost per AdjRW (from the costing study above). Regarding costs per inpatient admission, the unit cost per AdjRW (from the costing study) was multiplied by the AdjRW

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[1] To determine, the data were classified to be (1) patients with LOS less than one-third of the average lengths of stay in the DRG group (LOS is below the threshold - low outlier), (2) patients with LOS within one-third of the average lengths of stay in the DRG group (normal LOS - inlier) and (3) patients with LOS were greater than the outlier trim point of LOS of each DRG group.

from our stroke data set. Inflation was adjusted for using the consumer price index (CPI).

1. Cost of inpatient admission = **Equation (1)**
[(cost per AdjRW x (CPI_{2020}/CPI_{2019})) x AdjRW per admission]
+
[self-paid charge by patients x (CPI_{2020}/CPI_{x})]

2. Cost of outpatient visit = **Equation (2)**
[cost per outpatient visit x (CPI_{2020}/CPI_{2019})]
+
[self-paid charge by patients x (CPI_{2020}/CPI_{x})]

Treatment cost per patient = 1 + 2 **Equation (3)**

Where:
- cost per AdjRW stands for cost for a hospitalization differing by hospital level.
- AdjRW stands for adjusted relative weight which was automatically calculated and provided by NHSO
- CPIx stands for consumer price index (CPI) for the year of resource use
- CPI2020 stands for consumer price index for the year 2020

Once the total cost per inpatient admission or outpatient visit was defined, the total cost for an episode of care, or continuous inpatients stay (CIS), was determined. A CIS stands for an unbroken period of time that a patient is being treated as an inpatient[117]. The process describing the calculation of costs per patient is presented in Figure 3-1.

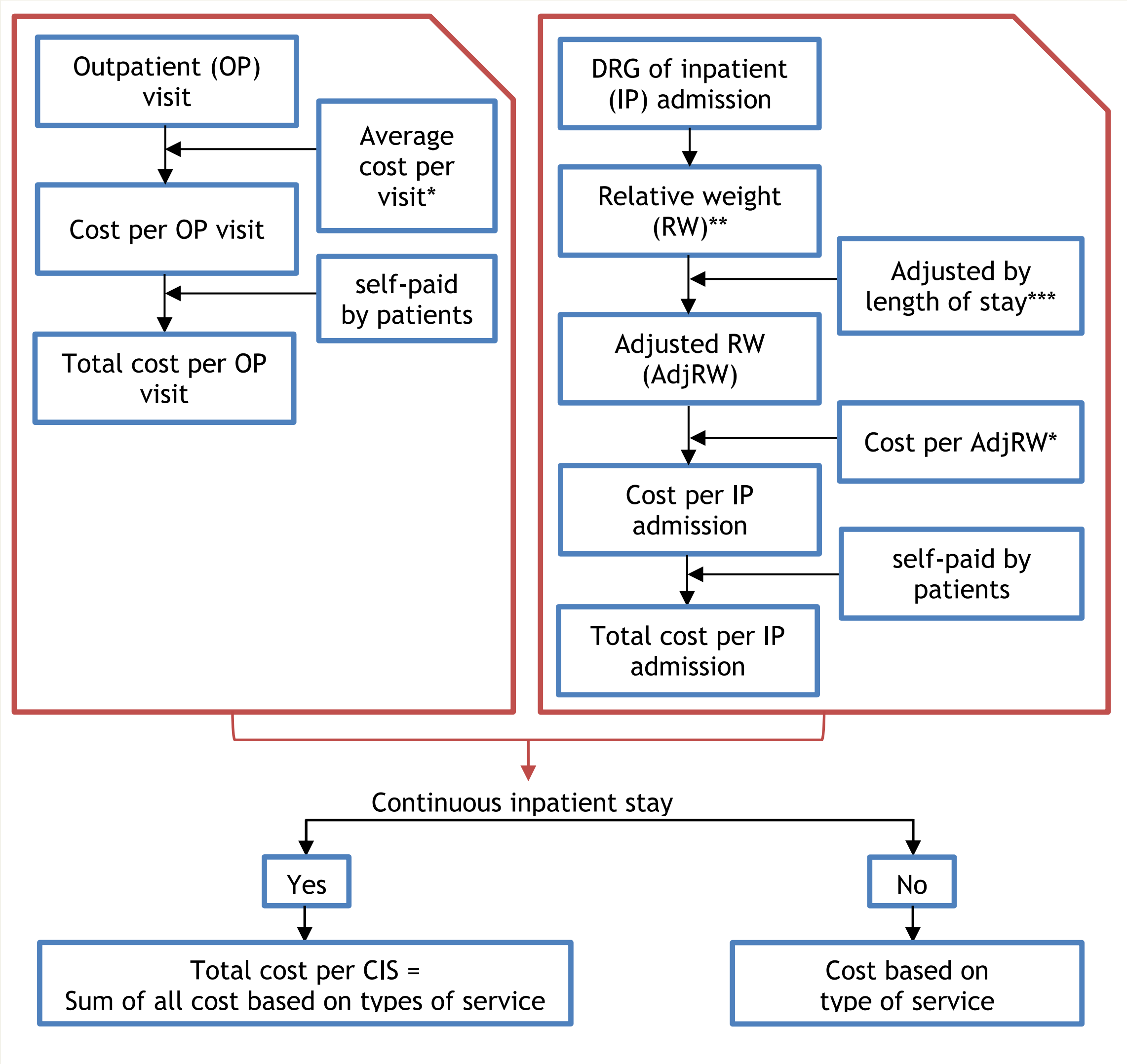

Figure 3-1 Cost calculation
*Cost from "The unit cost per disease phase 1 year 3 report" study[112]; **RW = mean charge of each DRG divided by aggregated mean charge of all patients[115]; ***Different formula for adjusting RW based on LOS[116]

Estimation of annual hospitalisation cost per patient

The following section presents an estimation of mean annual hospitalisation costs per patient, which was calculated summing up the costs from the previous section.

It is widely recognised that health service cost data (or expenditure) often have a high percentage of zero values, heavy right tails or positive skewness. From initial checks, the data also showed positive skewness and heavy right tails of cost values (Appendix 4 haemorrhagic stroke patients, Appendix 5 ischaemic stroke patients, Appendix 6 unspecified stroke patients). Typically, the most common statistical methods to estimate costs are Ordinary Least Squares regression (OLS), log-transformed OLS, and Generalised Linear Model (GLM) with a log link gamma distribution[118-121]. OLS regression is easy to apply and based on the central limit theorem or on the assumption of normally distributed error terms with constant variance (homoskedastic)[122]. However, OLS might not be suitable if data are right skewed and it may violate the normality assumption and the error term is non constant (heteroskedastic). To overcome this issue, a log-transformation of costs is commonly applied to achieve a more normal distribution, but back-transformation into the original units is required for interpretation of results[123]. One technique that can be applied here is Duan's smearing factor[124]. However, if the residual errors are non-constant, the smearing factor could also yield biased results and heteroskedasticity might still be present[125]. In addition the selection of a smearing factor is usually arbitrary[126]. Another approach for addressing heteroscedastic residual errors and estimating costs is to use GLM. GLM estimates costs on an untransformed scale and thus makes inferences about the mean costs directly. GLM with a gamma distribution and log link is widely applied in health economic studies[125, 127].

In order to address the issue of zero cost observations for some patients in some years, GLMs can be extended and estimated by using two-part models (TPM)[118, 122, 128]. Part 1 estimates the probability of incurring any healthcare costs and can be analysed using a logit or probit regression model. The second part estimates costs conditional on having incurred positive costs. It can be fitted using GLM with the same or a different set of variables used in the first modelling part. GLMs require specification of (1) a link function g(.), which relates the conditional mean to the predictors, and (2) a distributional family (D), which specifies the relationship between the variance and the mean estimated costs conditional on having incurred positive cost values. Finally, results from both parts are multiplied to calculate mean annual costs per individual patient.

Part 1, Pr(Y>0|X), was estimated with a logistic regression model (logit)[129, 130]. The dependent binary variable (Y) can be estimated in the form of a log odds ratio. Equation (4) shows the structure of the first component which denotes the probability of observing a positive cost.

$$\Pr(Y>0) = \frac{exp(\beta^{j} X_{it}^{j})}{(1+exp(\beta^{j} X_{it}^{j})} \qquad \textbf{Equation (4)}$$

Where: X_{it}^{j} is the variables at that could influence costs (j = 1, ... J); i is the patient i at time t; β^{j} is the estimated coefficient for variable at the j^{th}.

Part 2, GLM with a log link function and gamma distribution estimates costs conditional on having incurred positive cost values.

$$E(Y|Y>0,X) = \exp(\beta^{j} X_{i}^{j}) \qquad \textbf{Equation (5)}$$

Where βj is the coefficient on the j^{th} variable in the GLM equation

Therefore, mean estimated costs per individual patient can be calculated by multiplying the first and second part (Equation (6))

$$E(Y|X) = \Pr(Y>0|\ X) \times E(Y|Y>0,\ X) \qquad \textbf{Equation (6)}$$

Covariates

The selection of explanatory variables was based on a literature review and clinically relevant variables including age, sex, CCI, stroke subtype, LOS, hospital type at the incident stroke, received thrombolytic therapy at the incident stroke, received rehabilitation at the incident stroke, health region, and year of admission[18, 59, 131-134]. To select these variables for model fitting, univariable and multivariable regression were conducted in which the forward and backward stepwise selection were used to compare models.

For the first part, variables that were expected to impact on resource utilisation were included, namely age group, sex, CCI and LOS including the interaction between age group and CCI. The second part included the same variables that were used in the first part, but in addition variables that would affect costs were also included: stroke subtype, type of hospital, health region, receiving rehabilitation at admission, receiving thrombolysis during the incident inpatient admission and year of admission. All covariates entered the model as categorical variables.

- Age group

Age at incident inpatient admission or outpatient visit was converted to a categorical variable, where the youngest (age <40 years) served as the reference group. Age was categorised into 10 year age bands.

- Sex

Sex is one of the risk factors which influences many diseases including stroke. The reference group was female. It was assumed that differences in costs between men and women might occur.

- Comorbidity index scales

All SDXs were classified as severity of comorbidities using CCI as mentioned in the previous section. A set of 17 specific conditions based on ICD codes are used with a weight from 1 to 6 based on the adjusted 1-year mortality hazard ratio. The summation of these weights generates the Charlson comorbidity score for each patient. A zero score indicates no comorbidities. This thesis classified the CCI in to three categories: a score of zero (no comorbidity), score 1-2 and score ≥3. It was expected that patients who have more comorbidities would incur higher costs than those with no comorbidity (reference group).

- Length of stay

LOS was converted to a categorical variable which was dichotomised to LOS <3 days, LOS 3 to 7 days, LOS 8 to 15 days and LOS >15 days. This study identified the first group to be a reference group based on the literature review and mean of LOS from the patient characteristics data (quartile range) and it is hypothesised that longer LOS would be expected to impact on costs.

- Type of stroke

Stroke subtypes were ischemic, unspecified and haemorrhagic stroke (reference group).

- Rehabilitation

Stroke patients who received rehabilitation during the incident inpatient admission or outpatient visit were compared to patients who did not receive rehabilitation (reference).

- Thrombolytic therapy

Stroke patients who received thrombolysis during the incident inpatient admission or outpatient visit were compared to patients who did not receive this treatment (reference). This service was included in the model to take account of costs of implementing stroke care in the service plan policy[6].

- Health region

Generally, different geographical areas would have different costs of treatment. Therefore, geographical variation in service utilisation and treatment costs might reflect a variation in clinical practice and service etiquette. As Bangkok outperforms other regions in terms of technology advancements, it is used as the reference category for estimating costs.

- Hospital level

Hospitals were divided into six groups, comprising advanced-level, standard-level, mid-level hospitals, primary and community hospitals, non-MOPH hospitals which included university hospitals, military hospitals, other specialised hospitals, hospitals in the Bangkok area, and private hospitals/clinics.

Similar to health region, the type of hospital is also expected to impact on costs with higher level hospitals incurring higher costs due to the provision of more advanced treatments. This study used primary and community hospitals as a reference group because it is hypothesised that the cost of stroke care at this hospital level is lower than for other hospital levels.

Time to event analysis

Time to event analysis for all-cause mortality and the first recurrent stroke were carried out.

For all-cause mortality, patients who died on the admission date of the incident admission or outpatient visit (LOS = 0) were excluded from the analysis (N = 4,805). For the analysis of stroke recurrence, the first stroke diagnosis of each patient was designated the “index stroke”. A recurrent stroke is defined as an inpatient admission of any type of stroke occurring more than 21 days after the admission date of the index stroke admission[135-137]. Patients who died during their index stroke admission were excluded from the analysis of recurrent strokes (N = 41,294). This included patients who had several admissions for an episode of care, or CIS. However, to reflect local practice in Thailand, a CIS would include any outpatient visit followed by a transfer to inpatient admission on the same day. To calculate the numbers of patients experiencing a recurrent stroke events, patients who had only one outpatient visit or inpatient admission and who did not experience a recurrent stroke were excluded. Thus, there were

31,687 patients (35,026 events) over 4 years since their incident stroke (Figure 3-2).

In conclusion, the final number of incident stroke patients was 386,484, 340,403 patients for the analysis of all-cause mortality and 31,687 patients for recurrent stroke event.

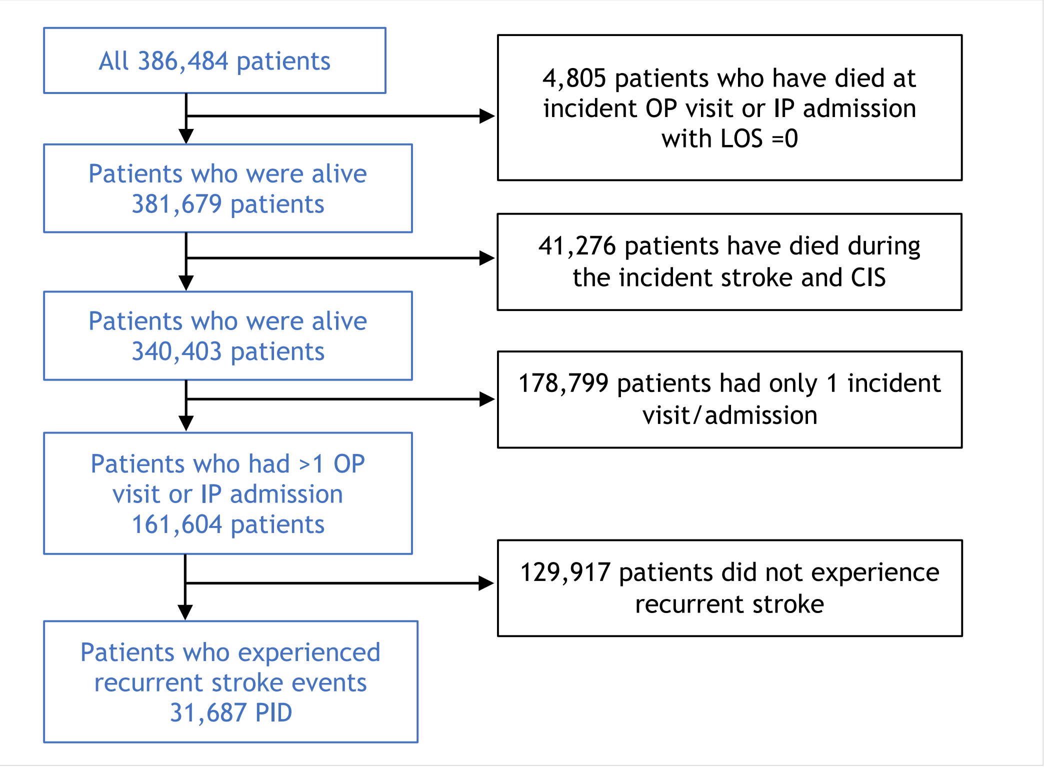

Figure 3-2 Data management and processes for stroke recurrences

Inferential analysis

Survival analyses of all-cause mortality, with survival time from date of the incident stroke until date of death, were conducted. For recurrent stroke, survival time was calculated from the admission date of the incident stroke until the hospitalisation of the first recurrent stroke. There are no standardised approaches to define the duration between index stroke and recurrent stroke in research studies, and different criteria have been used in the literature. These include a minimum of seven days, 21 days, or 30 days[135, 136, 138-140]. Upon reviewing the literature and after consultation with a clinical expert, a duration of 21 days between index stroke (admission date) and recurrent stroke was chosen to define recurrence[136, 138, 139]. In the remainder of this analysis, only right censored data was considered. Censoring occurred either at the end of the observational period (November 23rd, 2020) or death.

Survival analyses were performed in three parts as follows.

(1) a non-parametric method using the Kaplan-Meier survival analysis which estimated the survival probability from observed survival times. The survival function is denoted in Equation (7).

$$\text{Survival function} = S(t_k) = S(t_{k-1}) * \left(1 - \frac{d_k}{n_k}\right)$$ **Equation (7)**

Where:
d_k = the number of events at time t_k
n_k = the size of risk sets at time t_k

(2) a semi-parametric analysis was carried out using Cox proportional hazards regression which was used to investigate the effect of covariates on all-cause mortality (Equation (8)). The cox proportional hazards model assumes that the ratio of the hazards for any two individuals is constant over time. This assumption was tested using the Schoenfeld residuals method and the log-log plot.

$$h(t, X) = h_0(t)e^{\sum_{i=0}^{p} \beta_i X_i}$$ **Equation (8)**

Where:
X_i = covariate variables
$h_0(t)$ = baseline hazard function
β_i = the regression coefficients indicating the effect of each covariate X_i

In this regard, there was evidence of nonproportional hazards (Appendix 7) from the Schoenfeld residuals (Appendix 8) which were statistically significant for each of the covariates including a global test. To support the proportional hazards assumption, the association between Schoenfeld residuals and time must represent either a random or no pattern against time. However, the Schoenfeld residuals plot shows a non-random pattern against time. So, this is evidence of a violation. The results of log-log plots also showed a violation of the proportionality assumption (Appendix 9). For example, the estimated log cumulative hazard curves were unparallel over time between men and women meaning that the ratio of the hazards is not constant over time. In addition, a crossed curve also leads to proportional hazard violation as can be seen in health region covariate. For example, the hazard is greater in health region 11 than health region 5 at first; however, the hazard changes and is higher for health region 5 at the end.

To resolve this issue stratification on violating variables such as age group, rt-PA, stroke subtype, was carried out as well as a time-dependent variable approach[141]. The recurrence status variable, called a defined time-dependent variable, was used because the value for a given subject might differ over time t. Both approaches were not sufficient to resolve the issue of non-proportionality. Thus, parametric survival models were considered for analysis[141, 142].

(3) The following parametric distributions were explored. Generally, the hazard is assumed to be constant in the exponential model while the Weibull and Gompertz models have a monotonically increasing or decreasing hazard as it contains the distributional parameters that determine the shape of hazard models. Lastly, the log-logistic and log normal distribution have a increasing hazard to a maximum and then decreasing hazard. The Gompertz parametric model has been extensively used by medical researchers and other fields to model overall mortality and is also the standard distribution choice when modelling the risk of death or competing events[143]. In this study, the Cox-Snell residuals test and the Akaike's information criterion (AIC) were used to select the best fitting distribution. In particular, the Exponential distribution contains the simplest parametric model (Equation (9) and Equation (10)) for hazard and survival function respectively, which assumes the hazard is constant over time (t) while the Weibull and the Gompertz distribution contain shape parameters which represent the hazards' direction over time.

Exponential model

- Hazard function = h(t) = λ **Equation (9)**
- Survival function = S(t) = $\exp(-\lambda t)$ **Equation (10)**

where:

λ = scale parameter and $\lambda > 0$, for $0 \leq t < \infty$

Gompertz distribution

- Hazard function = h(t) = $\exp(\exp(\lambda) + \gamma t)$ **Equation (11)**
- Survival function = S(t) = $\exp\left[\frac{-\exp(\lambda)(\exp(\gamma t)-1}{\gamma}\right]$ **Equation (12)**

where:

γ = shape parameter

$\gamma>0$ = increasing hazard

$\gamma<0$ = decreasing hazard

Covariates

Variables used as covariates comprised sex, age group, CCI, stroke subtype, receiving rehabilitation during incident admission, receiving thrombolysis during the incident inpatient admission, recurrence status, LOS, type of hospital and health region. In addition, an interaction term between age group and CCI was included based on clinical evidence that most comorbid diseases become more common as people age. The details of these variables were described in the cost analysis section. For example, it was expected that stroke mortality is higher in male patients, patients with longer LOS or a higher CCI score. In terms of health region, hospitals in the Bangkok area tend to have more advanced technologies available and also a relatively high proportion of stroke specialists[19]. It is hypothesised that these regional differences could impact mortality rates.

In terms of all-cause mortality for patients with a recurrent stroke, stroke patients with at least one recurrent stroke during a four-year follow-up were assigned to a stroke recurrence group which was compared to patients who have not had any recurrent event (reference). It is expected that patients experiencing a recurrent stroke event would have higher mortality.

These covariates were used for model fitting by comparing the forward and backward stepwise selection. Both stepwise selections returned the same results which showed that the aforementioned covariates had the lowest AIC. Thus, these covariates were included in the model.

3.3 Results

Initially, there were 637,160 patients (3,332,533 records). No duplicate records or inconsistencies for patient characteristics were found. However, some patients died before their first admission and 216 PIDs were excluded. Additionally, data on admissions after death were deleted but no patient was excluded. The remaining 636,944 patients were checked for a stroke diagnosis (ICD-10: I60 - I69). There were 51,542 patients that had no stroke diagnosis as either PDX or SDX recorded. This result may be explained by the fact that when deleting data after their death date, the remaining data were not related to stroke services. The remaining data included 585,402 patients. This study used data between calendar year 2015 and 2016 as a look back period to ensure that the incident stroke event is captured. A further 194,894 patients were excluded with records in either 2015 or 2016. For the remaining 390,508 patients the age at admission was checked and a further 4,024 patients who were under 18 years were excluded. Following these steps, the final number of incident stroke patients was 386,484 (Figure 3-3). Further adjustments will be made for individual outcome measures. More details of each outcome were given in the next section.

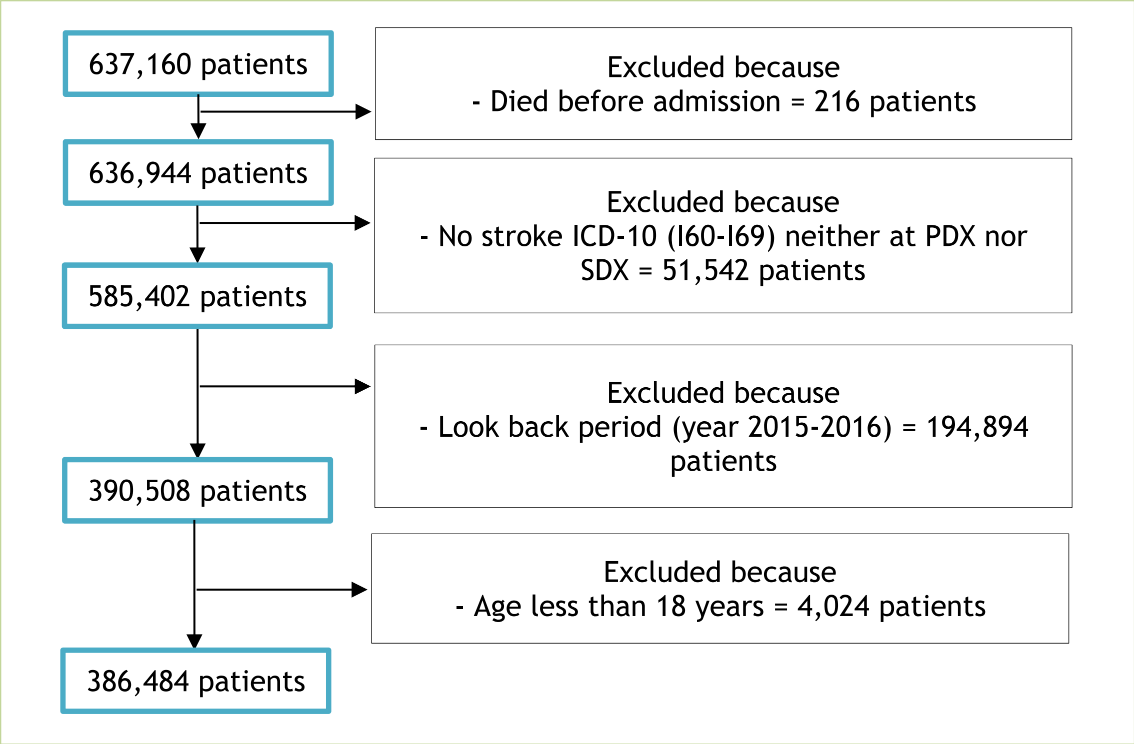

Figure 3-3 Step of data cleaning and data validation

The final data set for analysis included 386,484 incident stroke patients. Table 3-2 presents the number of incident stroke patients by year and Figure 3-4 illustrates the initial place (outpatient vs inpatient) where stroke patients were diagnosed and the number of transfers to another hospital. It is apparent that nearly 80% of patients who were diagnosed at an outpatient setting were transferred to an inpatient setting (either to the same or another hospital) and of these, around 65% were transferred on the same day of their diagnosis. In contrast, 82% of patients diagnosed with stroke in an inpatient setting stayed in inpatient. The number of patients in year 2020 was lower due to incomplete data for that year.

Table 3-2 The number of incident patients classified by year

Year	Number of patients	Men				Women			
		Haemorrhagic	Ischaemic	Unspecified	Total	Haemorrhagic	Ischaemic	Unspecified	Total
2017	138,251 (36%)	17,310 (23)	35,937 (47)	23,457 (31)	76,704 (100)	11,298 (18)	31,186 (51)	19,063 (31)	61,547 (100)
2018	138,112 (36%)	17,343 (23)	37,565 (49)	21,966 (29)	76,874 (100)	11,267 (18)	32,372 (53)	17,599 (29)	61,238 (100)
2019	105,279 (27%)	12,444 (21)	29,110 (50)	16,838 (29)	58,392 (100)	8,039 (17)	25,133 (54)	13,715 (29)	46,887 (100)
2020	4,842 (1%)	237 (9)	649 (24)	1,852 (68)	2,738 (100)	143 (7)	462 (22)	1,499 (71)	2,104 (100)
Total	386,484 (100%)	47,334 (22)	103,261 (48)	64,113 (30)	214,708 (100)	30,747 (18)	89,153 (52)	51,876 (30)	171,776 (100)

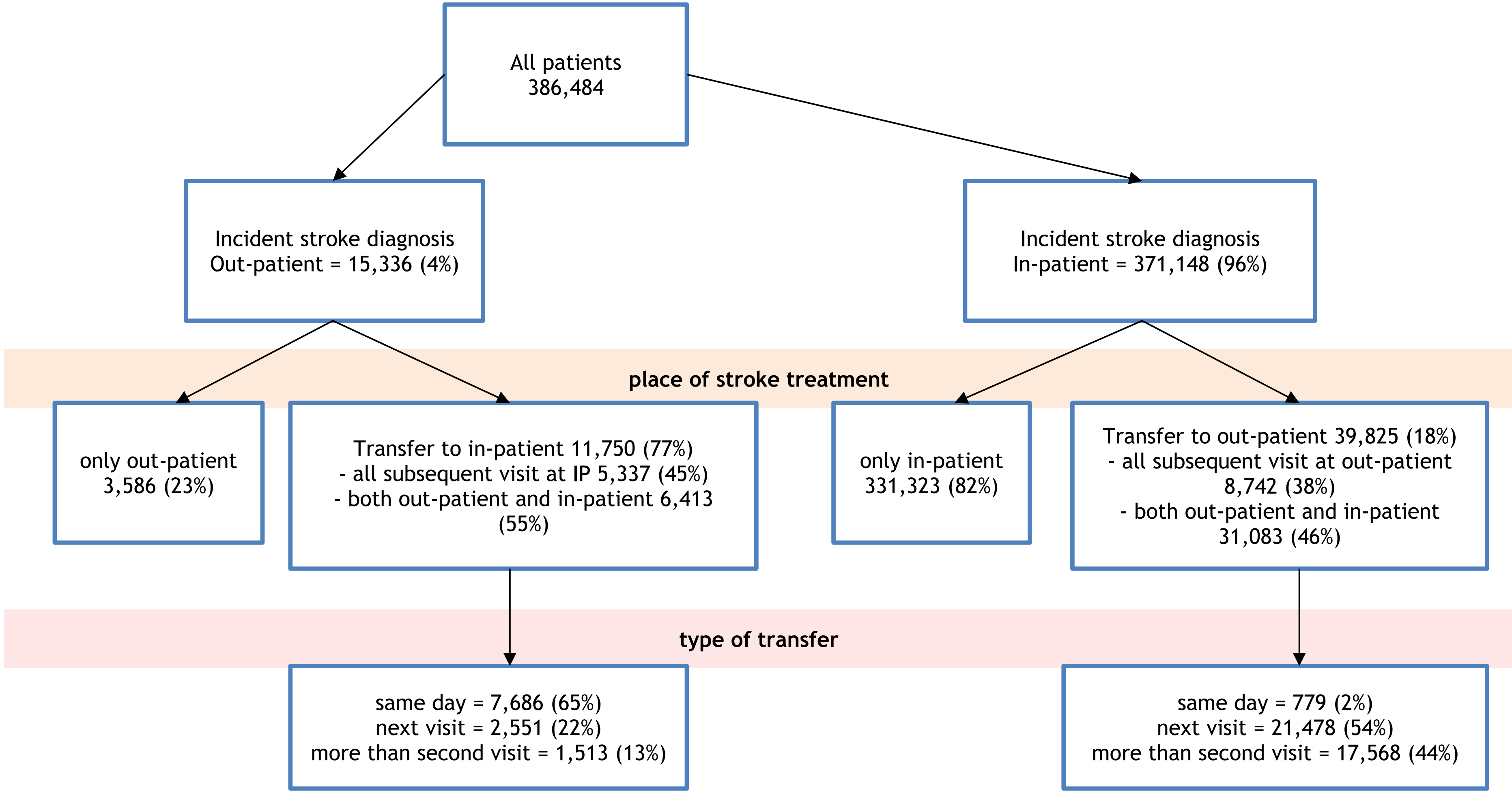

Figure 3-4 Number of transferred patients

3.3.1 Cohort characteristics by stroke subtype

Characteristics of patients classified by type of stroke are shown in Table 3-3. based on data at incident admission. Of the 386,484 patients who were diagnosed with stroke, the majority had ischaemic followed by unspecified and haemorrhagic stroke accounting for 50%, 30% and 20%, respectively. There were more male patients (N=214,708; 56%) than female patients, and the mean age of female patients (mean: 67.0; SD: 14.0) was higher than that for males (mean: 63.4; SD: 13.7) in all stroke subtypes. At the incident stroke admission, the mean LOS of haemorrhagic stroke was highest at around 10 days (mean: 9.9; SD: 16) while LOS for ischaemic and unspecified stroke were less than 7 days (ischaemic: mean: 6.7; SD: 10.9, unspecified: mean: 6.1; SD: 9.5). More than 60% of haemorrhagic and ischaemic stroke patients had no comorbidities (CCI score 0) while 68% of patients with an unspecified stroke had a CCI score of 1 to 2 which might imply that these patients could be more severely ill than patients with other subtypes. However, when considering all 17 components of the CCI, there was no distinction in any of the stroke subtypes for the top three comorbid diseases which indicated that the most common disease was cerebrovascular disease (CVD).

In terms of type of hospital, the highest percentage of incident stroke diagnoses was found to be made in advanced-level hospitals at 50% of haemorrhagic patients and 37% of ischaemic patients. Comparatively, 57% of unspecified stroke patients were diagnosed with their incident stroke at other hospital levels such as university hospital, other specialised hospitals, community hospitals, hospitals in the Bangkok area, private hospitals/clinics and military hospitals. It is obvious that imaging (CT-scan) was mostly carried out for patients with haemorrhagic and ischaemic stroke, however, the percentage of patients with ischaemic stroke receiving thrombolytic therapy was only 7%. Furthermore, during their incident admission, patients with ischaemic stroke were more likely to receive rehabilitation services compared to other subtypes. When considering the frequency of outpatient and inpatient utilisation, patients had on average four outpatient visits and two inpatient admissions in all stroke subtypes. Average stroke recurrence, after excluding patients who died during their incident stroke, was approximately one.

Table 3-3 Baseline characteristics at the first time of diagnosis with stroke

	Haemorrhage	Ischaemic	Unspecified	All
Number of patients - N (%)	78,081 (20)	192,414 (50)	115,989 (30)	386,484 (100)
Sex				
Men	47,334 (61)	103,261 (54)	64,113 (55)	214,708 (56)
Woman	30,747 (39)	89,153 (46)	51,876 (45)	171,776 (44)
Age (years)				
mean (SD)	60.8 (14.9)	65.5 (13.3)	67.0 (13.8)	65.0 (14.0)
- men	58.5 (14.5)	64.2 (12.9)	65.7 (13.6)	63.4 (13.7)
- women	64.3 (14.8)	67.1 (13.6)	68.5 (13.9)	67.0 (14.0)
median (IQR)	61 (50-72)	66 (57-75)	68 (58-77)	66 (56-75)
- men	58 (49-69)	65 (56-73)	67 (57-76)	64 (54-73)
- women	65 (54-76)	68 (58-77)	70 (60-79)	68 (58-78)
Age group				
age < 40	5,802 (7)	6,020 (3)	4,114 (4)	15,936 (4)
age 40 - 49	12,071 (15)	16,927 (9)	8,382 (7)	37,380 (10)
age 50 - 59	19,208 (25)	38,102 (20)	19,435 (17)	76,745 (20)
age 60 - 69	18,255 (23)	54,237 (28)	30,894 (27)	103,386 (27)
age 70 - 79	13,400 (17)	47,149 (25)	30,900 (27)	91,449 (24)
age 80 - 89	8,124 (10)	26,325 (14)	19,244 (17)	53,693 (14)
age > 90	1,221 (2)	3,654 (2)	3,020 (3)	7,895 (2)
Death age (years)				
mean (SD)	64.2 (15.0)	71.9 (12.7)	72.3 (12.6)	69.8 (13.9)
- men	61.3 (14.7)	70 (12.6)	70.7 (12.6)	67.5 (14.0)
- women	68.2 (14.5)	73.9 (12.4)	74.1 12.4)	72.4 (13.3)
median (IQR)	65 (53-79)	74 (64-81)	74 (65-81)	71 (61-80)
- men	61 (51-72)	71 (62-79)	72 (63-80)	69 (58-78)
- women	70 (58-80)	76 (67-83)	76 (67-83)	75 (64-82)
N (%)	41,109 (29)	56,623 (40)	43,512 (30)	141,244 (100)
LOS (days)				
mean (SD)	9.9 (16)	6.1 (9.5)	6.7 (10.9)	7.1 (11.6)
median (IQR)	5 (3 - 11)	4 (3 - 6)	4 (3 - 7)	4 (3 - 7)
Charlson comorbidity index				
score 0	47,528 (61)	126,531 (66)	32,920 (28)	206,979 (54)
score 1 to 2	30,058 (38)	64,024 (33)	79,041 (68)	173,123 (45)
score 3 or over	495 (1)	1,859 (1)	4,028 (3)	6,382 (2)
Comorbidity - top 3 diseases				
first rank	cerebrovascular disease (61%)	cerebrovascular disease (48%)	cerebrovascular disease (68%)	cerebrovascular disease (60%)
second rank	renal disease (14%)	renal disease (20%)	renal disease (12%)	renal disease (15%)
third rank	hemiplegia (9%)	hemiplegia (11%)	hemiplegia (8%)	hemiplegia (9%)
Hospital level				
advanced-level	39,348 (50)	70,960 (37)	24,260 (21)	134,568 (35)
standard-level	19,024 (24)	51,962 (27)	16,635 (14)	87,621 (23)
mid-level	4,230 (5)	20,158 (10)	8,675 (7)	33,063 (8)
others	15,479 (20)	49,334 (26)	66,419 (57)	131,232 (34)
Investigations				
imaging (CT-scan)	60,929 (78)	167,860 (87)	30,194 (26)	258,983 (67)
Medication				

	Haemorrhage	Ischaemic	Unspecified	All
rt-PA	178 (0.2)	12,951 (7)	459 (0.4)	13,588 (4)
Rehabilitation				
received	18,641 (24)	89,716 (47)	115,989 (15)	125,561 (32)
Number of admissions/visits*				
A. outpatient visits				
mean (SD)	3.7 (7.4)	3.7 (6.9)	4.2 (8.0)	3.9 (7.4)
median (IQR)	1 (1-3)	2 (1-4)	2 (1-4)	2 (1-4)
N (%)	16,651 (21)	51,335 (27)	38,085 (33)	106,071 (27)
B. inpatient admissions*				
mean (SD)	2.0 (2.1)	2.4 (2.4)	2.8 (3.1)	2.5 (2.6)
median (IQR)	1 (1-2)	1 (1-3)	1 (1-3)	1 (1-3)
N (%)	77,941 (99)	192,009 (99)	113,505 (98)	383,455 (99)
Frequency of recurrence**				
mean (SD)	1.2 (0.7)	1.2 (0.6)	1.2 (0.8)	1.2 (0.7)
median (IQR)	1 (1 - 1)	1 (1 - 2)	1 (1 - 2)	1 (1 - 2)
number of events - n (%)	5,774 (7)	20,173 (10)	9,079 (8)	35,026 (9)

*All data; **Exclude patients who were dead at the incident stroke

95,163 (28%) patients died during a four-year follow up after their incident stroke (Table 3-4), with 84,478 patients from the group without a recurrent stroke and 10,685 patients from the group that had at least one recurrent stroke event. When including patients who died during their incident stroke (46,081 patients), there were 141,244 (36.5%) patient deaths recorded.

Table 3-4 Number of patients who have died during a four-year follow up

	Haemorrhage	Ischaemic	Unspecified	All
Number of patients - N (%)	78,081 (20)	192,414 (50)	115,989 (30)	386,484 (100)
Patients who have died during incident stroke	24,759 (32)	12,755 (7)	8,567 (7)	46,081 (12)
Patients who are alive during incident stroke	53,322 (68)	179,659 (93)	107,422 (93)	340,403 (88)
A. no recurrence	49,001 (92)	160,887 (90)	98,828 (92)	308,716 (100)
- alive	34,161 (70)	122,958 (76)	67,119 (68)	224,238 (73)
- dead	14,840 (30)	37,929 (24)	31,709 (32)	84,478 (27)
B. recurrence	4,321 (8)	18,772 (10)	8,594 (8)	31,687 (100)
- alive	2,811 (65)	12,833 (68)	5,358 (62)	21,002 (66)
- dead	1,510 (35)	5,939 (32)	3,236 (38)	10,685 (34)

3.3.2 Cost analysis

The cost analysis conducted in this chapter quantifies the average cost (Thai Bath unit) and distribution of cost by year over a four-year period from 2017 - 2020. Univariate regression results are shown in Appendix 10 and multivariate regression results using TPM are presented in the next section.

Multivariable analysis using TPM

It is apparent from multivariable regression (Table 3-5) that patients aged between 40-59 years had a lower probability of accessing healthcare services and also incurred lower costs compared with patients aged <40. For example, the coefficient values of age between 40-49 years equals -0.033 implied that, once costs occurred, these were about 3% lower when compared to the costs incurred by patients aged less than 40 years (an exponent of -0.033 equals 0.968). Surprisingly, age did not seem to have a linear association with resource utilisations as it decreased in patients aged between 40-59 years and then increased in patients aged 60 and over. However, it could be concluded that the probability of incurring costs seemed to increase with increasing age, in particular in patients aged ≥60 years.

Having a high CCI score and more than one week of LOS seemed to increase the probability of accessing healthcare services. From the results of the second part, it appears that once costs were incurred, these were lower for patients with ischemic and unspecified stroke compared to patients with haemorrhagic stroke. A stroke patient who received rehabilitation incurred costs about 10% lower (an exponent of -0.104) compared to stroke patients who did not receive rehabilitation at the incident admission.

Table 3-5 Multivariable analysis of annual mean cost

Variable	Coefficient	95%CI	SE	Coefficient	95%CI	SE
	Part 1 (Logit)			Part 2 (GLM with log link)		
Age group (years)						
age <40	Reference					
age 40-49	-0.086	-0.113, -0.059	0.014	-0.033	-0.070, 0.004	0.019
age 50-59	-0.037	-0.062, -0.012	0.013	-0.033	-0.068, 0.001	0.018
age 60-69	0.077	0.052, 0.102	0.013	0.030	-0.005, 0.064	0.018
age 70-79	0.245	0.219, 0.271	0.013	0.089	0.054, 0.124	0.018
age 80-89	0.421	0.391, 0.450	0.015	0.085	0.049, 0.121	0.018
age ≥90	0.656	0.595, 0.717	0.031	0.021	-0.029, 0.071	0.026
Sex						
women	Reference					
men	-0.055	-0.063, -0.046	0.004	0.030	0.021, 0.039	0.005
CCI						
no CCI	Reference					
score 1 to 2	0.336	0.295, 0.376	0.021	0.279	0.233, 0.324	0.023
score ≥3	1.261	0.828, 1.693	0.221	0.445	0.266, 0.624	0.091
LOS group						
LOS <3 days	Reference					
LOS 3 to 7 days	-0.047	-0.056, -0.038	0.005	0.042	0.031, 0.052	0.005
LOS 8 to 15 days	0.124	0.110, 0.137	0.007	0.378	0.365, 0.391	0.007
LOS >15 days	0.367	0.348, 0.386	0.010	1.042	1.028, 1.056	0.007
Age group#CCI						
age 40-49# score 1 to 2	0.022	-0.026, 0.071	0.025	-0.011	-0.066, 0.043	0.028
age 40-49#score ≥3	-0.446	-0.929, 0.037	0.246	0.101	-0.118, 0.320	0.112
age 50-59# score 1 to 2	0.028	-0.016, 0.073	0.023	0.039	-0.011, 0.089	0.026
age 50-59# score ≥3	-0.166	-0.625, 0.293	0.234	0.297	0.097, 0.496	0.102
age 60-69# score 1 to 2	0.034	-0.010, 0.077	0.022	0.019	-0.030, 0.068	0.025
age 60-69# score ≥3	-0.306	-0.750, 0.138	0.226	0.146	-0.041, 0.332	0.095
age 70-79# score 1 to 2	-0.013	-0.057, 0.031	0.023	-0.056	-0.105, -0.007	0.025
age 70-79# score ≥3	-0.459	-0.901, -0.018	0.225	0.062	-0.123, 0.247	0.095
age 80-89# score 1 to 2	-0.056	-0.104, -0.008	0.024	-0.072	-0.123, -0.022	0.026
age 80-89# score ≥3	-0.614	-1.060, -0.167	0.228	-0.005	-0.194, 0.183	0.096
age 90up# score 1 to 2	-0.097	-0.185, -0.009	0.045	-0.077	-0.148, -0.005	0.037
age 90up# score ≥3	-0.624	-1.142, -0.105	0.264	-0.045	-0.260, 0.171	0.110
Stroke subtype						
haemorrhagic	Reference					

Variable	Coefficient	95%CI	SE	Coefficient	95%CI	SE
ischaemic				-0.354	-0.365, -0.342	0.006
unspecified				-0.339	-0.354, -0.324	0.007
Hospital levels						
primary and community	Reference					
mid-level				0.156	0.137, 0.175	0.010
standard-level				0.112	0.096, 0.128	0.008
advanced-level				0.046	0.032, 0.061	0.007
non-MOPH				0.520	0.495, 0.546	0.013
private hospitals and clinics				0.567	0.532, 0.603	0.018
Rehabilitation						
not received rehabilitation	Reference					
received rehabilitation				-0.104	-0.114, -0.094	0.005
Thrombolytic treatment						
not received thrombolytic	Reference					
received thrombolytic				0.126	0.102, 0.150	0.012
Health regions						
Bangkok	Reference					
1				-0.064	-0.093, -0.035	0.015
2				-0.034	-0.065, -0.003	0.016
3				-0.027	-0.062, 0.008	0.018
4				0.035	0.004, 0.066	0.016
5				-0.016	-0.049, 0.016	0.017
6				-0.023	-0.055, 0.008	0.016
7				0.011	-0.020, 0.042	0.016
8				-0.018	-0.048, 0.012	0.015
9				0.023	-0.009, 0.054	0.016
10				-0.015	-0.047, 0.017	0.016
11				-0.056	-0.090, -0.022	0.017
12				-0.039	-0.073, -0.005	0.017
Follow-up years						
1	Reference					
2				0.009	-0.001, 0.019	0.005
3				0.005	-0.005, 0.015	0.005
4				-0.296	-0.311, -0.280	0.008
Constant	0.217	0.192, 0.241	0.012	10.845	10.800, 10.890	0.023

<u>Estimated mean annual cost</u>

Results after combining both modelling parts showed that mean annual cost per patient was 37,179.43 Baht (SE: 97.62; 95%CI: 36,988.10 - 37,370.76 Baht). Estimated costs for all covariates, after adjusting for all other predictors, are presented in Table 3-6[2]. Overall, key variables that significantly contributed to an increase in cost were found to be age, LOS, CCI score and receiving thrombolysis during the incident inpatient admission. It appeared that, advanced age was leading to an increase in estimated annual costs conditional on having incurred positive costs. Longer LOS, especially more than one week, significantly increased cost by around 1.5 - 3 times or 15,308.68 Baht up to 64,134.81 Baht compared to the reference group (LOS 1-3 days). Moreover, patients who had a CCI score of 3 and over incurred costs twice as high as comparable patients who had a CCI score of zero or no comorbidity. Lastly, patients who received thrombolysis during the incident inpatient admission incurred higher costs as there was a difference of over 5,000 Baht in the amount of annual costs compared to patients who did not receive rt-PA.

Patients who received rehabilitation during their incident admission, incurred lower costs (approximately 3,806 Baht) compared to patients who did not receive rehabilitation at the incident admission. Closer inspection of the results shows that haemorrhagic stroke subtype seemed to be associated with higher costs than ischaemic or unspecified stroke. In addition, only three health regions has a higher cost than hospital in the Bangkok area, the majority of health regions (9 out of 12) had lower costs than the Bangkok area. Being admitted to non-MOPH and private hospitals (including private clinics) was associated with considerably higher costs than hospitals under MOPH. Finally, mean annual costs between sex and year of admission only showed a trivial difference.

[2] It should be noted that after combining both parts, the interaction terms disappeared because the mixture of part one and two are based on the marginal effect in which the main covariates absorb the interaction term effect.

Table 3-6 Mean annual cost per stroke patients

Variable	Cost	L95%CI	U95%CI	SE
Age group (years)				
age <40	34,751.99	33,902.84	35,601.13	433.25
age 40-49	32,458.10	31,915.64	33,000.55	276.77
age 50-59	34,374.65	33,970.12	34,779.18	206.40
age 60-69	37,562.22	37,207.94	37,916.50	180.76
age 70-79	40,110.51	39,722.04	40,498.98	198.20
age 80-89	41,496.81	41,008.08	41,985.53	249.36
age ≥90	41,186.96	39,986.89	42,387.02	612.29
Sex				
women	36,959.35	36,689.56	37,229.14	137.65
men	37,365.87	37,116.11	37,615.62	127.43
CCI				
no CCI	30,085.96	29,860.32	30,311.59	115.12
score 1 to 2	44,447.53	44,126.97	44,768.09	163.55
score ≥3	70,241.79	67,842.17	72,641.41	1,224.32
LOS group				
LOS <3 days	29,086.65	28,837.15	29,336.15	127.30
LOS 3 to 7 days	29,781.74	29,544.98	30,018.51	120.80
LOS 8 to 15 days	44,395.33	43,915.56	44,875.09	244.78
LOS >15 days	93,221.46	92,039.97	94,402.96	602.81
Stroke subtype				
haemorrhagic	48,599.22	48,099.20	49,099.25	255.12
ischaemic	34,125.00	33,879.20	34,370.80	125.41
unspecified	34,629.38	34,284.27	34,974.49	176.08
Hospital type				
primary and community	32,001.41	31,628.90	32,373.93	190.06
mid-level	37,401.68	36,805.94	37,997.43	303.96
standard-level	35,798.05	35,385.59	36,210.50	210.44
advanced-level	33,523.82	33,223.52	33,824.12	153.22
non-MOPH	53,847.02	52,727.59	54,966.45	571.15
private hospitals and clinics	56,440.28	54,608.24	58,272.31	934.73
Rehabilitation				
not received rehabilitation	38,490.47	38,258.46	38,722.48	118.37
received rehabilitation	34,684.90	34,381.33	34,988.47	154.88
rt-PA				
not received rt-pa	37,020.66	36,827.84	37,213.48	98.38
received rt-pa	41,986.10	40,991.72	42,980.48	507.34
Health regions				
Bangkok	37,843.69	36,942.68	38,744.70	459.71
1	35,506.96	35,029.75	35,984.17	243.48
2	36,573.41	36,018.92	37,127.90	282.91
3	36,838.72	36,004.36	37,673.08	425.70
4	39,181.82	38,287.13	40,076.51	456.48
5	37,231.40	36,538.27	37,924.52	353.64
6	36,966.71	36,300.87	37,632.54	339.72
7	38,275.02	37,629.32	38,920.72	329.44
8	37,172.71	36,658.41	37,687.02	262.41
9	38,706.39	38,122.47	39,290.31	297.92
10	37,290.50	36,647.70	37,933.30	327.97

Variable	Cost	L95%CI	U95%CI	SE
11	35,771.55	35,042.51	36,500.59	371.96
12	36,395.49	35,650.52	37,140.46	380.09
Follow-up years				
1	39,645.58	39,343.05	39,948.11	154.35
2	39,991.39	39,700.93	40,281.84	148.19
3	39,845.32	39,539.91	40,150.73	155.82
4	29,495.85	29,086.74	29,904.96	208.73

L95%CI: lower bound 95%confidence interval, U95%CI: upper bound 95%confidence interval

Table 3-7 shows the mean annual costs by stroke subtype after adjusting for all other predictors. What stands out in this table was the dominance of mean annual cost in patients with haemorrhagic stroke compared to patients with ischaemic and unspecified stroke. There has been a gradual increase in the mean annual costs of patients aged 50 years and over and these figures showed a similar trend in all stroke subtypes while the lowest mean annual cost was found in patients aged between 40-49 years. Compared with ischaemic and unspecified stroke, patients with haemorrhagic stroke incurred the highest mean annual cost in every age group. In the same way, there has been a steady rise in the mean annual cost by CCI score and there was a twofold increase in the mean annual cost of all stroke subtypes between no comorbidity and CCI scores of 3 or over. In terms of LOS, the mean annual cost of the LOS 1-3 days group was almost similar to the LOS 3-7 days group, in all stroke subtypes. A similar pattern was observed in thrombolysis during the incident inpatient admission, with higher costs in patients who underwent thrombolysis during the incident inpatient admission. When considering the types of hospital, patients who were admitted to private hospitals, including private clinics and non-MOPH hospitals, incurred higher costs than those who were admitted to hospitals under MOPH.

What is interesting was the slight decline in mean annual costs of patients who had rehabilitation during their incident admission in all stoke subtype. Also, it is apparent that there were three health regions, where patients incurred higher mean annual costs compared to the Bangkok area (as reference) namely health region 4, 7 and 9 (Figure 3-5). However, the mean annual costs were almost identical in all health regions.

Table 3-7 Mean annual cost per patient by stroke subtypes

covariates	Haemorrhagic		Ischaemic		Unspecified	
	Mean	(95%CI)	Mean	(95%CI)	Mean	(95%CI)
Age group (years)						
age <40	45,334.63	44,187.11-46,482.14	31,832.70	31,029.57-32,635.82	32,303.19	31,451.32-33,155.07
age 40-49	42,340.40	41,566.61-43,114.19	29,730.24	29,201.42-30,259.05	30,169.66	29,591.52-30,747.79
age 50-59	44,872.50	44,228.41-45,516.59	31,508.20	31,098.66-31,917.75	31,973.90	31,500.79-32,447.02
age 60-69	49,017.33	48,374.82-49,659.85	34,418.59	34,052.12-34,785.06	34,927.31	34,484.45-35,370.17
age 70-79	52,315.05	51,602.12-53,027.98	36,734.15	36,340.50-37,127.81	37,277.09	36,802.41-37,751.77
age 80-89	54,113.11	53,285.97-54,940.24	37,996.70	37,518.07-38,475.33	38,558.30	38,006.04-39,110.56
age ≥90	53,709.81	52,057.34-55,362.27	37,713.51	36,602.70-38,824.32	38,270.93	37,111.64-39,430.21
Sex						
women	48,312.91	47,749.11-48,876.71	33,923.96	33,626.00-34,221.92	34,425.37	34,040.44-34,810.30
men	48,844.65	48,306.82-49,382.49	34,297.34	34,007.69-34,586.99	34,804.26	34,425.57-35,182.95
CCI						
no CCI	39,232.48	38,806.33-39,658.63	27,547.94	27,318.50-27,777.38	27,955.11	27,596.55-28,313.66
score 1 to 2	57,922.64	57,228.40-58,616.89	40,671.65	40,299.67-41,043.62	41,272.78	40,852.69-41,692.88
score ≥3	91,481.82	88,225.80-94,737.85	64,235.96	62,031.00-66,440.92	65,185.38	62,974.56-67,396.20
LOS group						
LOS <3 days	38,525.18	38,012.24-39,038.12	27,051.29	26,793.71-27,308.88	27,451.12	27,122.58-27,779.66
LOS 3 to 7 days	39,448.02	38,961.16-39,934.89	27,699.29	27,445.53-27,953.05	28,108.69	27,780.02-28,437.36
LOS 8 to 15 days	58,793.03	57,998.83-59,587.24	41,282.81	40,776.92-41,788.70	41,892.98	41,318.05-42,467.91
LOS >15 days	123,421.00	121,689.10-125,152.90	86,662.75	85,434.16-87,891.34	87,943.64	86,574.12-89,313.17
Hospital type						
primary and community	41,862.84	41,205.10-42,520.58	29,394.91	29,000.20-29,789.61	29,829.37	29,460.68-30,198.05
mid-level	48,927.23	48,008.30-49,846.17	34,355.32	33,792.92-34,917.72	34,863.10	34,233.31-35,492.89
standard-level	46,829.43	46,152.45-47,506.42	32,882.31	32,481.18-33,283.43	33,368.31	32,873.44-33,863.19
advanced-level	43,854.38	43,334.41-44,374.36	30,793.31	30,486.40-31,100.23	31,248.45	30,831.00-31,665.89
non-MOPH	70,440.30	68,846.42-72,034.19	49,461.20	48,384.95-50,537.44	50,192.24	49,086.39-51,298.10
private hospitals/clinics	73,832.68	71,356.24-76,309.13	51,843.23	50,151.67-53,534.78	52,609.48	50,820.83-54,398.13
Rehabilitation						
not received rehabilitation	50,322.19	49,794.48-50,849.91	35,334.83	35,037.95-35,631.71	35,857.08	35,497.19-36,216.97
received rehabilitation	45,346.82	44,760.50-45,933.13	31,841.26	31,551.08-32,131.44	32,311.88	31,892.37-32,731.38

covariates	Haemorrhagic		Ischaemic		Unspecified	
	Mean	(95%CI)	Mean	(95%CI)	Mean	(95%CI)
rt-PA						
not received rt-pa	48,374.72	47,879.59-48,869.85	33,967.36	33,717.93-34,216.80	34,469.41	34,126.00-34,812.82
received rt-pa	54,863.03	53,429.08-56,296.99	38,523.28	37,617.82-39,428.73	39,092.66	38,097.97-40,087.35
Health region						
Bangkok	49,466.38	48,201.60-50,731.15	34,733.90	33,900.33-35,567.46	35,247.27	34,341.52-36,153.03
1	46,411.98	45,661.38-47,162.57	32,589.18	32,113.58-33,064.78	33,070.86	32,555.00-33,586.72
2	47,805.96	46,975.67-48,636.26	33,568.00	33,030.95-34,105.05	34,064.14	33,467.92-34,660.36
3	48,152.75	46,980.34-49,325.17	33,811.51	33,026.29-34,596.73	34,311.25	33,482.36-35,140.14
4	51,215.48	49,961.07-52,469.88	35,962.06	35,124.88-36,799.25	36,493.59	35,599.13-37,388.05
5	48,666.03	47,661.86-49,670.20	34,171.92	33,513.33-34,830.50	34,676.98	33,967.08-35,386.89
6	48,320.05	47,340.42-49,299.68	33,928.98	33,287.39-34,570.57	34,430.46	33,758.17-35,102.74
7	50,030.18	49,077.80-50,982.55	35,129.78	34,502.64-35,756.92	35,649.01	34,985.62-36,312.39
8	48,589.32	47,791.98-49,386.67	34,118.05	33,609.07-34,627.04	34,622.33	34,066.36-35,178.30
9	50,594.03	49,716.81-51,471.26	35,525.70	34,957.25-36,094.16	36,050.78	35,427.56-36,674.00
10	48,743.29	47,791.74-49,694.83	34,226.16	33,605.26-34,847.06	34,732.03	34,075.68-35,388.38
11	46,757.83	45,726.03-47,789.63	32,832.03	32,150.74-33,513.32	33,317.30	32,567.49-34,067.10
12	47,573.40	46,513.82-48,632.99	33,404.70	32,699.19-34,110.22	33,898.43	33,149.26-34,647.61

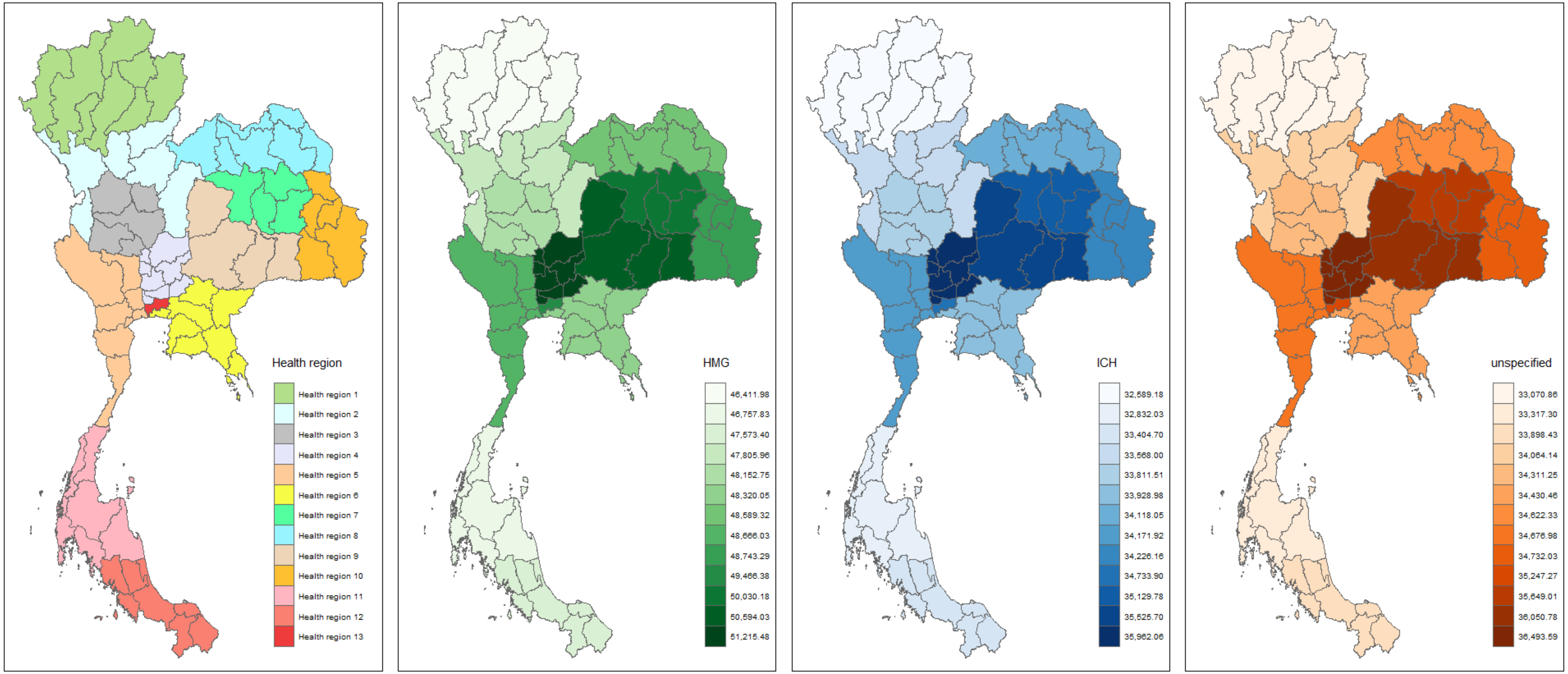

Figure 3-5 The mean annual cost per patient classified by stroke subtypes and health regions
Health region 13: Bangkok area

3.3.3 Survival analysis

Survival analysis conducted in this chapter examined all-cause mortality and the first recurrence of stroke. For all-cause mortality, survival time was calculated from the date of index stroke until date of death. Patients without a death record were censored on the last discharge date of all patients in this data, which was November 23rd, 2020. For recurrent stroke, survival time was calculated from the admission date of the index stroke until the admission date of the first recurrent stroke.

Kaplan-Meier plots

All-cause mortality

Kaplan-Meier curve in Figure 3-6 shows the 4-year probability of survival (all-cause mortality) after an incident stroke for all stroke subtypes which reveals that there is a clear trend of decreasing mortality during the four years following an incident stroke. The 1-year and 4-year probability of survival was 80% (95%CI: 80.4%-80.6%) and 66.5% (95%CI: 64.3% - 66.7%), respectively (Log-rank: $p<0.0001$).

Kaplan-Meier curves of all-cause mortality over 4-years classified by sex showed that the probability of survival in men was higher than the probability observed in women (Appendix 11). Survival probabilities for patients with haemorrhagic, ischaemic and unspecified stroke are shown in Appendix 12A. The ischaemic group had the highest survival rate (70.5%; 95%CI: 70.2%-70.7%) compared to other subtypes (unspecified: 60.6%; 95%CI: 60.2%-61.0%; haemorrhagic: 64.9%; 95%CI: 64.4%-65.5%). It should be noted that the survival rate in patients with unspecified stroke during the first year (Appendix 12B) after a first-ever stroke was significantly higher (77.4%; 95%CI: 77.2%-77.7%) compared to patients with haemorrhagic stroke (76.5%: 95%CI: 76.1%-76.9%); however, after the first year, patients with haemorrhagic stroke had a better chance to survive after stroke compared with patients who had an unspecified stroke. Furthermore, the older stroke patients had a lower probability of survival than those of younger age (<40 years) (Appendix 13). Likewise, among patients who had no comorbidities (Appendix 14), survival probability was higher compared to those patients with comorbidities. The median survival time could only be estimated for patients who had a CCI score ≥3, which was 467 days (95%CI: 421-510 days). In addition, the survival rate was higher in patients who received thrombolysis during the incident inpatient admission, but during the first 30 days up to three months since incident stroke, the probability of survival in patients who received thrombolytic therapy was slightly lower compared to the patients who did not receive thrombolytic therapy (Appendix 15).

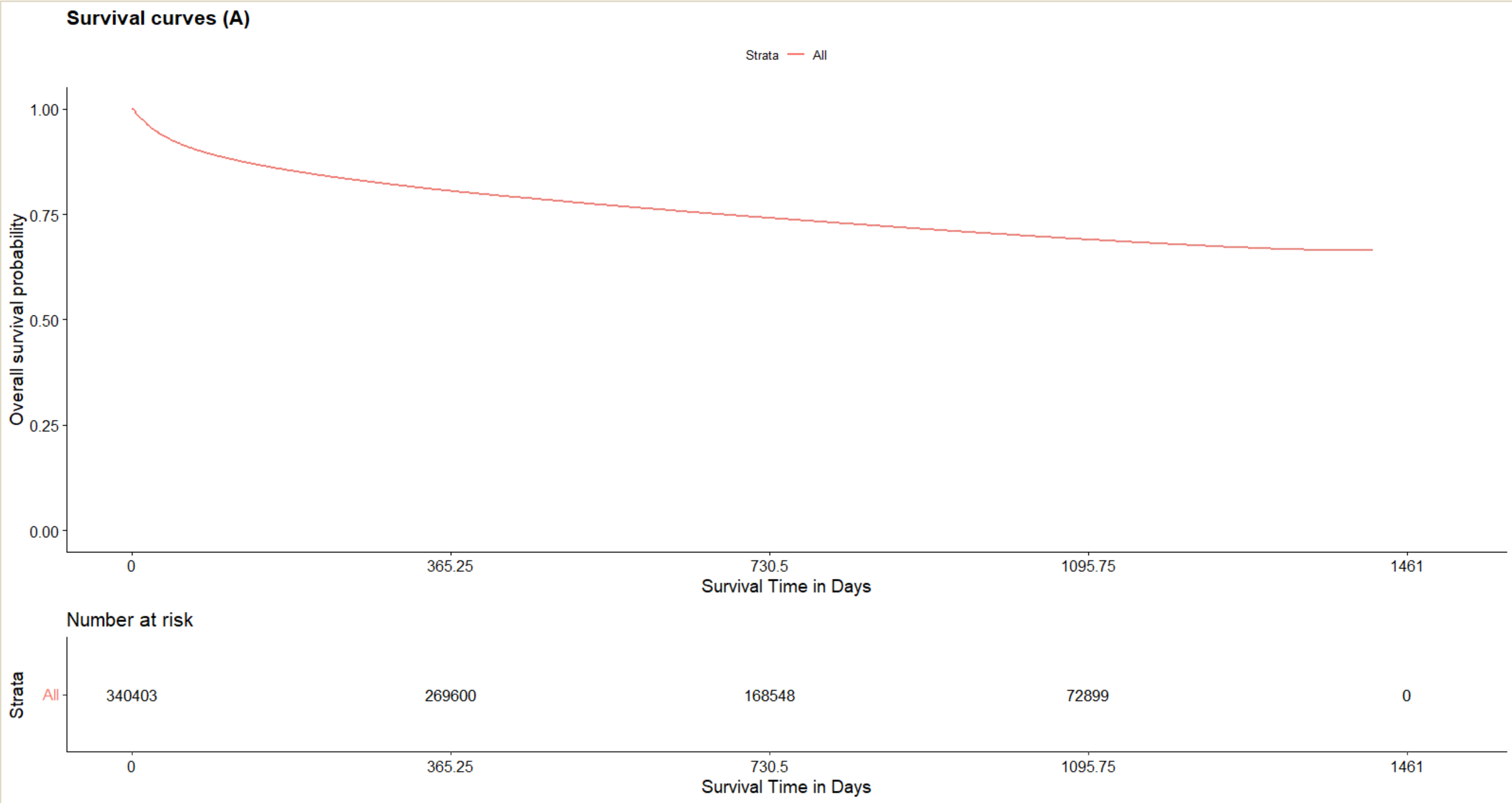

Figure 3-6 Kaplan-Meier curves of all-cause mortality

Recurrence-free survival

In terms of time from incident stroke to recurrence or recurrence-free survival (Figure 3-7), the estimated 1-year recurrence-free survival rate for all strokes was 92.3% (95%CI: 92.2%-92.4%). Patients with unspecified stroke showed the highest rate of recurrence-free survival - at approximately 0.938 or 93.8% (95%CI: 93.6%-93.9%), followed by patients with ischaemic stroke - at approximately 0.918 or 91.8% (95%CI: 91.7%-91.9%) and patients with haemorrhagic stroke - at 0.906 or 90.6% (95%CI: 90.4%-90.9%). Recurrence-free survival was significantly longer for patients with unspecified and ischaemic stroke compared to patients with haemorrhagic stroke. The 4-year probability of recurrence-free survival declined to 85.1% (95%CI: 84.9%-85.3%) and remained highest in patients with unspecified strokes at 86.8% (95%CI: 86.5%-87.1%). However, the probability of recurrence-free survival in patients with ischaemic stroke dropped noticeably (84.3%: 95%CI: 84.0%-84.5%) and seemed to be indistinguishable compared to patients with haemorrhagic stroke (84.6%; 95%CI: 84.2%-85.1%).

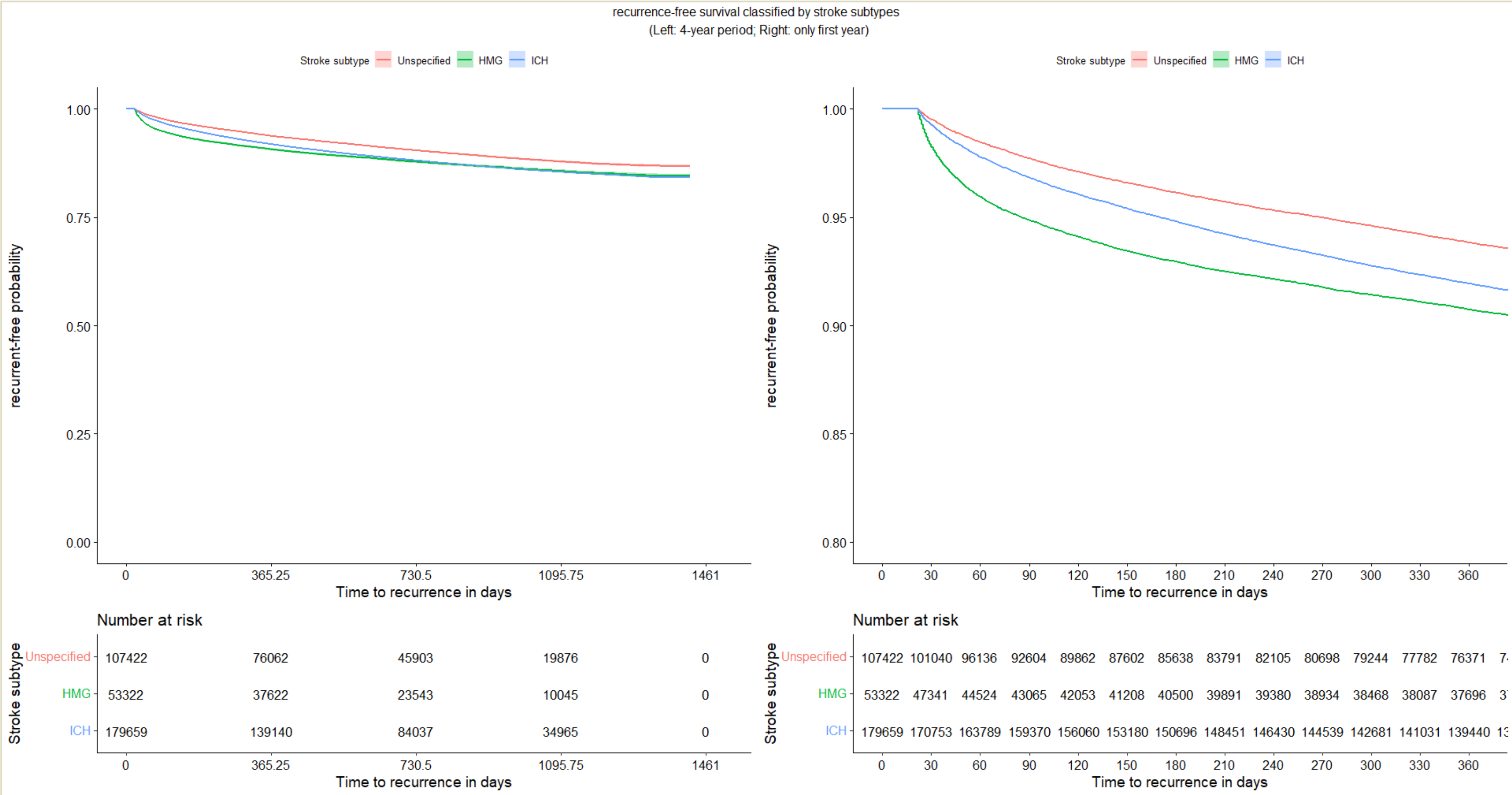

Figure 3-7 Kaplan-Meier curves of stroke recurrence

(Left: 4-year period; Right: only first year)

Parametric survival modelling

All-cause mortality

This section investigated parametric survival modelling to model the hazard functions of all-cause mortality following incident stroke. A comparison of each parametric model distribution (Appendix 16 - coloured lines) was conducted. The fitted survival curve from different parametric models for overall survival in all patients and classified by stroke subtype showed that all models, except the Exponential model, appeared to match the Kaplan-Meier estimates (Appendix 17). The distribution plots of the Cox-Snell residuals (with the exception of the Exponential distribution) were nearly identical and would fit the data of this study well (Appendix 18). These results were also supported by the AIC and Bayesian information criterion (BIC) (Appendix 19) which suggested that although the Lognormal distribution had the lowest AIC and BIC, there was a trivial difference between these distributions. Thus, the Gompertz distribution model was chosen.

Results from the Gompertz model for all stroke subtypes are presented in Table 3-8. After adjusting for all covariates, male patients had a 7% higher risk of all-cause mortality than their female counterparts (HR 1.071; 95% CI: 1.057-1.085). The risk of mortality of patients also increased with age, the risk of mortality was 17% higher in patients aged 40-49 years and increased to 57% in patients aged 50-59 years compared to patients aged <40 years (reference). There was a noticeable upward trend in the mortality risk for patients aged 70 – 79 years which was 2.47 times higher than that of under 40’s and reached 15.6 times for patients in the ≥90 age group compared with those aged <40 years. In other words, elderly stroke patients were more likely than younger patients to die, when other covariates were adjusted.

The risk of mortally for patients who had a CCI score of 1 to 2 was twice (HR 2.116; 95% CI: 1.917-2.337) that in patients who did not have any comorbidities at the incident admission and the mortality risk was more than 5-fold in patients who had a CCI score of 3 and over (HR 5.770;

95% CI: 4.177-7.971) compared to patients who had no comorbidity. Moreover, patients who had a recurrent stroke had a 28% increase in the risk of mortality compared to patients who had no recurrent stroke (HR 1.284; 95% CI: 1.260-1.308). There was a higher risk of mortality for patients with longer LOS (LOS >16 days - HR: 2.449; 95% CI: 2.393-2.506; LOS 7-15 days - HR: 1.817; 95% CI: 1.782-1.852; LOS 3-7 days - HR: 1.160; 95% CI: 1.142-1.179) as compared with patients who had LOS of less than three days. Lastly, almost all geographic areas were associated with a higher risk of mortality, the only exception was health region 5 (south central area), compared to the Bangkok area.

Three additional measures were associated with a reduction in mortality risk when other covariates were adjusted for. First, receiving thrombolytic therapy seemed to be associated with better health outcomes as it showed around 7% reduction in mortality rate (HR: 0.928; 95% CI: 0.892-0.964) for all stroke types in patients who underwent thrombolytic therapy during the incident admission compared to patients who did not receive thrombolytic therapy. Second, compared to patients who did not receive rehabilitation at the incident admission, receiving rehabilitation exhibited a 15% decrease in the risk of mortality (HR: 0.851; 95% CI: 0.838-0.863). Lastly, patients admitted to higher-level hospitals, except for the standard-level hospital and private hospitals/clinics, at the incident admission showed a reduction in the risk of mortality compared with those admitted to primary hospitals. Patients with ischaemic or unspecified stroke had a 23% reduction in the risk of mortality compared to patients with haemorrhagic stroke.

Table 3-8 All-cause mortality for patients with first-ever stroke (Gompertz model)

Covariate	Coef.	SE	Hazard ratio	L95%CI	U95%CI
Shape	-0.0021	0.00004	-	-0.0022	-0.0020
Scale/Rate	0.00018	0.000008	-	0.00017	0.00020
Female	1 [Reference]				
Male	0.069	0.007	1.071	1.057	1.085
Age<40	1 [Reference]				
Age 40-49	0.159	0.045	1.172	1.072	1.281
Age 50-59	0.453	0.042	1.573	1.449	1.708
Age 60-69	0.904	0.041	2.470	2.280	2.675
Age 70-79	1.521	0.040	4.579	4.230	4.956
Age 80-89	2.138	0.041	8.483	7.834	9.187
Age 90up	2.746	0.046	15.587	14.240	17.062
CCI: score 0	1 [Reference]				
CCI: score 1 to 2	0.750	0.051	2.116	1.917	2.337
CCI: score 3 or over	1.753	0.165	5.770	4.177	7.971
Haemorrhagic stroke	1 [Reference]				
Ischaemic stroke	-0.270	0.010	0.763	0.748	0.778
Unspecified stroke	-0.259	0.011	0.772	0.755	0.788
Not received rehabilitation	1 [Reference]				
Received rehabilitation	-0.162	0.007	0.851	0.838	0.863
Not received thrombolytic therapy	1 [Reference]				
Received thrombolytic therapy	-0.075	0.020	0.928	0.892	0.964
No recurrent stroke	1 [Reference]				
Having recurrent stroke	0.250	0.010	1.284	1.260	1.308
LOS <3 days	1 [Reference]				
LOS 3 to 7 days	0.149	0.008	1.160	1.142	1.179
LOS 7 to 15 days	0.597	0.010	1.817	1.782	1.852
LOS ≥16 days	0.896	0.012	2.449	2.393	2.506
hospital type: primary and community	1 [Reference]				
Mid-level	-0.072	0.013	0.930	0.906	0.955
Standard-level	0.002	0.011	1.002	0.981	1.023
Advanced-level	-0.099	0.010	0.905	0.888	0.923
Non-MOPH	-0.322	0.020	0.725	0.697	0.753
Private hospitals/clinics	-0.013	0.025	0.987	0.940	1.036
Bangkok	1 [Reference]				
Health Region 1	0.123	0.023	1.131	1.081	1.183
Health Region 2	0.107	0.024	1.113	1.061	1.166
Health Region 3	0.197	0.026	1.217	1.157	1.281
Health Region 4	0.230	0.024	1.259	1.202	1.318
Health Region 5	0.034	0.025	1.035	0.986	1.086
Health Region 6	0.133	0.024	1.143	1.091	1.197
Health Region 7	0.251	0.024	1.285	1.225	1.348
Health Region 8	0.223	0.024	1.250	1.194	1.309
Health Region 9	0.089	0.024	1.093	1.043	1.146
Health Region 10	0.219	0.025	1.245	1.185	1.308
Health Region 11	0.082	0.025	1.086	1.033	1.141
Health Region 12	0.176	0.025	1.193	1.135	1.254
Age < 40 # CCI score 0	1 [Reference]				
Age 40-49 # score 1 to 2	0.092	0.059	1.096	0.976	1.231
Age 50-59 # score 1 to 2	0.071	0.054	1.074	0.966	1.194
Age 60-69 # score 1 to 2	-0.085	0.052	0.919	0.829	1.018
Age 70-79 # score 1 to 2	-0.309	0.052	0.734	0.663	0.813
Age 80-89 # score 1 to 2	-0.530	0.052	0.588	0.531	0.652
Age 90up # score 1 to 2	-0.777	0.060	0.460	0.409	0.517
Age 40-49 # score 3 or over	-0.119	0.199	0.888	0.600	1.312
Age 50-59 # score 3 or over	0.068	0.175	1.070	0.759	1.507
Age 60-69 # score 3 or over	-0.378	0.169	0.685	0.492	0.955
Age 70-79 # score 3 or over	-0.876	0.168	0.416	0.299	0.579
Age 80-89 # score 3 or over	-1.246	0.169	0.288	0.207	0.401
Age 90up # score 3 or over	-1.666	0.189	0.189	0.130	0.274

Results from the Gompertz regression when modelled separately by stroke subtype are presented in Appendix 20. Overall, results for individual stroke subtypes were similar to those observed for overall stroke, as presented previously in Table 3-8, with some differences. Patients with unspecified stroke seemed to have the highest risk of mortality in terms of sex, with men having a 12% (HR: 1.121; 95%CI: 1.097-1.145) higher risk of mortality than their female counterparts. The risk of mortality was found to be higher for patients with ischaemic stroke than haemorrhagic and unspecified stroke, not only in all age groups but also in patients who had LOS greater than 7 days. As can be seen from Appendix 20, the risk of mortality in each age group for patients with ischaemic stroke was higher than the risk of mortality when looking at all strokes, as well as the other two stroke subtypes, especially, in patients aged ≥60 years (when compared to patients aged ≤40).

Likewise, results show considerable difference in risk of mortality for patients with ischaemic stroke, whose LOS was 7 days or longer and the other stroke subtypes. For instance, risk of mortality in patients with ischaemic stroke who had LOS greater than 16 days was 3.5 times (HR: 3.536; 95%CI: 3.414-3.663) higher than for patients who had LOS less than 3 days (reference). Additionally, risk of mortality in patients with ischaemic stroke who had LOS greater than 16 days was 2.4 times higher than for patients with unspecified stroke (HR: 2.399; 95%CI: 2.304-2.498). While risk of mortality was only 13% higher in patients with haemorrhagic stroke (HR: 1.130; 95%CI: 1.078-1.184) compared to the reference group. Third, only patients with ischaemic stroke who received services in other health regions, compared to the Bangkok area, had a statistically significant higher risk of mortality.

In terms of reduction in risk of mortality, when comparing with the risk of mortality of all stroke subtypes, the most remarkable result is that patient with ischaemic stroke who underwent thrombolytic therapy during the admission had a decrease in risk of mortality. Furthermore, patients who had LOS >3 days had an increased risk of mortality; however, only patients with haemorrhagic stroke who had LOS 3 - 7 and 7 - 15 days had a

37% and 24% reduction in mortality risk, respectively, compared to patients who had LOS of less than three days (reference).

These results provided important insights into the different associations of included covariates when mortality risk is modelled separately by stroke subtype and reveals findings that were masked when considering all stroke subtypes together (Table 3-8). This information will be useful for policy makers for stroke management of specific subtypes in Thailand.

Recurrence-free survival (RFS)

In terms of recurrent stroke event, a comparison of each parametric model distribution (Appendix 21 - coloured lines) was also conducted and a Gompertz distribution was selected for modelling RFS as there was a trivial difference between these distributions. Results from the Gompertz regression for all stroke subtypes, after adjusting for all covariates (Table 3-9), show that being male, aged between 60-89 years, having a CCI score of 1-2, unspecified stroke, received rt-PA, LOS, hospital type and health region were associated with RFS. It was found that male patients had prolonged RFS (HR 0.963; 95% CI: 0.943-0.984) compared with their female counterparts. RFS was longer in patients with a CCI score of 1 to 2 compared with patients with no comorbidity, with an HR 0.793 (95% CI: 0.709-0.887). Patients with unspecified stroke were less likely to suffer from recurrence than patients with haemorrhagic stroke (HR: 0.808, 95% CI: 0.778-0.840); however, it seemed to be indistinguishable in patients with ischaemic stroke.

In contrast, RFS remained slightly shorter in the older stroke patients aged 60-89 years (60-69 years-HR: 1.129; 95% CI, 1.052-1.212, 70-79 years-HR: 1.184; 95% CI: 1.101-1.273, 80-89 years-HR: 1.216; 95% CI: 1.124-1.316) than in patients aged <40 years (reference). Patients with LOS ≥16 days had a 68% increased risk of recurrence compared with patients with a LOS <3 days (reference) while RFS was longer in patients with a LOS between 3-15 days as opposed to patients with a LOS <3 days (reference). There is an increased risk of recurrence (HR: 1.174; 95% CI:

1.114-1.237) in patients who received thrombolytic therapy during the incident admission compared to patients who did not receive thrombolytic therapy.

Furthermore, patients admitted to mid-level, advanced-level, non-MOPH, and private hospitals had a higher risk of stroke recurrence ranging from 4%-17% compared to primary hospitals (reference). Lastly, being treated in health regions outside the Bangkok area (except health region 4) was associated with an increased risk of stroke recurrence, ranging from 8% to 35%.

Table 3-9 Recurrence free survival for all stroke subtypes (Gompertz model)

Covariate	Coef.	Std. Error	Hazard ratio	L 95%CI	U 95%CI
Shape	-0.002	0.0001	0.998	0.998	0.999
Scale/Rate	0.000	0.00001	-	0.0002	0.0003
Female	1 [Reference]				
Male	-0.037	0.011	0.963	0.943	0.984
Age<40	1 [Reference]				
Age 40-49	0.017	0.039	1.017	0.941	1.099
Age 50-59	0.051	0.037	1.052	0.979	1.131
Age 60-69	0.122	0.036	1.129	1.052	1.212
Age 70-79	0.169	0.037	1.184	1.101	1.273
Age 80-89	0.196	0.040	1.216	1.124	1.316
Age 90up	0.001	0.082	1.001	0.852	1.177
CCI: score 0	1 [Reference]				
CCI: score 1 to 2	-0.232	0.057	0.793	0.709	0.887
CCI: score 3 or over	-0.475	0.446	0.622	0.260	1.490
Haemorrhagic stroke	1 [Reference]				
Ischaemic stroke	-0.009	0.016	0.991	0.960	1.023
Unspecified stroke	-0.213	0.019	0.808	0.778	0.840
Not received rehabilitation	1 [Reference]				
Received rehabilitation	0.016	0.012	1.016	0.992	1.039
Not received rt-PA	1 [Reference]				
Received rt-PA	0.160	0.027	1.174	1.114	1.237
LOS <3 days	1 [Reference]				
LOS 3 to 7 days	-0.035	0.012	0.966	0.943	0.989

Covariate	Coef.	Std. Error	Hazard ratio	L 95%CI	U 95%CI
LOS 7 to 15 days	-0.072	0.019	0.931	0.897	0.966
LOS ≥16 days	0.518	0.021	1.678	1.610	1.750
hospital type: primary	1 [Reference]				
Mid-level	0.072	0.022	1.074	1.028	1.122
Standard-level	-0.028	0.018	0.972	0.938	1.007
Advanced-level	0.045	0.017	1.046	1.012	1.082
Non-MOPH	0.159	0.031	1.172	1.104	1.245
Private hospitals/clinics	0.105	0.041	1.111	1.025	1.204
Bangkok	1 [Reference]				
Health Region 1	0.125	0.036	1.133	1.056	1.216
Health Region 2	0.167	0.038	1.181	1.097	1.272
Health Region 3	0.115	0.042	1.122	1.033	1.219
Health Region 4	0.040	0.039	1.041	0.965	1.123
Health Region 5	0.095	0.039	1.100	1.018	1.188
Health Region 6	0.082	0.038	1.086	1.008	1.169
Health Region 7	0.140	0.039	1.151	1.067	1.241
Health Region 8	0.255	0.037	1.290	1.199	1.387
Health Region 9	0.305	0.038	1.356	1.260	1.460
Health Region 10	0.189	0.040	1.208	1.117	1.307
Health Region 11	0.281	0.040	1.324	1.225	1.431
Health Region 12	0.256	0.040	1.291	1.193	1.397
Age <40#CCI score 0	1 [Reference]				
Age 40-49#score 1 to 2	0.250	0.068	1.285	1.125	1.467
Age 50-59#score 1 to 2	0.290	0.062	1.336	1.183	1.509
Age 60-69#score 1 to 2	0.227	0.061	1.255	1.114	1.414
Age 70-79#score 1 to 2	0.175	0.061	1.192	1.057	1.344
Age 80-89#score 1 to 2	0.132	0.066	1.142	1.004	1.298
Age 90up#score 1 to 2	0.065	0.121	1.068	0.841	1.354
Age 40-49#score 3 or over	0.148	0.525	1.159	0.414	3.243
Age 50-59#score 3 or over	0.756	0.467	2.130	0.854	5.316
Age 60-69#score 3 or over	0.624	0.455	1.866	0.765	4.554
Age 70-79#score 3 or over	0.395	0.455	1.485	0.608	3.626
Age 80-89#score 3 or over	-0.001	0.468	0.999	0.399	2.500
Age 90up#score 3 or over	0.703	0.543	2.020	0.697	5.858

Results from the Gompertz regression when modelled separately by stroke subtype are presented in Appendix 22. Compared to RFS for all stroke subtypes sex was not significantly associated with the risk of recurrence for all subtypes. Patients with ischaemic stroke aged 50-89 years had a statistically significant higher risk of stroke recurrence, while risk of recurrence for other subtypes were not statistically significant. Patients with ischaemic stroke had a statistically significant higher risk of stroke recurrence in all groups of LOS, but patients with haemorrhagic stroke with LOS ≥16 days had a twofold risk of recurrence (HR: 1.916; 95%CI: 1.586-2.314). Only patients with unspecified stroke who received rehabilitation services had a lower risk of stroke recurrence (HR%: 0.882; 95% CI: 0.832-0.935) compared to the other subtypes. Moreover, risk of recurrence was higher and varied across all health regions in patients with unspecified stroke and haemorrhagic stroke compared to those treated in the Bangkok area.

3.4 Discussion

This is the first time that the recent Thai national administrative data between 2015-2020 from NHSO was used to provide the national-level assessment by (i) estimating the resource utilisation and costs of stroke patients across stroke subtypes and (ii) estimating all-cause mortality of incident stroke patients in Thailand.

3.4.1 Summary of main findings

Cohort descriptive

Overall, male patients outnumbered their female counterparts in all stroke subtypes. The mean age of men and women was 63 and 67 years, respectively. Mean LOS was 7.1 days and just over half of the stroke patients (54%) had no recorded comorbidity (CCI score 0). The type of stroke that occurred most frequently was ischaemic stroke (50%). Only around 32% of stroke patients received rehabilitation during their incident stroke admission and the percentage of thrombolytic therapy was 7% in patients with ischaemic stroke. Mean age at death was 70 years and patients with haemorrhagic stroke showed the lowest age at death. These results were lower than the expected life expectancy at year 2020 of the Thai population which is 76 years[144].

Estimating the resource utilisation and costs of stroke patients

The first aim was addressed in this section. Overall, estimated annual mean cost per patient was 37,179 Baht (SE: 98; 95%CI: 36,988 - 37,371 Baht). Key factors that significantly contributed to an increase in costs comprised higher age, long LOS, high CCI score and receiving thrombolytic therapy during the incident admission.

The important finding related to resource utilisation was LOS. It was found that mean LOS in this study (7 days), was noticeably shorter than in other global research[145-149]. For instance, mean LOS was 10 days in Germany[146], 17 days in Singapore[145], 27 days in China[147] and 40 days in Japan[150]. In this present study, LOS in patients with haemorrhagic stroke was 9.9 and 6.1 days for patients with ischaemic stroke. These findings are in agreement with another Thai study by Kongbunkiat et al. (2014)[18], who used NHSO data between 2004 - 2013 to identify stroke outcomes, which showed that average LOS for patients with haemorrhagic and ischaemic stroke were 10.7 and 6.3 days, respectively. Although the service plan strategy has not restricted the length of hospitalisation, the health care professionals seems to maintain the duration of treatment due to health care financing issues[151]. The same results between Thai studies are likely to be related to the DRG concepts to achieve cost containment, while the differences between other countries could be due to the variation of periods that counted after their hospitalisation. For instance, the period in the Japanese study was counted from acute until rehabilitation phase and the setting was stroke centres, where more severe stroke patients would be treated[150].

Another important finding to highlight was the percentage of patients receiving rehabilitation during their incident admission (32%). Although, this may appear to be in conflict with results in Chapter 2, where a high percentage of patients receiving rehabilitation services was reported, this could be due to a noticeably low number of respondents in the survey compared to the number of hospitals included in the NHSO dataset (over 1,000 hospitals, including primary level hospitals). However, this result is comparable with a previous international observational study by Langhorne et al. (2018), which indicated that, in LMICs, around 31% of participants received post-discharge rehabilitation, while this was 92% in high-income countries[60]. However, research on development of new rehabilitation services by Khiaocharoen et al. (2015)[45] indicated that access to rehabilitation services, for stroke patients, among 24 hospitals was 43% in status quo. However, when the new rehabilitation service – inpatient-based rehabilitation within first week after clinical outcomes were stable and for three days per week - was developed, under the new definition, only 13% of stroke patients would classify as fully receiving new rehabilitation services. The author suggested that the low level of rehabilitation services offered might be related to the following factors:

- the hub-and-spoke model could cause some loss to follow up while patients were being transferred from hub to spoke in other healthcare settings as outlined in Chapter 2

- awareness of patients towards the importance of rehabilitation and transportation problems[8]

- as Thailand uses the DRG approach for inpatient reimbursement, which only covers the acute treatment benefit package, it does not take account of inpatient-based rehabilitation services – and medical charges for reimbursement were regularly higher than the DRGs payments from NHSO[152, 153].

Another possible explanation is that there were different service delivery patterns in the different hospitals setting[154]. Indeed, the healthcare staff regularly referred patients back to a contracted community hospital close to where patients lived, but it could be due to the difficulty or inconvenience to attend rehabilitation care at the hospital or affordability of transportation costs including the inadequacy of district-level staffing for rehabilitation[8]. However, when considering the costs incurred by patients who received rehabilitation during their incident admission, results from this thesis showed that patients who received rehabilitation incurred lower mean annual costs, indicating that an initial higher investment in rehabilitation services has the potential to lead to lower future costs. This information is important for implementation of rehabilitation service improvements in stroke care. Unfortunately, the data set did not contain functional disability outcome measures or BI scores. This information could be used to support the improvement of rehabilitation programs post- acute stroke. Therefore, developing a national health information system in order to measure activities of daily living both in the acute- and post-acute phases and monitor health outcomes of stroke patients is important and should be taken into account by policymakers, especially, MOPH and all health insurance schemes.

As far as costs of stroke treatment is concerned, there were four important findings to be highlighted. The first important finding suggests that the mean annual cost incurred by patients with haemorrhagic stroke was highest. This was particularly apparent in patients with LOS of more than 15 days, a CCI score of 3 or over, and those admitted to non-MOPH hospitals, including private hospitals. These results are in line with recent studies[19, 155, 156], indicating that although haemorrhagic strokes are less common than ischaemic strokes, the cost that these patients incurred tends to be higher[18, 131, 150, 156, 157]. This could be because haemorrhagic strokes are more severe and require more resources to treat patients than ischaemic strokes. Moreover, estimated costs incurred by haemorrhagic stroke patients in this thesis were approximately 16,740 Baht lower than in a previous study by Khiaocharoen et al.[131] which had reported that the cost per haemorrhagic patient was 65,340 Baht. This difference may be due to the different methods of cost measurement as the authors used micro costing methods collected directly from two advanced-level hospitals while this present study used costs based on DRG values which had to be adjusted as they were initially designed for reimbursement. Although the costs estimated in this thesis were lower than in previous studies, it covers all hospitals in Thailand, thus ensuring national representation of costs. LOS in haemorrhagic patients was higher than that of other stroke subtypes which was consistent with previous studies[18, 148], both in Thailand and internationally, reporting that patients with haemorrhagic stroke had longer hospitalisations compared to patients with ischaemic stroke. Patients with haemorrhagic stroke are associated with a greater initial level of severity or poorer prognosis compared to ischaemic strokes[158, 159]. Furthermore, patients with haemorrhagic stroke are associated with a higher risk of mortality[18, 157, 160] and produces more severe neurologic consequences[161] than other stroke subtypes. Existing comorbidities (CCI) could give rise to high cost of treatment, increasing substantially in patients with CCI scores of ≥3 compared to patients in other categories. A high CCI score could also be associated with longer LOS resulting in increased cost of treatment[162-164]. Finally, patients with haemorrhagic stroke admitted to non-MOPH including private hospitals incurred higher costs than patients with other stroke types. A possible explanation is that, in a Thai context, non-MOPH hospitals were mostly classified as specialised hospitals, such as military hospitals or university hospitals, in which some might have more sophisticated technology. As explained above, haemorrhagic stroke patients have higher severity and mortality, and poorer functional outcomes than patients with ischaemic stroke. These patients require complex treatment and management[165], which may require more sophisticated technologies in these specialised hospitals[166].

The second important finding shows that costs tended to be higher in older age groups in all three subtypes, and cost in patients with haemorrhagic stroke was highest in all age groups. Furthermore, this study found that patients with haemorrhagic stroke were younger with a mean age of less than 60 years and men were more likely to have a stroke at younger ages compared to women. This result is consistent with prior research[18, 167-170] which indicated that the mean age of patients with ischaemic stroke was higher than in patients with haemorrhagic stroke and the factor of advanced age was more important in ischaemic stroke[167].

The third important finding is related to geographical variation in costs. It was found that patients living in three health regions, namely 4, 7 and 9, had higher costs than those living in the Bangkok area (reference). Due to a limited number of published research studies, both locally and globally, this result may be explained by the fact that these health regions have a successful stroke network system as well as having an active neurologist leader[171]. According to

Suwanwela et al. (2018)[171], the most successful stroke network and referral system is in the North-eastern part of Thailand and both health regions 7 and 9 are the biggest referral hub in this region of Thailand. Another possible explanation for this is that because these health regions have succeeded in network development, they might treat more severe patients who have been transferred from other regions.

The fourth important finding is related to the thrombolytic therapy. The percentage of patients with ischaemic stroke receiving thrombolytic therapy was only 7%. This is consistent with data published in the service plan strategies 2018 - 2022[6]. Furthermore, the percentage of thrombolytic treatment has gradually increased since 2008[27, 60]. Mean annual costs of patients receiving thrombolytic treatment was less than 40,000 Baht which is lower than the previous research reports[18, 59]. Costs of thrombolytic therapy may have played a role in the mean annual costs as patients who received thrombolytic therapy had higher mean annual costs compared to patients who did not receive thrombolytic therapy but it also played a vital role in improvement of mortality outcomes. Although the door-to-needle time is one of the main national KPIs showing a decreasing trend[6], the problem of low thrombolytic therapy prescription is related to health literacy of patients and families which is essential to the prescription for thrombolytic therapy[18].

Estimating all-cause mortality following incident stroke

The second objective in this chapter was to examine how the stroke service plan strategy affects health outcomes of stroke patients and whether these differ between stroke subtypes. The analysis in this section evaluated all-cause mortality following incident stroke. Overall, Kaplan-Meier curves of all-cause mortality showed the 1-year probability of survival for all subtypes was 80% while patients with haemorrhagic stroke was associated with a higher risk of death than those patients with ischaemic stroke. In terms of recurrence-free survival, the most important factor significantly associated with an increase in risk of recurrence after adjusting for all covariates comprised age between 60-89 years, received rt-PA, LOS ≥16 days, hospital type and non-Bangkok health region.

There were four key findings to be highlighted. First, the results from the parametric survival analysis showed that patients with ischaemic and unspecified stroke had a reduced mortality risk (23%) compared to patients with haemorrhagic stroke. This result is consistent with an earlier study using NHSO data from 2004 - 2013[73], which reported that the survival probability during the first 30 days post-stroke was higher in patients with ischaemic than haemorrhagic stroke. However, the survival probability >30 days post-stroke was considerably higher among patients with haemorrhagic than patients with ischaemic stroke, after adjusting for sex and stroke type, which is contrary to the result of this chapter.

Second, in terms of patient characteristics, men had a slightly higher mortality risk than women, this also accords with previous studies[172, 173]. Further, elderly stroke patients were more likely than younger patients to die, when other covariates were adjusted for. This finding is consistent with a recent Thai study which indicates that stroke in the elderly is associated with higher mortality.

Third, a comparison between health regions revealed large variations in mortality risk, indicating that patients living in other geographic areas than Bangkok had a higher risk of mortality. This is also comparable with previous Thai studies[73]. As quality of care may have an effect on stroke survival, the inequality in stroke care between health regions could be attributed to the differences in stroke management systems in each health region. There are more neurologists or specialists in the Bangkok area and scarcity of specialists/health staff in some health regions[19, 73]. Differences in quality of stroke care could be attributed to differences in advanced medical technologies.

Fourth, receiving rehabilitation was associated with a 15% decrease in the risk of mortality. It is somewhat surprising that the estimated mean annual cost tended to decrease by approximately 3,806 Baht per patient who received rehabilitation during the incident admission. It could be argued that providing rehabilitation at the incident admission could not only reduce risk of mortality but save direct medical cost. Previous research reported that early rehabilitation is beneficial after stroke[26, 174] and commencement of rehabilitation within the first two weeks after acute stroke is advantageous[174] for achieving functional independence[175], and improvement in activities of daily living[176]. Furthermore, there is a possibility that rehabilitation could improve quality of life of stroke survivors. For example, rehabilitation could have a beneficial effect for up to one year after discharge[177-180]. In addition, different rehabilitation delivery services could improve personal independence. Additionally, a cohort study in the UK[181] reported that there was an association between functional status at six months after stroke and long-term survival. Their findings also indicated that median survival was 12.9 years (95%CI: 10.0-15.9) for patients with independence in daily living and 6 years (95%CI: 5.7-6.4) for patients with some form of dependence. Therefore, positive effects on reducing dependency and survival could be beneficial from an early rehabilitation. However, the benefit of rehabilitation over the long-term remains unclear[182]. In Thailand, functional ability outcomes are currently recorded at the hospital level, while NHSO has only recently started a value-based programme for healthcare reimbursement towards new rehabilitation services provided under the IMC policy[51]. This could provide opportunities for focusing on effectiveness, quality of life as well as value for money to the Thai MOPH of the new rehabilitation policy implementation in Thailand.

3.4.2 Strength and limitations

This study is the first comprehensive analysis of recent Thai national stroke data to investigate costs and all-cause mortality of a nationally representative stroke cohort. It contains a large number of records, providing nearly complete coverage, except for the civil servant medical beneficiary scheme (CSMBS) and social security scheme (SSS), of all stroke patients admitted to hospital in Thailand and covered three stroke subtypes namely haemorrhagic, ischaemic and unspecified strokes.

In addition, to ensure that the data was compliant with the initial data request, even after four different versions of the NHSO data were received, validation and comparison steps were important. The first version of the data extract was received in December 2019, but many records could not be merged. The second and third extracts were missing important components of data such as PDX, discharge date, death status and socioeconomic status. Repeated data inspection and cleaning was extremely time consuming. Moreover, the Covid-19 pandemic contributed to delays in receiving data from NHSO. The final version of the linked NHSO data was received in February 2021, containing records from fiscal years 2015 - 2020. Thus, validation of the number of stroke patients was carried out by comparing numbers of the stroke cohort with numbers published in the NHSO annual report for the fiscal year 2019[113] (Appendix 23). The comparison revealed that there has been a slight decline in the number of thrombolytic therapy cases in fiscal year 2019. A possible explanation for this might be that the NHSO report was established before the audit system and data stored in the NHSO database were updated before retrieving this data set. In summary, the NHSO data extract was quite similar to results from the NHSO annual report and any small differences could stem from the different periods of retrieving data.

In addition to delays and inconsistencies in data extracts, other limitations include the lack of some important information that were not made available by NHSO, such as date of birth, cause of death, medicines, availability of stroke unit, and importantly, clinical outcome measures in particular the functional score using BI. Henceforth, it was not possible to evaluate the functional disability of individuals. Also, mortality was analysed based on in-hospital mortality only, patients dying at home were not included. Information on cause of death could also not be established under the current data capture, accordingly only all-cause mortality was considered in this chapter. Due to the difference in definition and durations to define recurrent stroke from the existing literature, this study considered strokes that occurred more than 21 days after the admission date of the index stroke admission, thus, any differences between this current study and other studies could stem from different durations. Finally, this study made an assumption on the history of previous strokes to determine incident stroke based on a two-year look-back period, rather than clinical history of patients.

In terms of cost measurements, unfortunately, the charge data of some patients showed zero or very small values, which might not reflect patients' resource utilisation or hospital costs[126]. With regard to these limitations, this study made reasonable assumptions, applying the recent national costing study on DRGs and AdjRW. Although these unit costs were not directly from all hospitals and only considered direct medical costs, they will reflect these better than using the reimbursement rates from NHSO or converting charges to costs.

From a methodological perspective, the large data set is likely to produce very consistent estimates. Even though there were some published articles relating to stroke using this national database, data were not up to date or only selected for a particular stroke subtype. For instance, Vongmongkol et al. (2018)[59] analysed data in fiscal year 2011 to 2014 and focused mainly on ischaemic stroke. Moreover, the comprehensive data used in this thesis were retrieved between year 2015 and 2020 which aligns with the service plan strategy 2018 - 2022. Findings from this chapter provide an important contribution to understanding patient characteristics, differences in resource utilisation and costs as well as all-cause mortality. The results from this chapter, such as the resource utilisation for inpatient and outpatient services and mean annual costs, will be used for further evaluation of the performance of the new rehabilitation services implementation under the service plan strategy 2018 - 2022[6].

This chapter is an example of utilising several research methods to answer research questions in real-world settings. A variety of analysis techniques and analysis tools were used which enabled the researcher to address the limitations or the weaknesses of each method, helping to strengthen the reliability and accuracy of the findings. For example, to perform cost measurement from claims data, Thai guidelines on measurement of costs[183, 184] for health economic evaluation recommend that adjustment of charges from a country database to costs can be conducted using the ratio of cost to charges (RCC). However, there might be heterogeneity in charging practice across hospitals and the charging rate can also vary between hospitals. Therefore, an average cost per relative weight (RW) derived from more detailed costing studies has been used. Moreover, a costing method should be selected based on the suitability of the nature of the data while in survival analysis, the proportional hazards assumption in cox regression was tested and methods were introduced to deal with the non-proportionality[141, 142].

Importantly, this chapter used the national administrative data which can inform routine clinical implementation in a real-world situation. Real-world data are increasingly important and provide great potential for generating evidence that may otherwise not be considered in decision making or would take a long time and be very costly in the case of RCTs. It therefore has the potential to improve the efficiencies of research studies[185]. The values of the real-world data such as the national stroke data used in this chapter enables a comprehensive assessment of services provided for and health outcomes of stroke patients. This data contained a broader and more comprehensive population and provided more robust data than studies that used only a single source of data e.g. studies carried out at only one hospital/setting[185, 186].

3.5 Conclusion

This chapter offers novel findings based on real-world practice as recorded in the Thai national administrative data from NHSO. Some of the issues emerging from findings in this chapter relate specifically to receiving rehabilitation and differences in clinical practices across Thailand. These information could be used to inform policy makers in terms of further service improvements in stroke care as there is a large body of evidence that early rehabilitation could help improve short-term and long-term outcomes and quality of life of stroke patients. Importantly, rehabilitation might help to save costs as well as contribute to a reduction in the risk of mortality. This study also shows that being admitted to a hospital outside of the Bangkok area was associated with noticeably lower costs than hospitals under the Bangkok area, after adjusting for all covariates.

Additionally, the need to measure and record health outcome measures of rehabilitation in the national level database, such as individual BI scores, should be emphasised. The findings also revealed key difference between stroke subtypes which could help determine measurements for stroke management towards mitigation of costs and to ensure that the quality of stroke services is adequate to preserve or improve health outcomes of stroke patients.

In addition to evaluating costs and health outcomes in this chapter, it is also important to evaluate the new rehabilitation policy, as introduced in

Chapter 1. The following chapter (Chapter 4) will therefore present the systematic review of existing economic evaluations of rehabilitation services for patients with stroke. This information can be adopted to inform the development of an economic evaluation of the new rehabilitation service that is appropriate for a Thai context.

Chapter 4 Systematic review of economic evaluation of rehabilitation services in stroke patients

4.1 Background and rationale

In chapter 1, the challenges in stroke care and rehabilitation were described. For example, some healthcare professionals refer stroke patients from the hospital directly to their home without any communication with the community hospitals; thus creating a gap in the continuation of post-stroke care. Patients lose the opportunity to access rehabilitation services in post-hospital care[30, 31]. Although, rehabilitation after stroke is known to be associated with better health outcomes, only few inpatients have access to it[45, 54]. Furthermore, the survey in Chapter 2 identified limited capacity of health personnel such as physiotherapists, occupational therapists, especially in rural areas, to provide rehabilitation services. Further evidence of low levels of rehabilitation offered to patients comes from the analysis of the national stroke data (Chapter 3) which showed that the percentage of patients receiving rehabilitation after their incident stoke was only 32%. This figure was lower than in developed countries with over 90%[60].

Thai clinical practice guidelines[25] recommend that stroke patients should start rehabilitation as soon as possible once medically stable, and they should receive rehabilitation services regardless of the severity of stroke. In 2019 the intermediate care (IMC) guideline for stroke, traumatic brain injury and spinal cord injury patients[51] has been endorsed as the new rehabilitation policy. It recommends that patients should receive rehabilitation services based on severity levels, assessed using the BI scale and physicians should consider either inpatient-based or outpatient-based or outreach-based rehabilitation programmes (Chapter1; Figure 1-3). Stroke patients should be followed up monthly or bi-monthly up to six months or until a BI score of 20 with no multiple impairment.

As mentioned in the previous chapter, it is important to evaluate the new rehabilitation services in terms of cost-effectiveness and also implementation. A review and critical appraisal of the existing evidence on effectiveness of rehabilitation as well as the cost-effectiveness of rehabilitation services for patients with stroke from other settings will help to inform the subsequent economic evaluation and value of implementation analyses. Results from the systematic review will be combined with health care resource utilisation and costs from real-world clinical practice data (Chapter 3) and will hence be used to inform the development of an appropriate economic model for the new rehabilitation policy in a Thai context. Indeed, national research and data are recommended by the Thai health technology assessment guidelines to be employed for economic evaluation to inform the policy decision making in Thailand. However, at present, only one study conducted cost-utility analysis (CUA) of rehabilitation services[62] but considered only short-term impacts on health outcomes of stroke survivors based on the new rehabilitation policy in Thailand. Therefore, this chapter aimed to systematically review existing economic evaluation models of stroke rehabilitation services to inform the development of an appropriate rehabilitation model, and to inform the evaluation of the new rehabilitation guidelines.

4.2 Methodology

4.2.1 Data sources and search strategy

Electronic databases were searched from Medline via the PubMed search engine, Embase via Ovid, and Centre for Reviews and Dissemination (CRD) which included: Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment Database (HTA), and National Health Service Economic Evaluation Database (NHS-EED). The search strategy included a combination of indexing terms including rehabilitation, stroke and economic evaluation. The Medical Subject Heading (MeSH) terms for titles or abstracts were employed and have been modified depending on databases (Appendix 24). The initial search was conducted in 2021 for studies published in the past 10 years until February 22nd, 2021. The search was updated by limiting the date range from February 23rd, 2021 to July 31st 2022 with no restrictions on publication language.

4.2.2 Study identification and selection

This systematic review included published economic evaluation studies of adult stroke patient rehabilitation when compared with usual care programmes or no rehabilitation with specified inclusion and exclusion criteria (Table 4-1). This review was conducted according to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)[187, 188]. The search terms were constructed based on a 'Population, Intervention, Comparator, Outcome, and Study design' (PICOS) approach[189].

The focus of this chapter is on rehabilitation services for achieving functional independence after the acute phase of stroke. The intervention was any rehabilitation services provided for stroke patients and the services were provided during the post-acute phase. The alternative interventions were either routine services or usual care or normal practice or no rehabilitation. The primary outcomes were costs and benefits measured either as clinical or health outcomes, such as severity scores, quality-adjusted life years (QALYs). Studies were excluded if they only reported costs or outcomes and if the rehabilitation services were related to substance abuse or addiction, pain management, supplement intervention, vision, hearing, pharmaceutical interventions or equipment introduction. In addition, studies were excluded if they reported only costs or outcomes.

Table 4-1 Inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
Population	stroke patients aged ≥18 years	
Intervention	rehabilitation services in the post-acute phase of care	- rehabilitation services in other phases or for health promotion or prevention - rehabilitation concerning substance abuse or addiction, pain management, supplement intervention, vision, hearing, pharmaceutical interventions or equipment introduction
Comparator	- routine services or usual care or normal practice - no rehabilitation	
Outcome	Any (No limitation)	
Study design	- full EE examining both the costs and outcomes - cost-effectiveness analysis (CEA), cost-benefit analysis (CBA) or cost-utility analysis (CUA)	- studies reporting only costs or outcomes - cost-minimisation analysis (CMA)

	Inclusion criteria	Exclusion criteria
Type of publication	journal publications and full text available	- opinion papers, editorial, letters - conference proceedings - case reports, qualitative research - clinical trial protocols, guidelines - systematic and other reviews
Languages	any (no limitation)	
Publication date	past 10 years up to 31 July 2022	

4.2.3 Data extraction

All three databases were searched and results transferred to Endnote (Clarivate Analytics, Philadelphia, PA). Title and abstract were screened according to the eligibility criteria. Additionally, the references of relevant articles were also searched to identify relevant additional articles.

A 10% sample of the included articles were randomly selected for validation by a second reviewer within this PhD supervisory team to ensure a comprehensive data extraction process. Any disagreements were addressed and resolved by discussions between the two reviewers. The completed data extraction was checked by a second reviewer. In case of multiple publications, the primary economic evaluation or completed report was selected and referred to in this chapter.

A tailored data extraction for detailed information of each study comprised general study characteristics (e.g. author, year of publication), population characteristics, intervention and comparators, perspective, type of economic evaluation and analytic approach (e.g. trial-based or model-based), time horizon and cycle length, costs including breakdown if available, discounting and price conversion, outcome measurement, valuation methods, assumptions, incremental cost–effectiveness ratios (ICER), uncertainty analyses, sensitivity analysis, main findings and concluding points. These items were developed and adapted based on the purpose of this thesis's aim[190-192].

4.2.4 Quality assessment of reporting of economic evaluation

To ensure the quality of selected studies, quality assessment was performed.

Assessment tools

Economic evaluations can either be trial-based or model-based. Trial-based economic evaluations are part of a clinical effectiveness study such as Randomised Controlled Trials (RCTs) or an observational study[193]. Model-based economic evaluations use data synthesis from a wide range of sources (RCTs, observational studies, trial-based economic evaluations, and other literature or reports) to develop an economic model[194].

There are several standardised assessment tools or checklists which can be used to assess whether the study has the appropriate components when reporting an economic evaluation. The Drummond and Jefferson checklist (or BMJ checklist)[195], the Quality of Health Economic Studies (QHES)[196] and the Consolidated Health Economic Evaluation Reporting Standards statement (CHEERS) checklist are suitable for both trial-based economic evaluations and model-based economic evaluations. The CHEERS checklist which contains 24 items under six main categories including: (1) title and abstract; (2) introduction; (3) methods; (4) results; (5) discussion; and (6) other, is recommended as a reporting tool for both trial-based and model-based economic evaluation[197, 198]. The Philips checklist[199] and the Consensus on Health Economic Criteria (CHEC) checklist[200] are suitable only for model-based economic evaluations. The Philips checklist is also one of the most widely used assessment tools and is recommended by the Cochrane Handbook for the assessment of the methodological quality of health economic evaluations[201, 202]. It focusses on three main components: (1) structure, (2) data and (3) consistency[198], that are very specific to how economic modelling was conducted. A description of the quality assessment tools and the comparison of items for each tool is shown in Appendix 25 and Appendix 26. In this thesis, the quality of reporting economic evaluations was assessed using the CHEERS checklist and the Philips checklist was used in addition to the CHEERS checklist.

<u>**Assessment scores**</u>

In terms of scoring, each question of the CHEERS checklist was scored based on the following criteria: (1) “Yes” if the article met the criteria in full, (2) “No” if the article did not meet the criteria, and (3) “Not applicable (NA)” if the question was not relevant to the article. Partial scores were not assigned. Therefore, the maximum possible score was 24. The Philips checklist was also scored using the same category – Yes, No and N/A - but with a maximum score of 60.

4.3 Results

4.3.1 Literature databases search results

After removing duplicate articles, a total of 2,359 articles were identified and, finally, 37 articles were included. Eight publications were published in multiple formats (article and report). These were included only once (N=4). Finally, there were 33 articles for review (Figure 4-1).

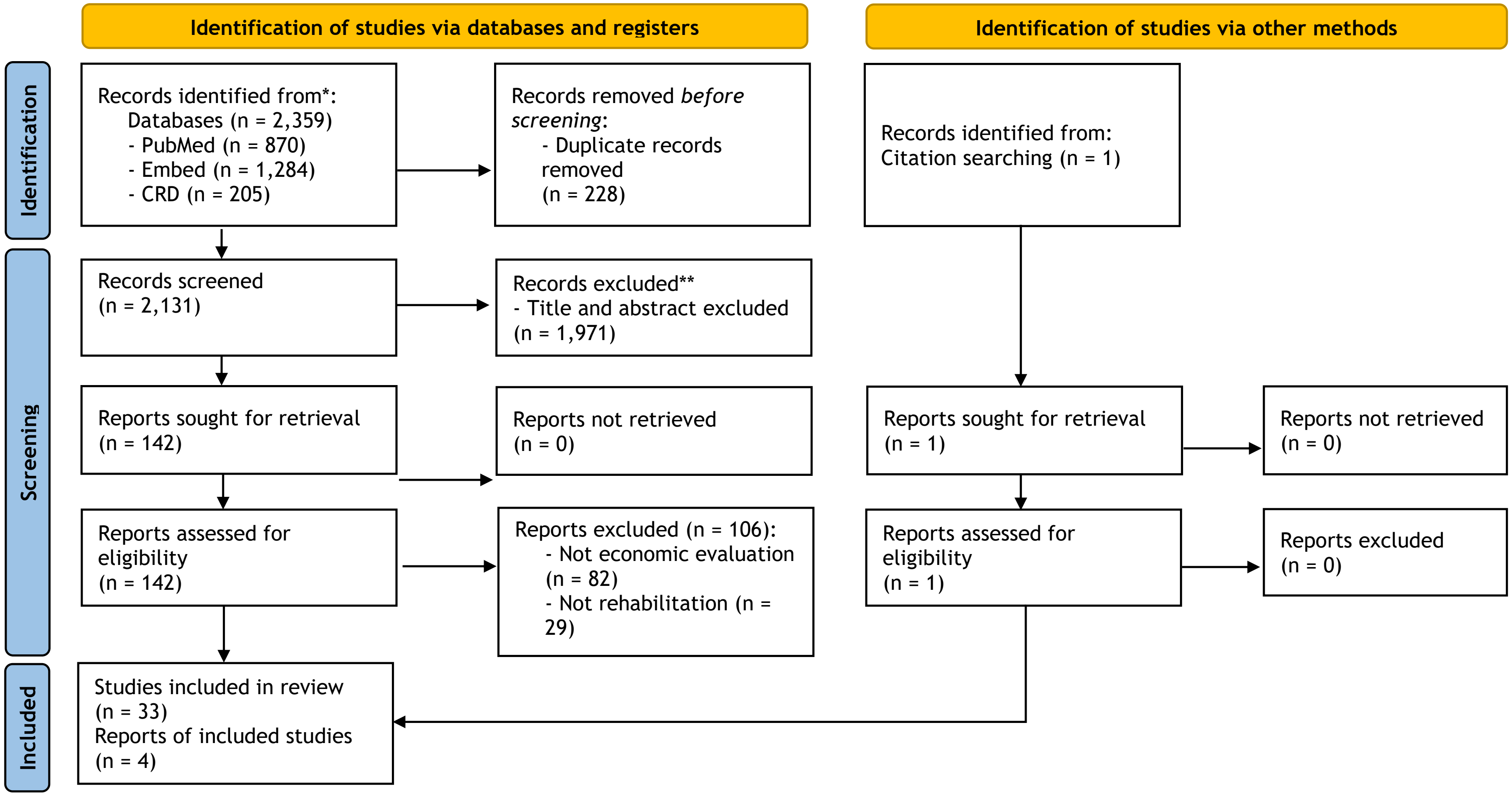

Figure 4-1 PRISMA flow diagram
CRD: Centre for Reviews and Dissemination

4.3.2 Study characteristics

Of the 33 articles, 20 studies were published between 2015 and 2020 (Table 4-2). Fourteen articles were from the United Kingdom (UK), three were conducted in Canada, two each in the Netherlands, Taiwan, United States (US) and multi-countries. The remaining articles were conducted in various countries. In terms of types of study, 18 articles were carried out using an RCT design, six articles used secondary data. In terms of the economic evaluation approaches, twenty-two articles used CUA, followed by seven using CEA, two articles used both CUA and CEA and the remaining two studies used CBA.

The economic evaluation studies were conducted from different perspectives, including a healthcare system/payer perspective which could be either the healthcare system or healthcare provider perspectives, e.g. the UK National Health Service (NHS) and personal social services (PSS) perspective or hospital perspective, (n = 16). There were eight studies conducted from a societal perspective, five studies from both healthcare payer and societal perspectives and four articles did not report their perspective. Of the 33 articles, only seven studies employed model-based economic evaluation with three studies using a Markov model, two studies employed a decision tree, and another two studies employed a decision tree followed by a Markov model.

Table 4-2 Study characteristics

Characteristics	No. of studies (%) (total = 33)
Year of publication	
2011 - 2015	13 (39)
2015 - 2022	20 (61)
Study country	
United Kingdom (UK)	14 (42)
Canada	3 (9)
the Netherlands	2 (6)
Taiwan	2 (6)
United States (US)	2 (6)
Multi-countries	2 (6)
Australia	1 (3)
China	1 (3)
Czech Republic	1 (3)
Japan	1 (3)
Malaysia	1 (3)
South Africa	1 (3)
Spain	1 (3)
Thailand	1 (3)
Type of study	
Randomised Controlled Trial (RCT)	18 (55)
Using secondary data	6 (18)
Based on RCT, but not alongside it	4 (12)
Prospective observational cohort study	3 (9)
Using previously published data	2 (6)
Time horizon	
1 month to 1 year	22 (67)
>1 year – 5 year	4 (12)
>5 year - lifetime	4 (12)
Not state	3 (9)
Type of economic evaluation approaches	
CUA	22 (67)
CEA	7 (21)
CEA and CUA	2 (6)
CBA	2 (6)
Economic evaluation perspective	
healthcare system/payer perspective	16 (49)
Societal perspective	8 (24)
Both healthcare system/payer and societal perspective	5 (15)
Not stated	4 (12)
Types of outcomes	
Improvement of rehabilitation services	16 (49)
Improvement of function, mobility or strength	10 (30)
Improvement of specific skills	5 (15)
Program for caregivers	1 (3)
Others	1 (3)

Characteristics	No. of studies (%) (total = 33)
Type of model	
No economic model	26 (79)
Markov	3 (9)
Decision tree and Markov	2 (6)
Decision tree	2 (6)

4.3.3 Key findings

A summary of the key findings from the selected studies is presented in Appendix 27. Findings can be summarised into four different areas of interest: (1) improvement of rehabilitation services, (2) improvement of function, mobility or strength, (3) improvement of specific skills, and (4) others.

(1) Improvement of rehabilitation services

Sixteen studies focussed on rehabilitation services improvements. Of these, four studies were conducted in the UK[203-206], the remaining studies were conducted in Canada (N=2)[207, 208], Taiwan (N=2)[209, 210] and multiple countries (N=2)[42, 211]. The remaining six studies were conducted in the Netherlands[212], South Africa[213], Spain[214], Malaysia[215], Japan[216] and Thailand[54]. There were 12 studies[42, 54, 203, 204, 206, 207, 209, 210, 212-215] that investigated complex interventions which were defined as any rehabilitation services (e.g. complex package of therapy) provided by more than one healthcare worker (e.g. multidisciplinary team)[50]. Two studies evaluated early rehabilitation[208, 211], and two focused only on occupational therapy[205, 216]. With regards to study setting, ten studies were conducted in hospital settings (inpatient department, outpatient department, rehabilitation ward)[42, 54, 203, 206, 208-213], two were conducted in care home residents[205, 216], two were at a community-based or primary care healthcentre[204, 215], and two were conducted at home[207, 214]. The most frequently used economic evaluation framework was CUA (N=11)[42, 54, 203-207, 211, 212, 215, 216], three studies employed CEA[208-210], and a further two employed CBA[213, 214].

The most frequently used perspective was a societal perspective (N=7)[42, 54, 207, 209, 212, 215, 216], six studies used a healthcare system/payer perspective[203, 205, 206, 208, 210, 213], two studies examined both healthcare system/payer and societal perspectives[204, 211]. However, one study did not state the study perspective[214].

The time horizon varied from one month to 35 years or until death. However, around 70% of studies had a time horizon of less than or equal to two years, while the remaining studies used a time horizon of five years up to 35 years or until death[42, 207, 209, 213].

Health outcomes used (CUA: N=11; CEA: N=1) can be separated into disease-specific outcome measures and generic outcome measures[217]. The most frequently used disease-specific outcome measures were the BI scale[54, 205, 210, 215], and the Modified Rankin Score (mRS)[42, 211]. The most frequently used generic outcome measure was the EuroQol five-dimension scale questionnaire (EQ-5D), either EQ-5D-3L or EQ-5D-5L (N=9)[42, 54, 203, 205-207, 210, 212, 215] to measure quality of life (QOL). One study used each of the following to measure outcomes: quality of life-4 dimension (AQoL-4D)[211], the short-form 36 (SF-36)[216] and General Health Questionnaire-12 (GHQ-12)[204].

In terms of cost-effectiveness results, 10 out of 16 studies showed the rehabilitation interventions evaluated in the studies were found to be value for money. These were six CUA, two CEA and two CBA studies. Two CUA studies concluded that the intervention was cost-saving. These were: community care access centre rehabilitation service at home[207], and home-based rehabilitation[42], which was found to be dominant over the conventional hospital-based rehabilitation (cost-saving in 24 out of 32 countries in Europe). Another four CUA studies concluded that the intervention was cost-effective, these included a combination of extended stroke rehabilitation and usual care[206], an integrated care pathway for post-stroke[215], usual rehabilitation services more than once[54], and occupational therapy for care home residents living with stroke-related disabilities[216]. Two CEA studies concluded that the intervention was cost-effective[208, 209]. These interventions were high intensity fast-track stroke rehabilitation within one week of discharge versus usual inpatient rehabilitation with no fast-track program[208], and a comparison of transferring stroke patients to the rehabilitation ward with rehabilitation order versus those with no rehabilitation therapy[209]. Lastly, two CBA studies concluded that the interventions showed a net saving. These interventions included an individualised 8-week workplace rehabilitation intervention programme complemented with a conventional therapy program versus usual rehabilitation (components of usual rehabilitation were not described)[214], and a study evaluating a virtual reality (VR)-based telerehabilitation program in the balance recovery compared to an in-clinic program using the same VR[213].

(2) Improvement of function, mobility or strength

Ten studies focused on interventions to improve mobility and strength. Of these, five studies were conducted in the UK[218-222], two studies were conducted in the US[223, 224] and the remaining three were conducted in Canada[225], Australia[226], and China[227].

Six studies investigated complex interventions comprising of an outdoor mobility therapy[219], higher physiotherapy intensity[225], group physical fitness sessions[221], the bobath rehabilitation[227], constraint-induced movement therapy (CIMT) for arm recovery[226], and a high intensity training by a walking task (e.g. stairs, overground, treadmill) with targeted intensities at 80% maximum of heart rate reserve[224]. Another four studies evaluated rehabilitation programmes using functional electrical stimulation devices for the correction of dropped foot[218], Nintendo Wii™ Sports[220] as a tool to improve affected arm function, and robot-assisted therapy in moderate to severe upper-extremity impairment[222, 223].

Four studies were conducted in hospital[222, 224, 226, 227], two studies in the community[219, 221] and one study at home[220]. The remaining three studies did not report their setting but conducted a modelling study, which used data from the published literature[225], and retrospective analyses using a hospital database[218, 223].

In terms of perspective, six studies indicated their perspective was from payer[219, 222-226]. One study considered provider and patient perspective[227], whereas three studies did not provide the perspective used[218, 220, 221].

A CUA framework was used in nine studies and one study was a CEA. Disease specific health outcomes were measured using the Action Research Arm Test (ARAT) for arm function measurement[220, 222, 226]. Three studies assessed the level of disability using the Nottingham Extended Activities of Daily Living (NEADL)[219], Stroke Impact Scale[223], and the BI scale[227]. Two studies measured gain in walking speed[218, 224]. For generic health outcome measures, three studies used the EQ-5D[220, 222, 225], another three studies performed the SF-36[219, 221, 224], the Health Utilities Index[223], health utility values suggested from the specialists[227] and one study did not state the type of measurement but reported that they used QALY gain from the economic report[218].

Four studies reported results that showed interventions were either cost-saving or cost-effective. One CUA study focusing on the intensity of physiotherapy[225] concluded that increasing the intensity of rehabilitation or functional strength training plus conventional physiotherapy might result in cost saving (reduction in incremental cost, and a small incremental gain in QALYs). The other three CUA studies concluded that the intervention was cost-effective. These included a group-based physical fitness programme delivered by qualified exercise professionals[221], the Bobath rehabilitation[227] and walking with using a functional electrical stimulation device[218].

Four CUA studies suggested that the interventions were not cost-effective. These studies included the Nintendo Wii Sports™ to improve affected arm function[220], activities to increase outdoor mobility complement local travel information and verbal advice[219], introducing CIMT into routine practice for arm recovery[226]. Lastly, performing high intensity training practiced walking tasks targeting up to 80% maximum heart rate reserve[224].

Results were controversial in the remaining two CUA studies focusing on robot-assisted therapy. The study conducted in the US found that delivering robot-assisted therapy plus usual care had a lower average cost but showed an increase in QALYs. There was, however, much uncertainty with wide confidence intervals around the ICER[223]. Another study conducted in the UK suggested that robot-assisted training was not likely to be cost-effective at any cost per QALY gained[222].

(3) Improvement of specific skills

Five studies focused on rehabilitation for specific skills. Of these, three studies conducted a speech and language or communication skills intervention[228-230], one study evaluated behavioural therapy[231], and another assessed cognitive therapy[232]. Four studies were conducted in the UK[228-231] and the remaining study was carried out in the Netherlands[232]. With regards to study setting, two studies were conducted in either or both hospital and community setting[228, 231], speech and language therapy departments[229, 230], and rehabilitation centres[232].

The most frequently used economic evaluation framework was CUA (N=4)[228-230, 232] and one CEA[231]. The perspective most frequently used was healthcare system/payer perspective[228-231] and only one study used a societal perspective[232]. For the measurement of health outcomes, disease-specific health outcomes were measured in one CEA study which used change in the Stroke Aphasic Depression Questionnaire Hospital (SADQH21) scores[231]. For generic health outcome measures, the EQ-5D was used in all four CUA studies[228-230, 232].

In terms of cost-effectiveness results, two CUA studies[229, 232] concluded that the intervention was likely to represent a cost-effective intervention. These interventions were a computer therapy for people with long-standing aphasia which had a 75.8% chance of the intervention being cost-effective at a willingness to pay (WTP) threshold of £20,000 per QALY gained[229], and a cognitive behavioural therapy augmented with occupational and movement therapy with the probability of the intervention being cost-effective being approximately 76% at a WTP threshold of €40,000 per QALY gained[232].

The two remaining studies conducted early well-resourced flexible speech and language therapy by NHS speech and language therapists[228] and a combination of computerised word finding for SL therapy and usual care[230]. They concluded that these interventions were unlikely to be cost-effective. However, it was found that a combination of computerised word finding for SL therapy and usual care was likely to be cost-effective for a subgroup of the population consisting of patients with mild or moderate aphasia[230]. Additionally, the CEA study concluded that behavioural therapy resulted in some convincing savings in resource utilisation[231].

(4) Others

There were two studies in this group. The first study focused on a structured training programme for caregivers in stroke rehabilitation units compared to usual care (as recommended in national clinical guidelines for stroke year 2008) in the UK[233]. Another study evaluated early inpatient rehabilitation in the Czech Republic which classified patients into five different disability groups: self-sufficient (category 1), partly self-sufficient (category 2), those that require an enhanced level of supervision (category 3), most severely disabled patients or immobile (category 4), and unconscious (category 5)[234]. The former study employed CUA (no economic model) with both healthcare system/payer and societal perspective. The health outcome measurements were generic using the EQ-5D. The former study concluded that the control group (usual care) dominated in both perspectives and both costs and QALYs, thus, the training programme for caregivers in stroke rehabilitation units was less likely to be cost-effective than usual care. The latter study employed CEA and did not state the perspective used; however, this seems to be from a healthcare system/payer perspective. Only disease specific health outcomes were measured using the average increase in BI and the functional independence measure. Finding in both studies indicate that the interventions were not cost-effective; however, a sub-group analysis in the latter study, showed that the intervention proved to be most effective for partly self-sufficient patients. Besides, inpatient rehabilitation appeared to be the least effective intervention for the most severely disabled patients (disability category four).

4.3.4 Results of existing model-based economic evaluations

In terms of the existing decision-analytic models to evaluate stroke rehabilitation, seven studies employed a model-based economic evaluation[42, 207, 221, 225-227, 230]. These studies were conducted in these countries: the UK (n = 2)[221, 230], Canada (n = 2)[207, 225], Australia (n=1)[226], China (n=1)[227] and multiple countries in Europe (n=1).

A. Types of economic evaluation and modelling approaches

Economic evaluation framework

There were one CEA study and six CUA studies. The CEA study employed a decision tree (Figure 4-2)[226]. In terms of studies using CUA framework, one study[221] employed a decision tree (Figure 4-3), three studies[225, 227, 230] employed a Markov model (Figure 4-4 to Figure 4-6), and the remaining two studies[42, 207] used a combination of decision tree and Markov model (Figure 4-7 and Figure 4-8).

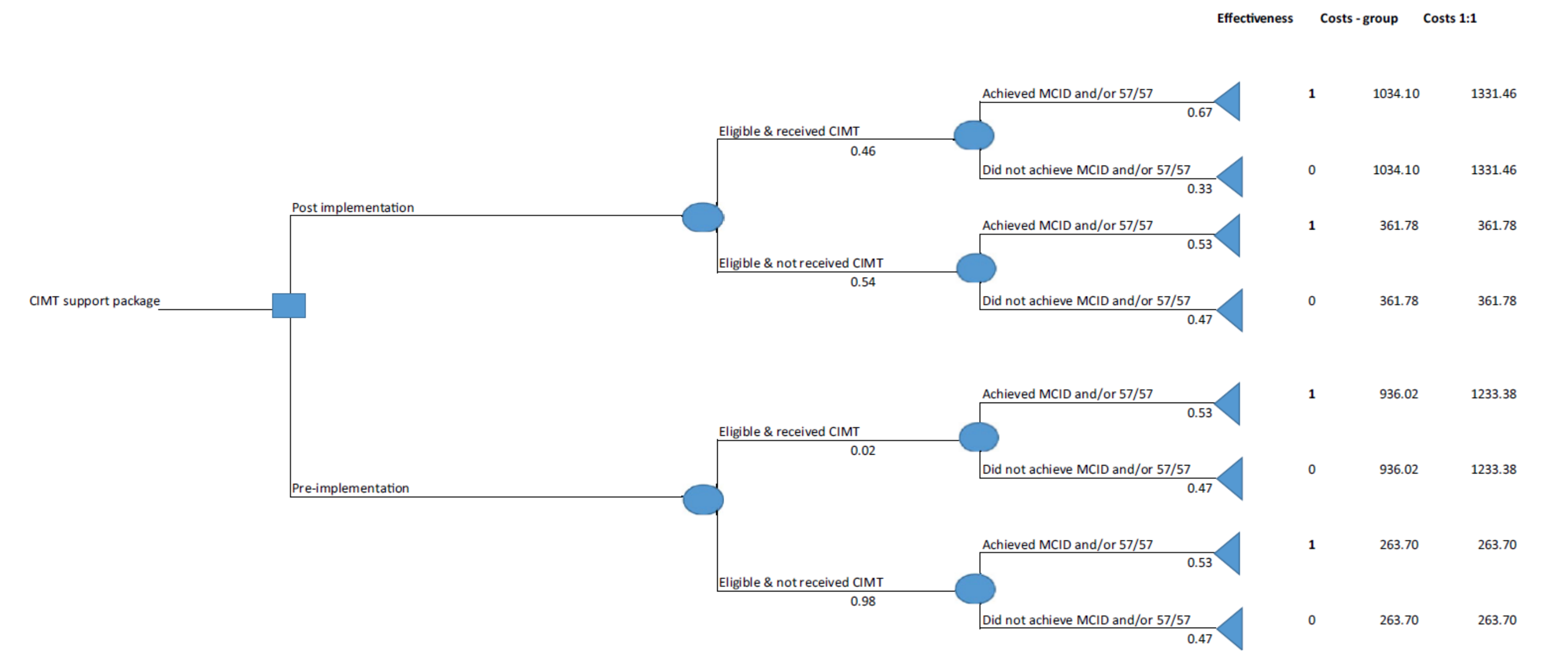

Fig. 1 CIMT decision analytic tree structure, showing costs (in Australian dollars), probability of uptake and outcomes. *CIMT* constraint-induced movement therapy, *MCID* minimal clinically important difference

Figure 4-2 Constraint-induced movement therapy implementation in neurorehabilitation
Figure by Christie et al[226]

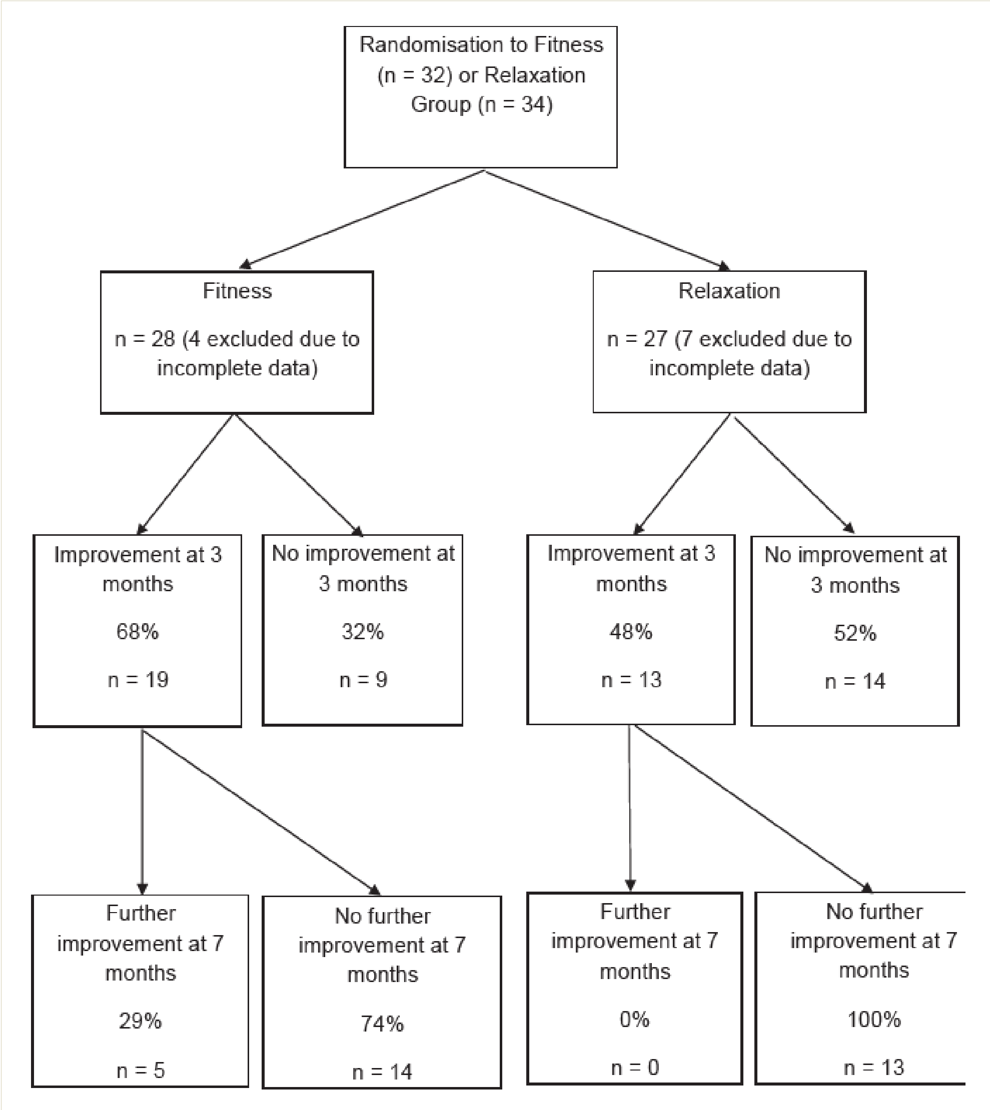

Figure 4-3 Decision tree of mixed physical fitness training intervention
Figure by Collins (2018)[221]

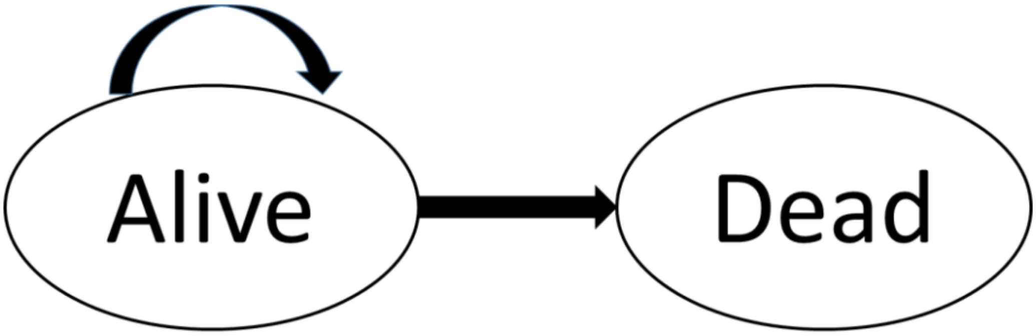

Figure 4-4 Markov model of an increased intensity of physiotherapy training
Figure by Chan (2015)[225]

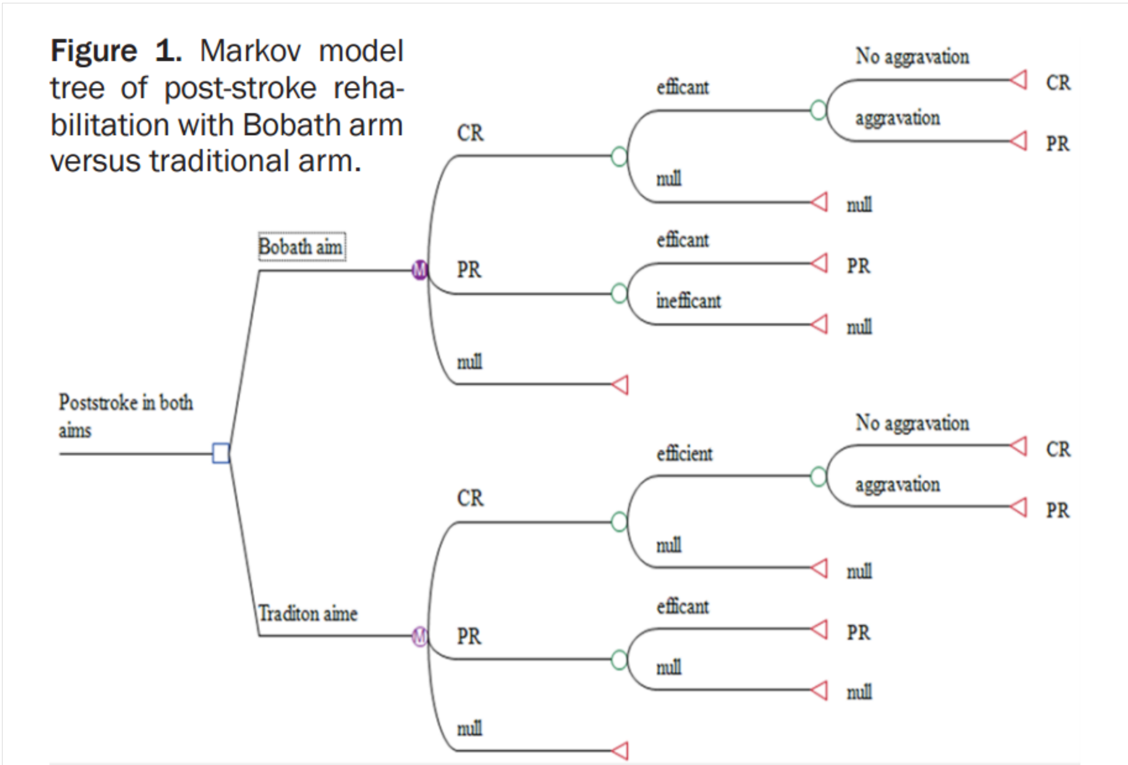

Figure 4-5 Markov model of Bobath rehabilitation vs traditional massage
Figure by Geng et al (2018)[227]
Health state comprises (1) complete rehabilitation (CR), (2) partial rehabilitation (PR) and (3) inefficacy (Null)

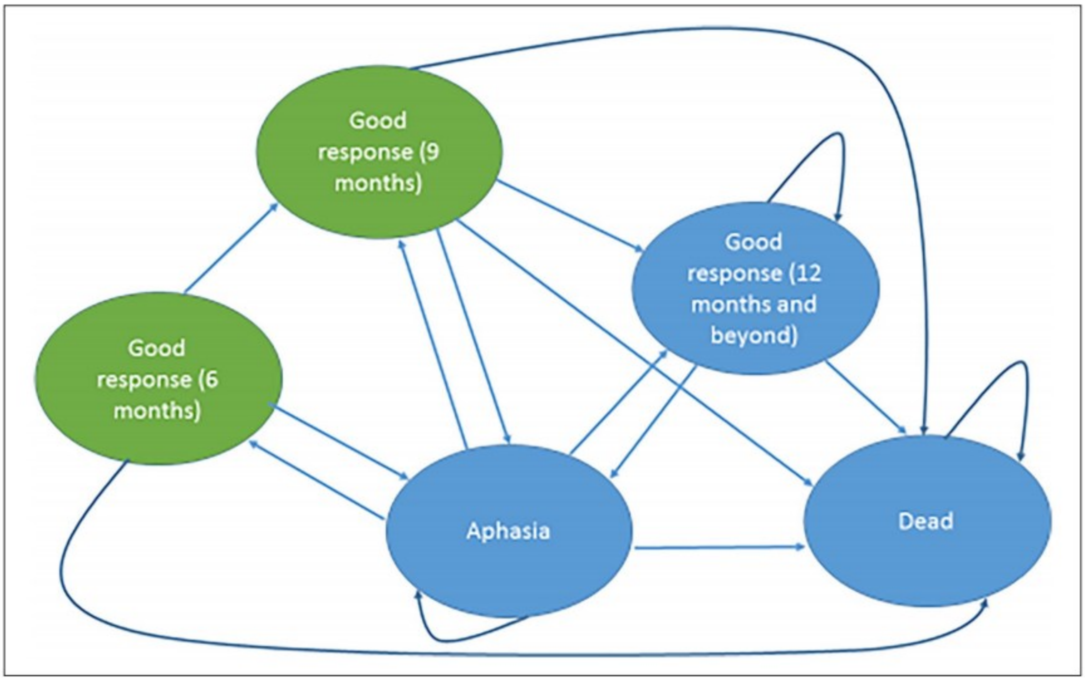

Figure 1. Markov model structure.
Each oval represents a health state. Participants begin in the 'Aphasia' health state and transition through the model in three-month cycles according to data on response and relapse from Big CACTUS. Arrows illustrate possible pathways through the model. Health states coloured in green represent 'tunnel states', which means that participants can only reside in these states for one modelled cycle before transitioning to a different health state. Death could occur from any health state. No new responses were assumed to occur after 12 months – from that point onwards participants in the 'Good response (12 months and beyond)' health state either retain a good response, relapse to the 'Aphasia' health state or die. From 12 months onwards people in the 'Aphasia' health state either remain in that health state or die.

Figure 4-6 Markov model of computerised word finding therapy intervention
Figure by Latimer (2020)[230]

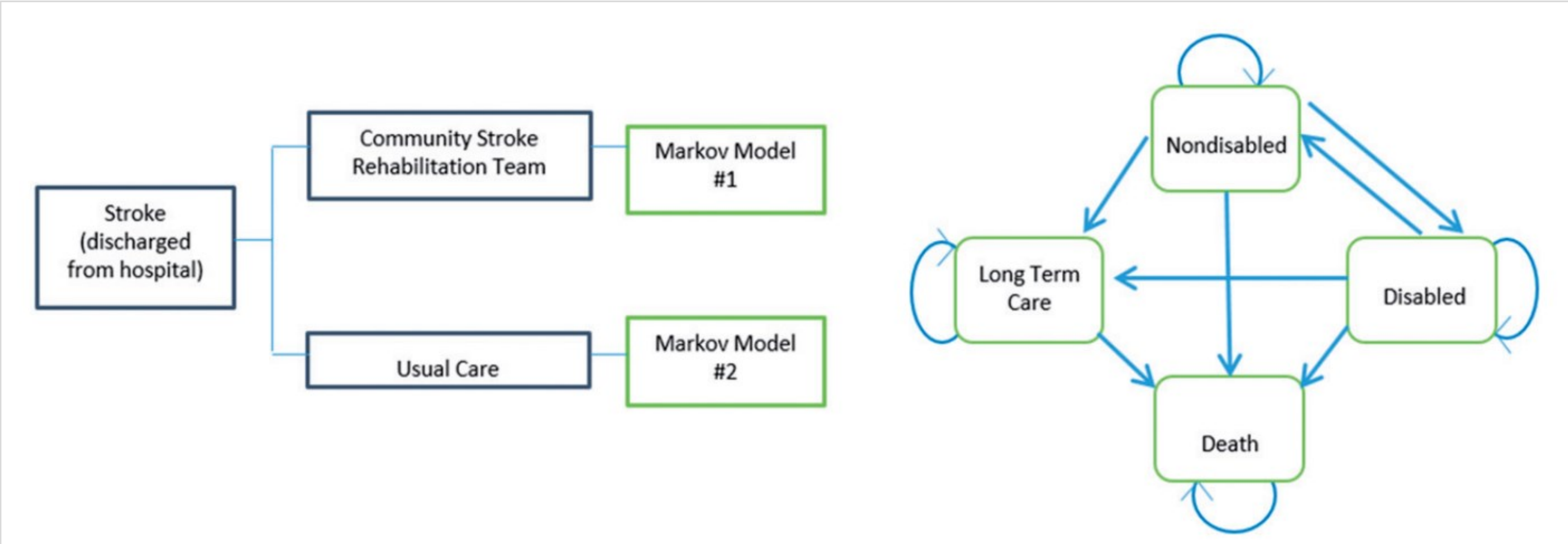

Figure 4-7 Decision tree and Markov model of the Community Care Access Centres (CCACs) rehabilitation services intervention
Figure by Allen (2019)[207]

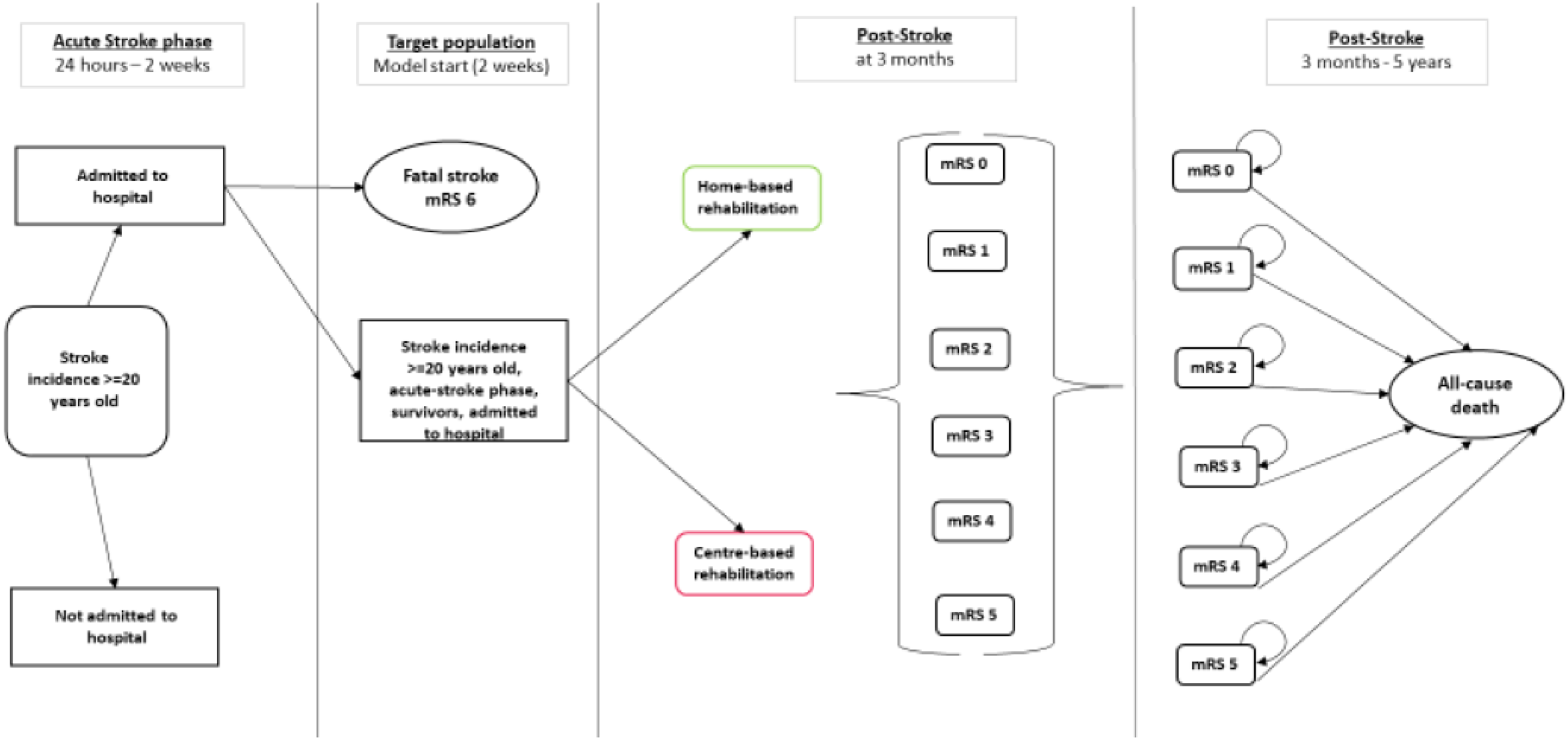

Figure 4-8 Decision tree and Markov model of the home-based stroke rehabilitation
Figure by Candio et al[42].

Model structure and health states

A decision tree in two studies evaluated interventions targeted at specific improvements of function, mobility or strength[221, 226]. The decision tree in the CEA study was designed to reflect the clinical pathway of CIMT in practice starting at the time from determining a patient's eligibility for CIMT to completion of the CIMT programme. The decision tree used in the CUA study was designed to compare between a physical fitness training intervention and a relaxation intervention, then evaluated the QALY gain at 7 months.

Two CUA studies, which employed a Markov model, focused on interventions targeted at specific improvements of function, mobility or strength. The first model[225] compared between higher physiotherapy intensity and a conventional physiotherapy. They explained that the functional improvements associated with higher-intensity physiotherapy did not result in changes to the stroke disease trajectory in either the short term or long term e.g. progression of disease, or risk for future strokes or other comorbidities. Thus, the Markov model was considered to have only two states which were 'alive' and 'dead'. The second model[227] focused on the Bobath rehabilitation compared to traditional treatment (traditional massage). The Markov model comprised three states including complete rehabilitation (CR), partial rehabilitation (PR), and inefficacy. Another CUA study, which employed a Markov model, focused on the computerised word finding therapy plus usual care compared to usual care alone (face-to-face usual speech and language therapy)[230]. The model included three health states: aphasia, good response at 12 months and dead, and another two tunnel states: good response at 6 and 9 months.

The remaining two studies[42] used a combination of decision trees and Markov models. Both studies focused on improvements of rehabilitation services. The economic model of the first study[207] consisted of a decision tree which compared either CSRT intervention or usual care. The health states in the Markov model comprised a 'nondisabled' (completely independent in activities of daily living), 'disabled' (living in their own home but requiring assistance for activities of daily living), 'long-term care' (resides in a LTC or assisted living facility), and 'death' state. The second study focused on home-based versus centre-based rehabilitation across 32 European countries. Eligible patients (e.g. patients who survived the critical phase of two weeks) entered the decision tree and were simulated to receive either home-based or centre-based rehabilitation. Afterward, patients entered to the Markov model conditional on a given level of functional independence on the 3-month mRS score. The health states comprised the mRS score varying from 0 (no disability) to 5 (bedridden and death).

Time horizon and cycle length

Time horizons used for the modelling studies comprised lifetime[225, 230], 35 years or until death[207], five years[42, 227] and less than one year[221, 226]. The cycle lengths varied from one month[227], three months[230], six months[207] and one year[42]. One study did not state their time horizon[225].

Perspective

The most commonly used perspective was that from a healthcare system/payer[221, 225, 226, 230]. Two studies used a societal perspective[207, 227] and the remaining study considered both healthcare system/payer and societal perspectives[42].

Sources of data

The data used in three studies came from various primary sources, e.g. observational studies, and secondary/national or government data supplemented by literature-based sources for long-term projections[42, 221, 226, 227]. One study used in-trial data collection (economic evaluation alongside RCTs)[230], and two studies used data based on a published RCT[207, 221].

B. Measurement and valuation of costs

Costing approaches

Cost components and measurement also varied due to the research objectives and perspectives. The majority of studies measured costs using the ingredients approach, i.e., multiplying unit of resources used and unit cost. The most common component was direct medical costs, particularly costs related to the new intervention or treatment of interest. Sometimes, this cost included training costs for implementation of new interventions[221, 230]. However, overhead costs associated with the new intervention were estimated in only one study[221]. The other components related to direct medical costs used in these studies included cost of hospitalisation, outpatient attendance, primary health care, medicines, devices, medical supplies, lab tests, transportation or ambulance service, and health professionals' travel/visit costs.

In terms of direct non-medical cost in the selected studies, one study included out of pocket expenses of patients[207] and one study included informal care costs[42]. With regards to indirect costs of patient (such as lost productivity or leisure time costs), only one study had taken this into account; however, this study included productivity loss only in patients aged less than 65 years[42].

Cost-Effectiveness Ratio

The ICER, which represents the additional cost per extra unit of effect, was used to present results in all six CUA studies[42, 207, 221, 225, 227, 230]. The CEA study used the proportion of patients who achieved a clinically meaningful improvement in arm function on the disease specific health outcome measure; thus, the ICER presented the cost per additional person gaining a meaningful change in arm function[226]. The WTP thresholds were also used to judge whether an intervention is cost-effective. Most studies employed a threshold of £20,000 per QALY gained. Some studies used WTP thresholds based on their setting. For example, one study conducted in Canada[207] considered a WTP of $20,000 per QALY, while two other studies reported that the country's gross domestic product (GDP) per capita was used as the cost-effectiveness threshold[42, 227]. However, these levels differed with one study indicating to have used three times their mean GDP[227] as a threshold, while another study used the country's per-capita GDP[42].

Price conversion and discounting

Four studies reported price conversion or inflation rate adjustment, using the Consumer Price Index[207, 209, 225, 230]. Four studies reported the discount rate used but this varied from 3%-5%[42, 207, 225] annually and was applied to both costs and outcomes. Another study did not report their discount rate, despite the time horizon being over one year[227].

C. Measurement and valuation of consequences

All six CUA studies evaluated only the generic health outcomes, four studies used EQ-5D[42, 207, 225, 230], one study used SF-36 and converted into QALYs[221], and one study consulted specialists to estimate utility values of each arm in the decision-tree[227]. However, some disease-specific health outcomes, namely functional strength improvement, change of BI of disability level were used for the initial health states and transition probabilities between health states[42].

D. Other economic evaluation components

Model uncertainty

Sensitivity analyses were mostly performed to assess the uncertainty of economic modelling. Four CUA studies conducted both one-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA)[42, 207, 225, 227], one CUA study performed only scenario analyses[221] and one study performed PSA and sub-group analysis[230]. One CEA study also performed OWSA and scenario analyses[226].

A selection of parameters were varied for OWSA. The most commonly used were the transition probabilities, duration of effect, costs of new interventions (especially costs of physiotherapist), mortality risk, utility values, and discount rate[42, 207, 225-227, 230]. On the subject of scenario analyses, three studies performed scenario analyses. Allen et al. (2019)[207] conducted scenario analyses by setting all transition values of a disabled to nondisabled health state in the CSRT equal to the usual care values and changed discount rates. Collins et al. (2018)[221], comparing the fitness training group to usual care, conducted three scenario analyses by (i) assuming a zero cost for the usual care group, and assumed an improvement of 0.01 in QOL, (ii) physical fitness classes (intervention) were continued for up to 12 months and, (iii) a reduction in attendees per class from seven to less than seven attendees per class. Lastly, Christie et al. (2022)[226], performing CEA on CIMT for arm recovery compared to standard rehabilitation upper limb therapy, conducted scenario analyses by assuming 80% uptake in the intervention arm and all therapy delivered within existing resources.

Overall, the parameters that cost-effectiveness results were most sensitive to were; cost of new interventions, health care costs including costs and time of health specialist, reducing the delivery and uptake of intervention, inpatient rehabilitation length of stay, and utility values.

Model assumptions

Several assumptions were made regarding the effectiveness. In the improvement of rehabilitation services group, Allen et al.[207], who evaluated between the CCACs rehabilitation services by CSRTs and usual care (no or limited further rehabilitation services), assumed individuals would no longer transition from the disabled health state to the nondisabled health state after 1 year (two Markov cycles). In addition, Candio et al.[42], who compared home-based rehabilitation and conventional hospital-based rehabilitation, assumed either type of intervention would impact functional independence (measured by mRS) at three months. They also assumed the same probabilities of mRS – as health states - at 3-month following hospital-based rehabilitation group with that observed in a UK-based (Oxford Vascular Study)[235].

Several assumptions were made regarding the transition probabilities. In the improvement of rehabilitation services group, Candio et al.[42], assumed that all participants remained alive during the three months from hospital admission in the decision tree until entering the Markov model and assumed the same mortality risk and QOL, irrespective of the country in Europe. In the improvement of function, mobility or strength group, Collin et al.[221], evaluating a physical fitness training intervention and muscular relaxation, assumed there was a maximum capacity of attendance in each class for both intervention and control group. They also assumed that a deterioration in QOL was not considered as it was assumed that if participants were deteriorating, they would not continue with the intervention. Chan[225] assumed the probability of dying being constant over time for patients who live beyond 10 years post-stroke. They also assumed the utility improvements at 6-week follow up were maintained for up to two years and the utility scores for intervention and comparator groups were identical. Christie et al.[226], who evaluated the CIMT programme for arm recovery versus standard rehabilitation upper limb therapy, assumed some patients may decline CIMT due to personal preference and assumed equal effectiveness of group and individual CIMT therapy.

Assumptions were also made around costs. Candio et al.[42] assumed informal care costs would be required for 50% of stroke patients who were identified with mRS scores = 3, and for 100% of stroke patients with mRS scores = 4 or 5. Candio et al.[42] also assumed that patients of each country would receive the same type and level of care and gain benefit from the intervention; hence, the resources needed for the rehabilitation intervention were already available and no heterogeneity of treatment protocols. At last, Chan[225] assumed physiotherapists did not require additional rehabilitation facilities or training to accommodate their increased workload and no downstream costs were associated with the intervention.

E. Conclusion of economic evaluation studies

Three studies reached similar conclusions showing that the rehabilitation intervention was cost-saving[42, 207, 225]. These included providing community stroke rehabilitation teams services at home, compared to not providing any therapy, higher-intensity physiotherapy during inpatient rehabilitation after stroke, compared to standard levels of physiotherapy, and home-based rehabilitation compared to centre-based (hospital-based care). Two studies also indicated that rehabilitation interventions were found to be cost-effective[221, 227]. These included group-based physical fitness interventions after stroke services compared to muscular relaxation interventions, and providing Bobath rehabilitation, compared to traditional massage. Additionally, one study showed that adding computerised word finding therapy for speech and language therapy to usual care (face-to-face usual speech and language therapy) in people with aphasia post-stroke was more likely to be cost-effective in a sub-group of patients only[230]. In particular, this intervention was unlikely to be cost-effective for the general population with aphasia post-stroke but it was more likely to be cost-effective for people with mild or moderate aphasia post-stroke. Only one study[226] concluded that planning to deliver the CIMT implementation package and introducing CIMT into routine practice in relation to arm function could be considered poor value for money.

4.3.5 Quality assessment of economic evaluation publications

The CHEERS checklist

All 33 studies were quality-assessed using the CHEERS checklist (Figure 4-9) This assessment showed small variations in reporting quality. All studies showed a minimum of 70% of the 24 questions that could be answered with 'yes'. The red line shows the percentage of 'yes' when excluding questions that had been answered with 'NA'. This means that most studies were clearly reporting well against 80% of the individual items. The answer to all 24 questions of the CHEERS checklist is depicted in Figure 4-10 for each reviewed study (distribution of overall scores of each question excluding NA answer is shown in Appendix 28). Most studies apparently described the study title and abstract, objectives, population and setting, comparators, health outcomes, resource used and cost, analytical methods, estimated costs and outcomes, and discussion. The items that were not answered with 'Yes' comprised discount rate, currency, price date, including a conversion, characterising uncertainty which was recommended to describe the effects of sampling uncertainty of the study and study perspective.

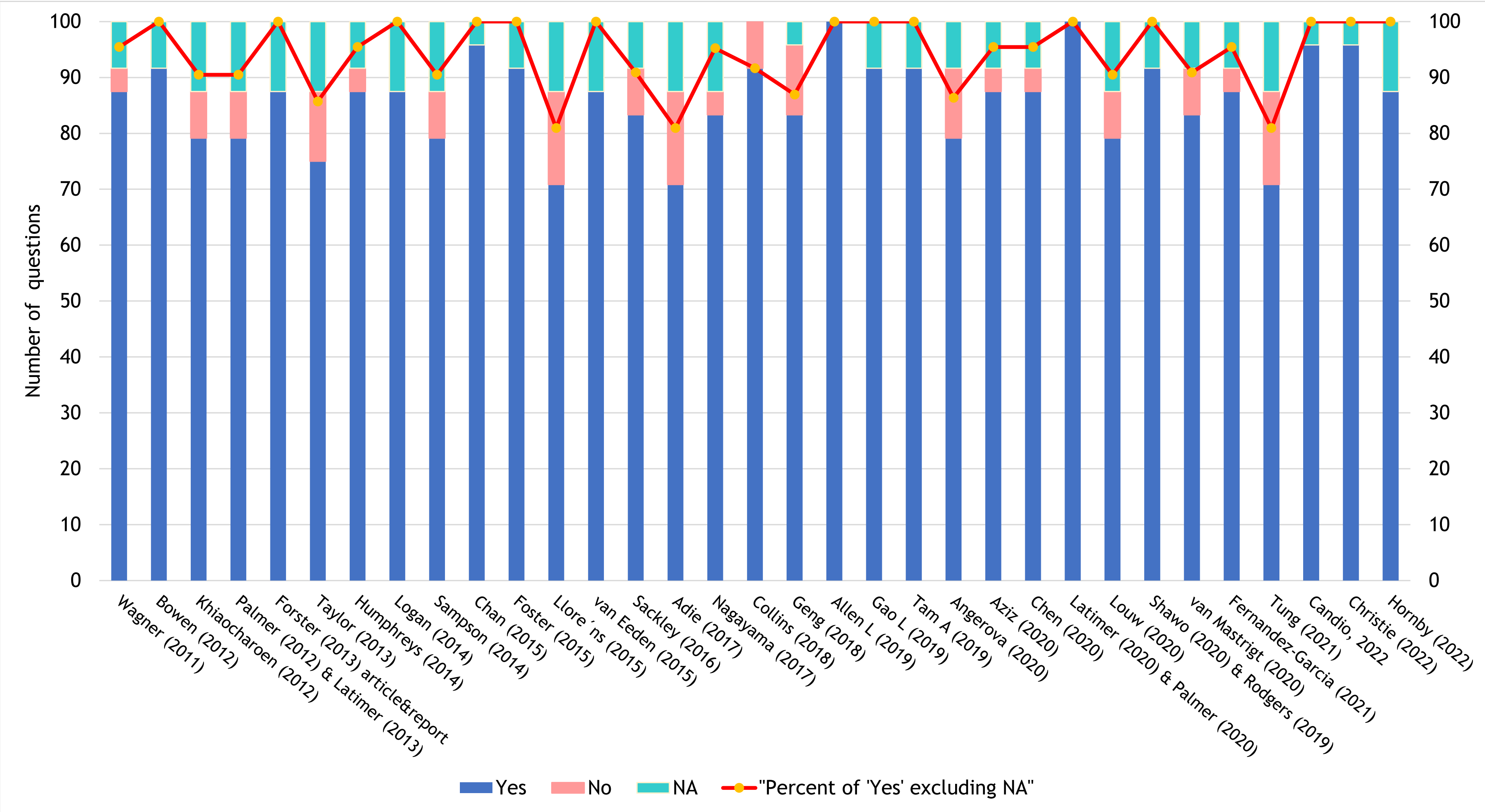

Figure 4-9 An assessment of the eligible studies using the CHEERs checklist

no	CHEERS checklist Items	Wagner (2011)	Bowen (2012)	Khiaocharoen (2012)	Palmer (2012) & Latimer (2013)	Forster (2013) article&report	Taylor (2013)	Humphreys (2014)	Logan (2014)	Sampson (2014)	Chan (2015)	Foster (2015)	Llorens (2015)	van Eeden (2015)	Sackley (2016)	Adie (2017)	Nagayama (2017)	Collins (2018)	Geng (2018)	Allen L (2019)	Gao L (2019)	Tam A (2019)	Angerova (2020)	Aziz (2020)	Chen (2020)	Latimer (2020) & Palmer (2020)	Louw (2020)	Shawo (2020) & Rodgers (2019)	van Mastrigt (2020)	Fernandez-Garcia (2021)	Tung (2021)	Candio, 2022	Christie (2022)	Hornby (2022)
Title and abstract																																		
1	Title	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
2	Abstract	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Introduction																																		
3	Background & objectives	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Methods																																		
4	Target population & subgroups	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
5	Setting & location	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
6	Study perspective	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	✓	✗	✓	✗	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
7	Comparators	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
8	Time horizon	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✗	✓	✓	✓	✓	✓	✗	✓	✓	✓
9	Discount rate	✗	✓	✗	✓	✓	✓	✗	✓	✗	✓	✓	✗	✓	✓	✗	✗	✗	✗	✓	✓	✓	✗	✗	✓	✓	✓	✓	✓	✗	✗	✓	✓	✓
10	Choice of health outcomes	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
11	Measurement of effectiveness	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓
12	Measurement & valuation of preference based outcomes (If applicable)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
13	Estimating resources & costs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
14	Currency, price date, & conversion	✓	✓	✗	✗	✓	✓	✓	✓	✗	✓	✓	✗	✓	✗	✗	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓
15	Choice of model										✓							✓	✓	✓						✓						✓	✓	
16	Assumptions										✓							✓	✓	✓						✓						✓	✓	
17	Analytical methods	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓
Results																																		
18	Study parameters	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
19	Incremental costs & outcomes	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
20	Characterising uncertainty	✓	✓	✓	✗	✓	✗	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓
21	Characterising heterogeneity (If applicable)	✓	✓					✓				✓			✓			✓		✓	✓	✓	✓	✓	✓	✓		✓	✓	✓				
Discussion																																		
22	Study findings, limitations, generalizability, and fit with current knowledge	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Other																																		
23	Source of funding	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓
24	Conflicts of interest	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓

✓ = Yes ✗ = No (blank) = NA

Figure 4-10 CHEERS score for each reviewed study

The Philips checklist

The Philips checklist was used for critically appraising all model-based EE in this thesis. All seven studies using an economic model to evaluate cost-effectiveness were assessed in terms of their overall quality (Figure 4-11). The bar graph shows the maximum score of 60 that can be achieved. Several items were found to be not applicable (NA). This was the case, for instance, in decision-analytic models using a decision tree where the assessment of the criterion asked for cycle length.

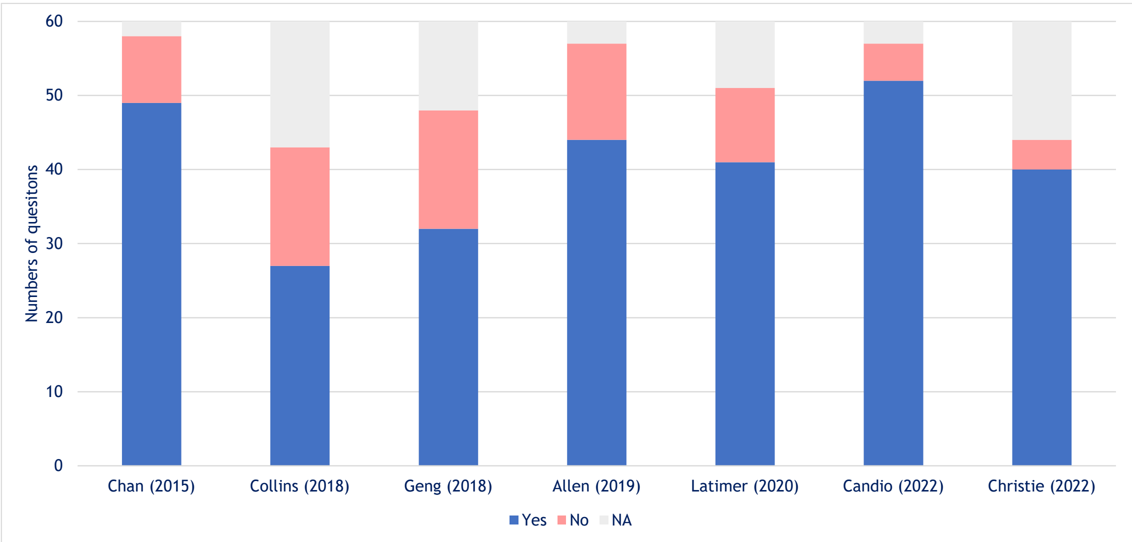

Figure 4-11 Overall Philips checklist scores of selected studies conducting economic model

In general, most studies reported well in terms of the structure domain (Figure 4-12). Studies stated their decision problem clearly, the objectives of the evaluation and perspective of the analysis were consistent with the decision problem. The model structures, strategies/comparators represented the clinical pathway. However, there were some structural concerns noticed such as sources of data used to develop the model structure. Studies generally stated and justified the study time horizon, and model cycle length.

no.		Dimension of Quality	Questions for Critical Appraisal	Chan (2015)	Collins (2018)	Geng (2018)	Allen (2019)	Latimer (2020)	Candio (2022)	Christie (2022)
Structure										
1	S1	Statement of decision problem/objective	Is there a clear statement of the decision problem?	✓	✓	✓	✓	✓	✓	✓
2			Is the objective of the evaluation & model specified & consistent with the stated decision problem?	✓	✓	✓	✓	✓	✓	✓
3			Is the primary decision maker specified?	✓	✗	✗	✗	✗	✓	✓
4	S2	Statement of scope/perspective	Is the perspective of the model stated clearly?	✓	✗	✓	✓	✓	✓	✓
5			Are the model inputs consistent with the stated perspective?	✓	NA	✓	✓	✓	✓	✓
6			Has the scope of the model been stated & justified?	✓	✗	✓	✓	✓	✓	✓
7			Are the outcomes of the model consistent with the perspective, scope & overall objective of the model?	✓	✓	✓	✓	✓	✓	✓
8	S3	Rationale for structure	Has the evidence regarding the model structure been described?	✓	✗	✓	✗	✓	✓	✓
9			Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	✓	NA	✓	NA	✓	✓	✓
10			Have any competing theories regarding model structure been considered?	✓	✓	✓	✓	✓	✓	✓
11			Are the sources of data used to develop the structure of the model specified?	✗	✓	✗	✗	✓	✓	✓
12			Are the causal relationships described by the model structure justified appropriately?	✓	✗	✗	✗	✓	✓	✓
13	S4	Structural assumptions	Are the structural assumptions transparent & justified?	✓	✓	NA	✓	✓	✓	✓
14			Are the structural assumptions reasonable given the overall objective, perspective & scope of the model?	✓	✓	NA	✓	✓	✓	✓
15	S5	Strategies/Comparators	Is there a clear definition of the options under evaluation?	✓	✓	✓	✓	✓	✓	✓
16			Have all feasible & practical options been evaluated?	✓	✓	✓	✗	✓	✓	✓
17			Is there justification for the exclusion of feasible options?	✓	NA	✗	✗	NA	✓	✓
18	S6	Model Type	Is the chosen model type appropriate given the decision problem & specified causal relationship within the model?	✓	✓	✓	✓	✓	✓	✓
19	S7	Time Horizon	Is the time horizon of the model sufficient to reflect all important differences between options?	✓	✓	✓	✓	✓	✓	✓
20			Are the time horizon of the model, the duration of treatment & the duration of treatment effect described & justified?	✓	✓	✓	✓	✓	✓	✓
21			Has a lifetime horizon been used? If not, has a shorter time horizon been justified?	✓	NA	✓	✓	✓	✓	NA
22	S8	Disease states/pathways	Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question & the impact of interventions?	✓	✓	✓	✓	✓	✓	✓
23	S9	Cycle length	Is the cycle length defined & justified in terms of the natural history of disease?	✓	NA	✓	✓	✓	✓	NA

Figure 4-12 Scoring of structure domain of the Philips checklist

In terms of data domain (Figure 4-13), it seems that the methods used for data identification were adequate in most studies. However, most of them did not explain the choice between data sources or how the quality of the data had been assessed. This could be a result of information inadequacy in the literature. Additionally, uncertainty in economic models is unavoidable, the methods of assessment of four main types of uncertainty, namely methodological, structural, heterogeneity and parameter, were recommended as well as the justification of the omission of particular forms of uncertainty analyses. Clearly, none of these reviewed studies addressed all types of uncertainty. However, parameter uncertainty was addressed in all studies, e.g. OWSA or PSA were carried out to assess the impact of these parameters on results, while the assessment of uncertainty due to heterogeneity for different sub-groups was performed in only one study.

The final domain assessed consistency of data (Figure 4-14). The majority of studies assessed external consistency, in other words, they compared their results and discussion with previous modelling studies.

no.		Dimension of Quality	Questions for Critical Appraisal	Chan (2015)	Collins (2018)	Geng (2018)	Allen (2019)	Latimer (2020)	Candio (2022)	Christie (2022)
Data										
24	D1	Data identification	Are the data identification methods transparent & appropriate given the objective of the model?	✓	✓	✓	✓	✓	✓	✓
25			Where choices have been made between data sources, are these justified appropriately?	✓	✓	NA	✓	✓	✓	✓
26			Has particular attention been paid to identifying data for the important parameters in the model?	✓	✓	NA	✓	✓	✓	✓
27			Has the process of selecting key parameters been justified & systematic methods used to identify the most appropriate data?	✓	✗	✓	✓	✗	✓	✓
28			Has the quality of the data been assessed appropriately?	✓	✗	✗	✗	✗	✓	✓
29			Where expert opinion has been used, are the methods described & justified?	✓	NA	NA	NA	NA	NA	NA
30	D2	Pre-model data analysis	Are the pre-model data analysis methodology based on justifiable statistical & epidemiological techniques?	✓	✗	✓	✓	✓	✓	✓
31	D2a	Baseline Data	Is the choice of baseline data described & justified?	✓	✓	✗	✓	✓	✓	✓
32			Are transition probabilities calculated appropriately?	✓	✓	✗	✓	✓	✓	✓
33			Has half-cycle correction been applied to both cost & outcome?	✓	NA	✗	✗	✗	✓	NA
34			If not, has this omission been justified?	NA	NA	✗	✗	✗	NA	NA
35	D2b	Treatment Effects	If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques?	✓	NA	NA	✓	NA	✓	NA
36			Have the methods & assumptions used to extrapolate short-term results to final outcomes been documented & justified?	NA	NA	NA	✓	NA	✓	NA
37			Have alternative assumptions been explored through sensitivity analysis?	✗	NA	NA	✓	NA	✓	NA
38			Have assumptions regarding the continuing effect of treatment once treatment is complete been documented & justified?	✓	NA	NA	✗	NA	✓	NA
39			Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis?	✓	NA	NA	✗	NA	✗	NA
40	D2c	quality-of-life weights (utilities)	Are the utilities incorporated into the model appropriate?	✓	✓	✓	✓	✓	✓	NA
41			Is the source for the utility weights referenced?	✓	✓	✓	✓	✓	✓	NA
42			Are the methods of derivation for the utility weights justified?	✓	✓	✓	✓	✓	✓	NA
43	D3	Data incorporation	Have all data incorporated into the model been described & referenced in sufficient detail?	✓	✓	✓	✓	✓	✓	✓
44			Has the use of mutually inconsistent data been justified? (i.e. are assumptions & choices appropriate)?	✓	✓	✓	✓	✓	✓	✓
45			Is the process of data incorporation transparent?	✓	✓	✓	✓	✓	✓	✓
46			If data have been incorporated as distributions, has the choice of distribution for each parameter been described & justified?	✓	NA	NA	✓	✓	✓	NA
47			If data have been incorporated as distributions, is it clear that second order uncertainty is reflected?	✓	NA	NA	✓	✓	✓	NA
48	D4	Assessment of uncertainty	Have the four principle types of uncertainty been addressed?	✗	✗	✗	✗	✗	✗	✗
49			If not, has the omission of particular forms of uncertainty been justified?	✗	✗	✗	✗	✗	✗	✗
50	D4a	Methodological	Have methodological uncertainties been addressed by running alternative versions of the model with different methodological assumptions?	✗	✗	✗	✓	✗	✓	✓
51	D4b	Structural	Is there evidence that structural uncertainties have been addressed via sensitivity analysis?	✗	✗	✗	✓	✗	✗	✗
52	D4c	Heterogeneity	Has heterogeneity been dealt with by running the model separately for different sub-groups?	✗	✗	✗	✗	✓	✗	✗
53	D4d	Parameter	Are the methods of assessment of parameter uncertainty appropriate?	✓	✓	✓	✓	✓	✓	✓
54			Has probabilistic sensitivity analysis been done, if not has this been justified?	✓	NA	✓	✓	✓	✓	✓
55			If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly & justified?	✓	✓	✓	✓	NA	✓	✓

✓ = Yes ✗ = No

Figure 4-13 Scoring of data domain of the Philips checklist

no.		Dimension of Quality	Questions for Critical Appraisal	Chan (2015)	Collins (2018)	Geng (2018)	Allen (2019)	Latimer (2020)	Candio (2022)	Christie (2022)
Consistency										
56	C1	Internal consistency	Is there evidence that the mathematical logic of the model has been tested thoroughly before use?	✓	✗	✗	✓	✗	✓	✓
57	C2	External consistency	Are the conclusions valid given the data presented?	✓	✓	✓	✓	✓	✓	✓
58			Are any counterintuitive results from the model explained & justified?	✗	✗	✗	✓	✓	✓	✓
59			If the model has been calibrated against independent data, have any differences been explained & justified?	✓	NA	✓	NA	NA	NA	NA
60			Have the results of the model been compared with those previous models & any differences in results explained?	✗	✗	✓	✓	✓	✓	✓

✓ = Yes ✗ = No

Figure 4-14 Scoring of consistency domain of the Philips checklist scores

4.4 Discussion

The aim of this systematic review was to summarise and assess existing economic evaluations and economic models of rehabilitation in post-stroke patients. Findings from this review will inform the evaluation of the new rehabilitation policy in Thailand, which is presented in Chapter 5.

4.4.1 Summary of main findings for economic evaluations

The review included 33 studies, undertaken in 14 settings with heterogeneity in healthcare systems, population characteristics, interventions and comparators, and perspectives. To-date, evidence has been limited to developed countries such as the UK, Canada, and the US. Even though, the CUA framework and the generic outcome measure such as EQ-5D were most frequently used, most studies relied on RCT data with a short-term horizon. Although, the EQ-5D was the most commonly used outcome measure, several tools were used in the reviewed studies, e.g. SF-36, HUI. This could affect results[217], in particular, the ICER value as based on these measurements utility scores were generated, which were dissimilar and scaled differently; thus, estimated values are not exactly comparable and these can have implications for the comparability of health outcome analyses and interpretation of economic evaluation studies[236, 237]. The evidence of the difference in utility scores or QOL estimates related to different measurement tools can be seen in several published studies[238-242]. For example, SF-6D presented absence of ceiling and floor effects[239], and could result in less favourable results in cost-effectiveness analysis than EQ-5D[241].

There were several areas of interest related to the economic evaluation of rehabilitation interventions. Nearly half of the reviewed studies (49%) evaluated rehabilitation services improvement (group 1), followed by improvement of function, mobility or strength in patients with stroke (group 2). Overall, the majority of new rehabilitation interventions/services were likely to be cost-saving or cost-effective, but they were unlikely to represent good value for money in other groups, for instance, improvement of speech and language therapy. These cost-effective interventions comprised home-based rehabilitation, occupational therapy, extended rehabilitation, fast-track rehabilitation and transferring patients to the rehabilitation ward. In addition, there were conflicting results in a group focusing on improvement of function, mobility or strength. These could be due to a variation between studies concerning the intervention or comparator components or definition, perspective and the scope of costs. Moreover, the various methods used in these studies could be attributable to the study purpose and data availability in the respective setting. This chapter supports evidence from a previous systematic review[243] which accessed the cost or cost-effectiveness studies related to integrated care arrangements compared to usual care in people with stroke.

The economic evaluation of these reviewed studies especially those that focussed on rehabilitation services improvement (group 1) were in line with the new Thai rehabilitation policy[51] recommending providing rehabilitation therapy for post-stroke patients. Therefore, the economic model that will be adapted to evaluate the new rehabilitation policy in Thailand, will be discussed in the next section.

4.4.2 Summary of main findings for model-based economic evaluations

Although most studies conducted their economic evaluation by employing a CUA framework, only seven studies used economic models to assess cost-effectiveness of rehabilitation interventions. The most common modelling approach was a Markov model - a static economic model. Different approaches to model-based economic evaluation of stroke rehabilitation are likely to be related to different study purposes or objectives of the researcher or healthcare decision-maker to compare rehabilitation interventions within a country-specific context.

Inspection of the results suggests that the seven identified economic models were moderately heterogeneous in terms of model structure, data source, cost measurements, time horizon, and methods to assess uncertainty. For instance, the main cost component comprised direct-medical costs, especially costs related to the new intervention. However, most of these studies barely considered overhead costs of interventions or indirect costs, particularly, those related to productivity loss. Furthermore, there was a lack of economic modelling studies that considered stroke patients according to subgroups. As presented in Chapter 3, different types of stroke were associated with different risks of mortality. In addition, the analysis in Chapter 3 confirmed that receiving rehabilitation at incident stroke was associated with lower annual costs of treatment and also a lower risk of mortality. A possible explanation for this exclusion might be that most stroke patients were elderly and the authors considered that productivity loss might be negligible compared to costs of implementing new interventions due to the perspective aspect.

Of the seven studies, only two studies[42, 207] evaluated the cost-effectiveness of stroke rehabilitation service improvement (group 1). Both studies focussed on home-based rehabilitation services using a societal perspective and concluded stroke rehabilitation was likely to be cost- effective compared to usual care. The first study was a home care rehabilitation by the community stroke rehabilitation teams (CSRTs) compared to those patients who are unable to access traditional outpatient rehabilitation services. The second study was a home-based rehabilitation programme compared to centre-based rehabilitation, where the patient would only receive conventional hospital-based care (either inpatient or outpatient). Although both studies presented similar results, their methodologies were different. For example, different tools for measuring disability levels to classify stroke survivors into health states, time horizon between lifetime versus five years, variation in assumptions, and cost components. It is worth highlighting that albeit using the same societal perspective, there were noticeable differences in the scope of cost components, especially, neglecting of costs of lost productivity including informal care. These could introduce bias to the cost-effectiveness results as costs might be underestimated and could bias ICER results[244].

Although advancements have been made in stroke care management, it could be noticed that the number of cost-effectiveness studies of post-acute stroke rehabilitation services seemed to be considerably lower compared to the number of studies focusing on endovascular treatment in acute stroke care, as mentioned in Chapter 1. It could be implied that the improvement of rehabilitation services, such as service development, infrastructure, human resources, still lags behind the development of advanced technologies for acute-phase stroke treatment and/or stroke prevention[245]. The importance of rehabilitation services needs to be recognised as rehabilitation is one essential component in the value chain of improving the quality of stroke care in any health system. Additionally, CEA studies of both types of therapy were conducted mostly in developed countries, while there was a limited number of studies conducted in LMIC settings. This is an important issue to recognise for the Thai MOPH when they are working on developing and improving these health care services.

4.4.3 Quality assessment

Overall, all economic modelling studies performed well against frameworks on best practice for reporting an economic evaluation and economic modelling. There was an upward trend for more recent studies in terms of the average ‘yes’ scores compared to prior studies. According to the Philips checklist which contains items additional to the CHEERS checklist, several economic modelling studies rarely explained whether data quality had been appropriately assessed. Also, only sensitivity analysis to assess parameter uncertainty was usually undertaken. The absence of these uncertainty assessments due to methodological or structural factors, and heterogeneity may have an impact on study results. For instance, structural uncertainty would matter in the absence of good quality evidence on the history of disease and the structure of the decision-analytic model would be affected. Uncertainty due to heterogeneity could affect results between subgroups of patients.

4.4.4 Strengths and limitations of the systematic review

This chapter identified and assessed existing economic evaluations for stroke rehabilitation services to inform the development of an appropriate rehabilitation model. This systematic review provided insight into the existing evidence in terms of evaluating rehabilitation programmes for stroke survivors. It also identified existing economic models to help guide the evaluation of the new Thai rehabilitation policy, which is presented in the next chapter. To interpret the reviewed studies appropriately, the quality assessment of economic evaluations was carried out using the CHEERS and Philips checklists. This review included studies undertaken in the past 10 years as it was hypothesised that these studies would best reflect the most recent and up-to-date clinical practice in delivering stroke rehabilitation services as well as the effects of treatments. Some limitations also need to be considered when interpreting the findings. Firstly, due to heterogeneity in cost components, outcome measures, assumptions, and the type of intervention between studies, a comparison between studies was difficult and can only be described in a narrative way. Secondly, because of the time constraints, only 10% of randomly selected studies were assessed and checked independently by a second reviewer.

4.5 Implications for future research

Learnings from the economic evaluation and model-based studies

As mentioned earlier, most of the reviewed studies were carried out in developed countries with differences in several economic evaluation components. For example, costs related to rehabilitation interventions or components of the intervention and the number of health care professionals will differ greatly between jurisdictions. This is evident in the study undertaken by Candio et al[42] conducted in several European countries. The findings indicated that, of 32 European countries, home-based rehabilitation was found to be cost-saving in 24 countries but cost-effective in the remaining eight countries. Therefore, it is important to conduct an economic evaluation within a specific context.

Implications for future research are as follows:

- Heterogeneity in justifying the disability levels, cost and health outcome measurements, and the way data or model inputs were assessed could limit the ability to express meaningful ICER and comprehensive conclusions on the rehabilitation services.

- Productivity loss associated with informal care could impact on cost-effectiveness results in the economic evaluation. From a health care payer perspective, these costs may not impact results but might place huge financial constrain on patients and families when taking a societal perspective, as recommended by most HTA agencies[190, 246-248]. Therefore, costs related to lost productivity and/or informal care should be considered to reflect real world scenarios of providing rehabilitation services. Additionally, overhead costs should be taken into account when evaluating a new intervention that has infrastructure or trained staff requirements associated with its use.

- Future studies should consider their own context of relevant alternative intervention options and data. Responsible interpretation of the economic evaluations' results will take into account each study's sensitivity analysis approach and input ranges and whether the inputs are varied in a manner that reflects the practical context for the decision makers' application.

Additionally, there is a limited number of economic evaluations, including those employing an economic model for stroke rehabilitation programmes in Thailand[54, 61, 62, 249]. There is currently no economic evaluation that assesses the new stroke rehabilitation policy and its long term outcomes. Thus, a de novo economic modelling study of rehabilitation services for stroke survivors is needed in response to this policy to inform decision makers, such as MOPH – a provider, NHSO – a health purchaser - and health system researchers, for further rehabilitation policy implementation.

Based on the review and quality assessment and also taking into account context, the economic evaluation presented in Chapter 5 will adapt the economic model developed by Allen et al.[207]. This was identified to be the most suitable model because the rehabilitation programme was evaluated by comparing between patients who received rehabilitation services at home, delivered by the health care professionals, and those who had received no (or limited) further rehabilitation therapy services. The Markov model evaluated rehabilitation programmes depending on the functional status of post-stroke patients. This model also evaluated outcomes over a long-term time horizon. The quality assessment showed good quality in both the CHEERS and Philips checklists. This model also appeared to be inclusive of all the relevant health states which can be applied and adopted to the Thai rehabilitation economic model because the health states were similar to the recommendations in the new Thai rehabilitation guidelines[51].

4.6 Conclusions

Though, there were many cost-effectiveness studies for stroke rehabilitation interventions with several areas of interest, findings from all 33 studies in the systematic review in this chapter showed that there was a limited number of studies employing an economic model to assess cost-effectiveness of rehabilitation services compared to some acute care therapy/interventions such as endovascular therapy[34, 35, 38, 39]. Among reviewed studies, evidence has been limited to developed countries such as the UK, Canada, and the US, for both economic evaluations and economic models of rehabilitation services. Although, the most frequently used economic evaluation framework was CUA, the data sources mainly relied on RCT studies, using a short-time horizon and a healthcare system/payer perspective.

Almost half of reviewed studies assessed the improvement of rehabilitation services which were mainly conducted in hospital settings e.g., inpatient/outpatient department or rehabilitation ward. The most frequently used health outcomes for rehabilitation service improvements were EQ-5D as generic outcome measure, while BI and mRS scores were the most frequently used disease-specific outcome measures. However, many studies used or assumed the effectiveness of rehabilitation only over the short-term such as 1 - 2 years. A decision tree and Markov model were the main model structures employed to carry out economic modelling. There were only two economic modelling studies conducted in relation to rehabilitation service improvements and both performed well in the quality assessment. While results showed that stroke rehabilitation interventions were likely to be cost-effective from either healthcare system/payer or societal perspective, the heterogeneity was reflected in the characteristics of these studies. This included differences in cost components, health outcome measures and assumptions made. The parameters that cost-effectiveness results were most sensitive to comprised intervention costs, health care service costs, reducing the delivery and uptake of intervention, inpatient rehabilitation length of stay, and utility values.

In considering the above, results suggested that some of the heterogeneity can be controlled by the researcher, such as type and level of functional ability, cost components, health outcome measures and perspectives. However, some of the heterogeneity cannot be controlled when related to modelling choice decided by researchers/modellers, such as assumption made on data input to the model or model structure. These could have an impact on cost-effectiveness results in the economic evaluation. Therefore, further studies should consider relevant intervention options, model structures, methods and data that reflects the practical context for the decision makers' application. This chapter highlights challenges and variation between studies in terms of intervention or comparator components or definition, methodological approaches and uncertainty of data and parameters used in the economic evaluation. As uncertainty in economic models is unavoidable, the methods of assessment of uncertainty were recommended as well as the consideration of data availability in the respective setting. These could help inform researchers to strengthen the reliability and accuracy of further economic evaluations within a country-specific context.

Currently, there is no economic evaluation that assesses the new stroke rehabilitation policy and its long term outcomes; hence, a de novo economic modelling study of the new policy of rehabilitation services is needed in response to inform the Thai decision makers and stakeholders. Allen's economic model[207] was considered to be the most suitable model to adapt to an evaluation of the new Thai rehabilitation policy. The study by Allen et al. also showed a good quality in both checklists and also appeared to be inclusive of all the relevant health states related to stroke rehabilitation in post-stroke patients.

The next chapter will develop the economic model of rehabilitation therapy for Thai stroke patients, followed by a value of implementation analysis of the new rehabilitation policy in order to evaluate the cost-effectiveness of this policy implementation and to inform Thai policy makers in terms of future planning of rehabilitation service delivery and efficiency of health care resource allocation.

Chapter 5 Economic evaluation of rehabilitation services in Thai stroke patients

5.1 Introduction

How to allocate scarce resources while maximising outcomes when introducing a new healthcare policy, especially in resource limited settings, is important for decision-making. Economic evaluation has received increasing attention and is widely accepted by decision makers to inform policy decisions regarding cost-effectiveness of new health technologies. In Thailand, the economic evaluation of new technologies is the preferred method for policy decision making before including it in the benefit package or National List of Essential Medicines (NLEM)[190, 250]. However, the economic evaluation of new technologies does not usually consider implementation. Even if new services or technologies prove to be cost-effective, these might not be implemented perfectly or immediately into clinical practice in the real world.

As mentioned in chapter 1 that stroke rehabilitation interventions contain a set of complex interventions[251, 252], e.g. a multidisciplinary of health care professionals, several service components which are designed to optimise functioning of individuals and improve functional abilities from their illness[47]. It could be more challenging to evaluate complex interventions as these complex interventions are prone to be more variation than a single health technology such as medication or diagnosis instruments[251, 253]. It is also important to consider whether the implementation process is influenced by the complex interventions. For example, the rehabilitation therapy might be deviated from the recommendations in the guidelines and protocols owing to decisions made by health care professionals and/or patients and families. Thus, the implementation decision when planning for implementation such a complex intervention is important. As mentioned, health technologies that showed cost-effective may not automatically or perfectly implement into practices, complement a nonadherence or nature of complex intervention, can lead to inefficiencies in the health service provision and resource allocations. Thus, the value of implementation framework[217, 253, 254] which determines cost-effective health intervention and implementation efforts can help to inform decisions related to the expected efficiency losses, maximum return on investment by way of the expected level of implementation and strategies to promote implementation in health system and have impacts on routine practice[254, 255].

Therefore, the objectives of the evaluation in this chapter included: (1) to determine the cost-effectiveness of adopting the new rehabilitation service policy in post-stroke care in Thailand, (2) to examine the potential value of implementation on implementation of the new rehabilitation service policy for future eligible stroke cohorts.

This chapter is structured into six main topics: (1) background and rationale, (2) current rehabilitation services for patients with stroke, (3) the development of a bespoke rehabilitation economic model for post-stroke care in Thailand, (4) methodology, (5) results, and (6) discussion and conclusion.

5.2 Background and rationale

There is general agreement of benefit of rehabilitation in the literature, for example, improved functional ability[256, 257] or an improvement in being able to carry out activities of daily living[49], and reduced disability[258]. Furthermore, a prospective multi-centre study conducted in Thailand in 2009[256, 259] indicated that intensive inpatient rehabilitation, regardless of the disease being treated, was being more effective and efficient - improvement in terms of average BI scores improvement per one length of stay (LOS) - than a non-intensive rehabilitation program.

Over the past decade, only four economic evaluation studies of rehabilitation services in patients with stroke were undertaken in Thailand. Of these, three studies were carried out before the endorsement of the new rehabilitation policy[54, 61, 249] and only one study[62] was conducted to align with the new rehabilitation guidelines. Srisubut A. et al[62], performed CUA study with a short time horizon of 6 months. The author evaluated the cost-effectiveness of rehabilitation interventions between inpatient-based rehabilitation (N=50) and outpatient-based rehabilitation program (N=30) in community hospital which has been being a lead role model for other hospitals. However, there were some limitations from this study. For example, the outpatient-based rehabilitation program as a comparator may not be generalisable to standard care being implemented. Based on literature review, there has been a limited access and provide rehabilitation services before endorsement the new rehabilitation policy. Most of Thai studies reported a monthly follow up; thus, the intensity, in real practices, was estimated to be lower than this study[54, 61, 249, 260]. Additionally, currently, no research has been done to evaluate the cost-effectiveness of the new rehabilitation policy or long-term health outcomes in Thailand.

Overview of economic evaluation

As mentioned above, economic evaluation can be used as a tool to inform policy makers regarding introducing new healthcare policies. A CUA approach is one of the most common and preferred type of economic evaluation because this approach accounts for both quantity (in terms of life year gains) and quality of life (QOL) - called the 'QALY' as the measure of health outcome. The QALY is a common metric that enables a comparison between several types of health interventions[217, 261] and can be used for most disease areas, allowing for comparisons of interventions across disease areas[190, 250].

In terms of costs in economic evaluations, generally, these are commonly considered based on the perspective the evaluation takes, which helps to identify components of costs[184]. Components of costs can be divided into (1) direct medical costs, including all costs associated with health services; (2) direct non-medical costs, including costs borne by the patient and family as a consequence of the disease (e.g. transportation to health facilities, meals, accommodation and informal care by carer); and (3) indirect costs or productivity costs, including costs associate with loss of the ability to work due to illness, disability and death[217, 262] of patient.

Estimated mean cost and QALYs were used to calculate the Incremental cost-effectiveness ratio (ICER)[190, 261, 263, 264]. The ICER was calculated by using incremental cost per incremental QALYs. The new intervention is considered to be cost-effective on the condition that the ICER per QALY gained is less than the given WTP threshold.

Furthermore, the ICER can be considered in terms of net benefit approach[265] which represents the value of the intervention in a monetary term. Both ICER and net benefit approach share some common requirements as both require a pre-defined WTP threshold and QALYs. The net benefit approach takes into account both net monetary benefit (NMB) and net health benefit (NHB) such as QALY or health value of implementation[254, 255]. If the benefit of new health technology was more than its implementation costs, it represents the benefits gain to the Thai MOPH in terms of money or health, in other words, the new intervention is worthwhile for MOPH to investment in the implementation their new policy given the certain WTP threshold.

Overview of value of implementation

In addition to economic evaluations, another analytic framework using a Bayesian decision-theoretic approach can also help to inform decisions related to the implementation efforts by way of the expected value of implementation[254, 255] and consider whether the additional benefits and costs of a specific implementation strategies of a technology will be worthwhile investing in. Although, a new health technology deemed cost-effective or cost-saving, it might not be possible to achieve perfect implementation or immediate uptake by healthcare professionals to be provided in clinical practice. Limited implementation due to scarce resources is also possible. Also, non-adherence by either patients or healthcare professionals could impact on efficiency if implementation is below the initially expected level.

An example of the application of the value of implementation framework for decision-making is presented by Hoomans et al (2009)[253] who identified mitoxantrone plus prednisone/prednisolone versus docetaxel plus prednisone/prednisolone (three weekly) as the optimal treatment for metastatic hormone-refractory prostate cancer patients in the UK. The study results indicate that at a WTP of £30,000 per QALY, the perfect implementation rate suggested that it was worthwhile investing in strategies that implement the optimal treatments regimens. This is also exemplified in the work undertaken by

Faria et al[266] who evaluate the value of implementation activities in increasing the utilisation of novel oral anticoagulants (NOACs) for stroke prevention in the National Health Service (NHS) in England and Wales. The results demonstrated that there was value in additional implementation efforts to improve utilisation of NOACs to the NHS at a WTP threshold of £20,000 per QALY gained. In addition, an additional investment of £3.66 million in an educational activity that increases utilisation by 5% generated additional 71 QALYs or £1.42 million in terms of monetary equivalent compared with the use of these resources on other NHS activities[266].

Hence, the value of implementation approach can help inform policy decisions of how to invest in implementation technologies/initiatives given the limited of resource allocation, such as funds that could be shared with other health-generating interventions. In the case of stroke rehabilitation therapy, as can be seen in the previous chapter (Chapter 4), rehabilitation services were deemed to be cost-saving or cost-effective worldwide including in the Thai setting. Nevertheless, the practices and new rehabilitation policy still have variable service delivery and service uptake in a Thai contexts. For example, differences in supportive policies and rehabilitation fund, health care professionals and facilities adequacy, and appropriate payment systems from payers due to receiving low reimbursement rate[65, 267, 268].

In contrast, cost-effective health technologies can benefit to health service delivery and patients if these technologies are used routinely in clinical practices. Thus, the effective implementation strategies are required and the value of implementation can help examining to what extent the new health technology implementation provides value for money.

5.3 Current rehabilitation services for patients with stroke

Findings from the survey chapter (Chapter 2) indicated that the proportion of inpatient rehabilitation was highest in advanced-level hospitals and lowest in mid-level hospitals. In addition, the proportion of hospitals being able to provide IMC services was also lowest in mid-level hospitals. Although, majority of hospitals reported that they are able to provide these facilities, findings from Chapter 3 showed a low percentage of stroke patients receiving rehabilitation together with a low frequency of hospital attendances following their stroke. The availability of these facilities would seem to conflict with what is being offered to patients. The findings from Chapter 3 which contained data between 2015-2020, supported that the endorsement of the IMC guidelines for stroke patients[51] in 2019, aiming to increase accessibility to the rehabilitation provision, is necessary as the rehabilitation utilisation remains low.

5.4 Methodology

This section outlines methods employed for the economic evaluation of a rehabilitation intervention for patients with stroke to estimate cost-effectiveness. The CUA approach was conducted from a provider and societal perspectives over a lifetime horizons. Incremental cost-effectiveness ratios (ICERs) were estimated and the Thai WTP threshold of 160,000 Baht per QALY gained was applied.

A decision tree and Markov model from the economic evaluation study by Allen et al[207] is adapted to reflect a Thai context. Economic model by Allen et al. contained health states and provided parameters in relation to the degree of disability and also followed up for the long-term care. The economic model also appeared to be inclusive of all the relevant health states related to stroke rehabilitation in post-stroke patients which are similar to the recommendation from the new Thai rehabilitation guidelines. Some of transitional probabilities from Allen et al were also incorporated into the Markov model in this thesis.

Addition to the economic evaluation, the expected value of perfect implementation and the expected value of actual implementation approaches are presented to establish the value of implementation, to the Thai MOPH, of a new rehabilitation service for stroke patients. A five-year time horizon was evaluated to reflect a five-year programme of investment in health policy which is related to the service plan strategy. All analyses were conducted using Microsoft Excel.

5.4.1 Study population

In the base-case analysis, the incident patients with stroke, which was diagnosed at the hospital, were assumed to enter the model at 65 years of age. This assumption was based on the mean age of patients with stroke derived from the findings in Chapter 3.

5.4.2 Type of study

The CUA study was employed in this thesis as this approach accounts for both quantity (in terms of life year gains) and quality of life (QOL) - called the 'QALY' as the measure of health outcome which is a common metric allowing for comparisons between several types of health interventions.

5.4.3 Study intervention and comparators

Based on the new rehabilitation guidelines, home programmes should be suggested for patients who had a BI score of >15 without multiple impairment. For a BI score of <15 or a BI score of >15 with multiple impairment, physicians should consider either inpatient or outpatient rehabilitation or out-reach rehabilitation programmes. These are either followed up for 6 months, or until they reach a BI score of 20 and were classified as intervention group. In this study, the inpatient-based rehabilitation was selected as base case because the IMC guidelines focus on this patient group and set the targeted outcome indicators as a national KPIs.

The comparator group were patients who received usual care or conventional care. In this study, usual care or conventional care is defined as patients who needed rehabilitation therapy but did not receive this service or did not receive rehabilitation therapy following the new rehabilitation guidelines.

5.4.4Model structure and study design

This thesis used a decision tree to reflect a short-term outcomes of rehabilitation therapy, followed by a Markov model to estimate the long-term cost-effectiveness of the rehabilitation services intervention.

Model structure

The decision tree (Figure 5-1, Left side), representing the rehabilitation intervention and usual care in post-acute stroke patients, was constructed to reflect on the functional ability levels of rehabilitation services in the first 6 months since stroke and short-term costs.

Overall, at the beginning of the post-acute stroke phase, patients who received the rehabilitation intervention would enter the decision tree and it was determined that they would get inpatient-based rehabilitation for 14 days. Then, an assessment of their functional ability would take place at 6 months. While those who received usual care or conventional care would enter to the no rehabilitation intervention in the decision tree. The proportion of stroke patients who have a certain BI score at 6 months is used to determine the respective health state in the Markov model that is being entered following the decision tree.

In terms of Markov model (Figure 5-1 - right side) reflecting the long-term health outcomes following strokethe BI score at 6 months was used to determine which health state patients would enter. The Markov model contains four health states depending on the functional ability of stroke. Based on Thai rehabilitation guidelines[51], a BI of 20 stands for ‘non to mild’ disability, a BI of 11 to 19 stands for ‘moderate to severe’ disability, a BI of 0 to 10 stands for ‘LTC’ health state. Death is an absorbing state. All four health states of the model are represented by circles, transitions between health states are represented by arrows.

After the stroke cohort was partitioned based on functional ability levels, they enter the Markov model based on these. Patients may maintain their disability level, transition to higher disability levels or die at any time. The proportion transitioning to the next health state would depend on the current health state. Existing evidence shows functional ability could either decline or remain stable for up to two years[260]. Therefore, it was assumed that individuals in the rehabilitation arm would not transition from ‘non to mild’ to ‘moderate to severe’ in cycle 1 or would remain in the ‘non to mild’ state until the end of the first year after entering the Markov model. After this, the transition probability from ‘non to mild’ to ‘moderate to severe’ was applied following the second cycle and extrapolated to the end of the model. For example, patients with a BI score of 20 were classified as ‘non to mild’ when entering the model (cycle 0). Patients would remain in this state for year 1, after which they may experience a decline in functional ability and move to the ‘moderate to severe’ state or the ‘LTC’ state or die in year 2 or at any time thereafter. Then, costs were summarised from cost incurred for each stroke cohort multiplied by the time spent on the certain health state. Similarly, the QALY were summarised from life year gained multiply by utility in a particular health state. Finally, the total costs, and total QALYs, over lifetime horizon were evaluated by summation across all health states.

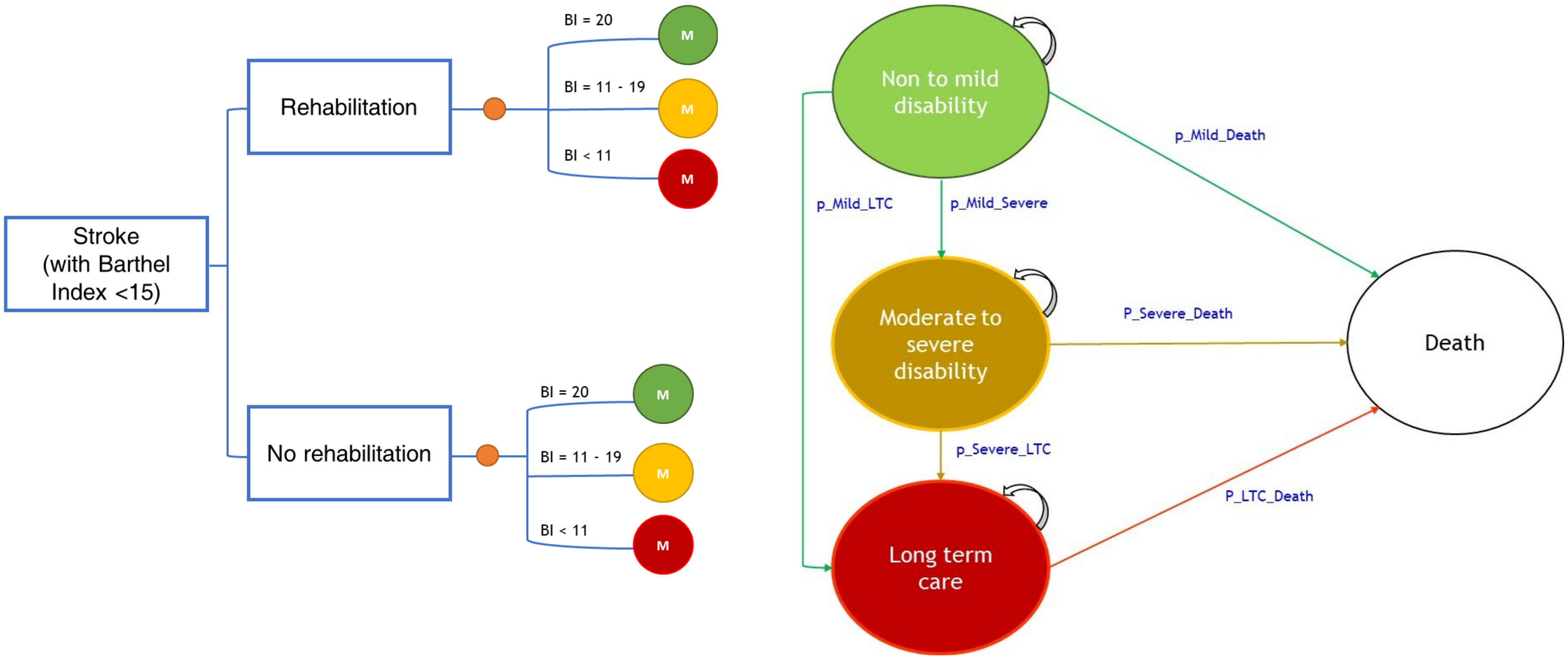

Figure 5-1 Decision tree and Markov model of the new rehabilitation services intervention

Time horizon and cycle length

The cycle length in the Markov model was one year. Costs and outcomes were extrapolated to 35 years or until patients in the cohort reached the age of 100 years[269].

Discount rate

A discount rate of 3% per annum was employed for both costs and outcomes as suggested by the Thai HTA guidelines[190, 270]. The following equation was used for generating discounted values:

discounted value = original value/(1+R)^{n} **Equation (13)**

where:

R = the discount rate used

n = the number of years

Perspective

A provider perspective and societal perspective were employed in this economic evaluation. The provider perspective incorporated all costs and outcomes related to health care interventions. However, the societal perspective included all costs and benefits regardless of who incurs the costs and benefits which means this perspective is the most comprehensive viewpoint the economic evaluation study[217, 271]. These were conducted based on the recommendation in the Thai HTA guidelines[184, 190].

Cost measurements

Resource use and costs were obtained from various sources including the national stroke administrative data that was analysed in Chapter 3. Costs were taken into account according to perspective. For a provider perspective, direct medical costs (e.g. intervention costs, treatment costs, out-of-pocket expenses related to stroke) were included. For a societal perspective, direct non-medical costs (e.g. transportation, accommodation and meals for patient and carers) and informal care costs due to loss of productivity of carers, were added to the former component. As recommended by Thai HTA guidelines[184, 190], a price conversion or inflation rate adjustment[272] using the consumer price index, was performed to inflate to the year of analysis (Appendix 24).

The parameters used in the model presented in Table 4-2. A gamma distribution was used for cost parameters. All costs were reported in 2021 Thai baht. In addition, the measurement and valuation of costs are presented below.

(1) Intervention costs

The intervention costs for the 6-month rehabilitation programmes were adopted from Srisubut et al. who included costs related to rehabilitation therapy but excluded costs of stroke treatment during the acute phase of care. These costs were collected using activity-based costing methods in year 2019. In this thesis, costs from Srisubut et al.[62] were applied as a one-off cost in patients who received rehabilitation therapy before entering the (cycle 0) Markov model and were assumed to be similar, irrespective of the disability level.

(2) Usual care costs

The Thai national stroke administrative data analysed in Chapter 3 was used to analyse costs of patients who did not receive rehabilitation. Length of stay (LOS) values obtained from a local study in patients with stroke in 2012[131], were used to classify patients by their functional ability levels. LOS of 1-2 days was used to represent the ‘non to mild’ functional ability group, LOS of 3-7 days was used to represent the ‘moderate to severe’ functional ability group and LOS of 8 days or more was used to represent patients in the ‘LTC’ functional ability group. After classification, direct medical costs comprising treatment cost and costs paid out-of-pocket by patients were estimated. These costs were estimated and counted until 6 months but excluded cost related to the incident stroke admission.

For any subsequent admissions, mean LOS per admission, frequency of inpatient admission and outpatient attendance were also extracted for the estimation of direct non-medical costs. Transportation costs and food costs were derived from the standard cost list for HTAs in Thailand[183] and applied for both patients and carers. The total direct non-medical costs were the summation of Equation (14) and Equation (15).

Regarding informal care costs, cost of productivity loss of carers was derived from the national income of Thailand 2020 which reported gross national income (GNI) per capita per year (Appendix 30)[273]. This was adjusted using the CPI to reflect 2021 prices. This value was then divided by 52 to get a cost of productivity loss per week. A six day week was further assumed to generate a daily cost of productivity[184], equalling 708.82 Thai baht per day. Calculation of costs is shown in Equation (16).

The analysis did not take account of productivity costs of patients because patients were above retirement age (>60 years), and also to avoid double counting as described above.

direct non-medical costs for patient **Equation (14)**
= (unit cost of transportation x frequency of inpatient admission per year) +
(unit cost of transportation x frequency of outpatient attendance per year)

direct non-medical costs for carer **Equation (15)**
= (food cost x number of meals per day x frequency of inpatient admission per year x LOS per admission) +
(food cost x number of meals per day x frequency of outpatient attendance per year)

informal care cost of carer **Equation (16)**
= (GNI per day x number of carer x frequency of outpatient attendance per year) +
(GNI per day x number of carer x frequency of inpatient admission per year x LOS per admission)

GNI: gross national income

(3) Health-state costs

Costs associated with each health state are those of health services used after discharge from 6-month rehabilitation therapy. The Thai national stroke administrative data (Chapter 3) were used to estimate annual costs of outpatient attendance or cost per inpatient admission per patient for each functional ability group. The yearly costs were assumed to be equal every year starting from cycle 1 until the end of the Markov model. The same methods described above for direct non-medical costs, including informal care costs, were used to generate costs of each health state in the Markov model.

Outcome measures

Thai HTA guidelines recommend using EQ-5D for measurement and valuation of HRQoL[250, 274]. This study used utilities from Srisubut et al[62] which collected HRQoL using EQ-5D-5L in stroke patients at month 6th and differentiated utilities after rehabilitation therapy based on disability level as recommended by the new rehabilitation guidelines; thus, this thesis assigned these utilities to each health state. Next, the utilities were multiplied with life expectancy (years of life remaining for a patient following a particular intervention) in a given health state to generate QALYs for the stroke cohort.

Analytical method

Equation (17) shows the formula of ICER. The new intervention is considered to be cost-effective on the condition that the ICER per QALY gained is less than a WTP threshold (λ). In Thailand, a WTP threshold of 160,000 Baht was used as recommended by Thai HTA guidelines[190].

Incremental cost effectiveness ratio (ICER)

$$= \frac{\text{Incremental cost } (\Delta\text{Costs})}{\text{Incremental QALY } (\Delta\text{QALY})} \qquad \textbf{Equation (17)}$$

$$= \frac{\text{incremental cost between new intervention and comparator}}{\text{incremental outcome between new intervention and comparator}}$$

5.4.5 Model transition probabilities

A summary of the model parameters used in the base-case analysis is provided in Table 4-2. Due to limited evidence on the new rehabilitation policy in Thailand, the proportion of stroke survivors entering the model at different health states was estimated from Srisubut et al[62]. Proportions represented the number of patients entering each health state in the Markov model after receiving rehabilitation at 6 months. Transition probabilities between health states were assumed to follow a Dirichlet distribution which is a multivariate generalisation of the beta distribution (conditional beta distribution). The Dirichlet distribution represents polytomous transitions thus representing transition probabilities from a given state to all of the other model states (more than 2 options)[275].

The first-year outcomes of the conventional inpatient rehabilitation programme in six university hospitals and three rehabilitation centres were taken from Kuptniratsaikul V. et al.[276]. The changes of the BI scores between discharging from hospital and at month 12 was used as a transitional probability for health states in the Markov model.

The transition probabilities between health states were derived from Kuptniratsaikul et al[276] and Allen et al[207]. A Beta distribution (α,β), where α is the number of successes, β is the number of failures, was applied to these binomial outcome parameters which express values between zero and one. Yearly probabilities were obtained by converting probabilities from a 6-month cycle into a rate using Equation (18) and then transforming back to a one-year cycle probability using Equation (19).

per-cycle rate **Equation (18)**
$= -\ln(S(t))/ t$

where:
$S(t)$ = the 6 month cumulative probability
t = time

per cycle (12 months) probability **Equation (19)**
$= 1-\exp^{(-rt)}$

where:
r = the per-cycle rate
t = time

In addition, it is assumed that the effect of rehabilitation therapy could be maintained for up to one year after ending rehabilitation therapy[260]. In this regard, there was no rehabilitation treatment effect from cycle 2 until the end of the model. In terms of mortality, all transition probabilities of each health state to death as a result of stroke were derived from Allen et al[207] due to a lack of Thai local data related to functional disability levels. Furthermore, annual mortality rates in the general Thai population were added to each health state in the model. These annual mortality rates were compared to the general Thai population and this data were derived from age- and sex-specific mortality rates from the WHO Life tables for Thailand[269]. Additionally, utilities as obtained from Srisubut et al[62] were assumed to differ by health state but not by intervention or comparator group (Appendix 31).

Table 5-1 Parameters and source of parameter used in economic model

Parameter	Point estimate	SE	Probability distribution	alpha	beta	Reference
Proportion of patients who received rehabilitation under the intermediate care (IMC) programme						
Proportion of patient who entered to 'non or mild' health state	0.240	0.060	Dirichlet	12	38	[62]
Proportion of patient who entered to 'moderate or severe' health state	0.600	0.069	Dirichlet	30	20	[62]
Proportion of patient who entered to 'long-term care (LTC)' health state	0.160	0.051	Dirichlet	8	42	[62]
Proportion of patients who received usual Care						
Proportion of patient who entered to 'non or mild' health state	0.233	0.076	Dirichlet	7	23	[62]
Proportion of patient who entered to 'moderate or severe' health state	0.600	0.088	Dirichlet	18	12	[62]
Proportion of patient who entered to 'LTC' health state	0.167	0.067	Dirichlet	5	25	[62]
Transitional probability						
'Non to mild' health state to 'Moderate to severe' health state	0.286	0.160	Beta	2	5	[276]
'Non to mild' health state to LTC health state	0.017	0.008	Beta	4.50	267.51	[207]
'Non to mild' health state to Death	0.049	0.016	Beta	8.53	166.47	[207]
'Moderate to severe' health state to LTC health state	0.072	0.021	Beta	11	141	[276]
'Moderate to severe' health state to Death	0.099	0.026	Beta	13.47	122.53	[207]
LTC health state to Death	0.220	0.002	Beta	11,839.29	41,899.71	[207]
Costs						
1. Cost of rehabilitation programme (one-time off)						
1.1 Direct medical costs	18,300.20	-	assumed to be fixed	-	-	[62]
2.2 Direct non-medical and informal care cost	59,127.19	-	assumed to be fixed	-	-	[62]
2. Cost of usual care group from post-acute phase to 6 months (one-time off)						
2.1 Direct medical costs						
- 'Non to mild' health state (OP: treatment)	1,535.44	8.79	Gamma	30,482.51	0.05	stroke data*
- 'Non to mild' health state (IP: treatment)	36,637.93	502.63	Gamma	5,313.32	6.90	stroke data*

Parameter	Point estimate	SE	Probability distribution	alpha	beta	Reference
- 'Non to mild' health state (OP: out-of-pocket)	19.68	3.35	Gamma	34.52	0.57	stroke data*
- 'Non to mild' health state (IP: out-of-pocket)	550.06	44.84	Gamma	150.47	3.66	stroke data*
- 'Moderate to severe' health state (OP: treatment)	1,414.04	4.27	Gamma	109,687.14	0.01	stroke data*
- 'Moderate to severe' health state (IP: treatment)	31,548.87	211.33	Gamma	22,287.09	1.42	stroke data*
- 'Moderate to severe' health state (OP: out-of-pocket)	23.14	2.47	Gamma	87.74	0.26	stroke data*
- 'Moderate to severe' health state (IP: out-of-pocket)	398.53	15.31	Gamma	677.32	0.59	stroke data*
- LTC health state (OP: treatment)	1,450.85	5.12	Gamma	80,325.70	0.02	stroke data*
- LTC health state (IP: treatment)	44,926.07	376.29	Gamma	14,254.41	3.15	stroke data*
- LTC health state (OP: out-of-pocket)	26.02	3.03	Gamma	73.60	0.35	stroke data*
- LTC health state (IP: out-of-pocket)	527.03	24.63	Gamma	457.79	1.15	stroke data*
2.2 Direct non-medical costs						
Travel cost (single trip)	98.12	4.83	Gamma	412.49	0.24	[183]
Food cost	33.85	2.45	Gamma	190.27	0.18	[183]
Number of meal per day	3.00	-	Normal	-	-	assumption
Income per capita per day	708.82	-	Normal	-	-	[273]
number of caregivers	1.00	-	Normal	-	-	assumption
'Non to mild' health state (OP attendance)	2.95	0.05	Gamma	3,198.50	0.001	stroke data*
'Non to mild' health state (IP admissions)	1.85	0.01	Gamma	19,532.61	0.000	stroke data*
'Non to mild' health state (LOS day per 1 admission)	6.15	0.06	Gamma	11,088.71	0.001	stroke data*
'Moderate to severe' health state (OP attendance)	2.32	0.02	Gamma	12,307.97	0.0002	stroke data*
'Moderate to severe' health state (IP admissions)	1.83	0.01	Gamma	84,668.64	0.00002	stroke data*
'Moderate to severe' health state (LOS day per 1 admission)	6.15	0.03	Gamma	47,866.64	0.0001	stroke data*
LTC health state (OP attendance)	2.61	0.03	Gamma	7,493.35	0.0003	stroke data*
LTC health state (IP admissions)	1.90	0.01	Gamma	58,832.70	0.00003	stroke data*
LTC health state (LOS day per 1 admission)	8.67	0.05	Gamma	29,379.29	0.0003	stroke data*
- 'Non to mild' health state (direct non-medical and informal care cost)	12,552.72	-	-	-	-	Calculation**

Parameter	Point estimate	SE	Probability distribution	alpha	beta	Reference
- 'Moderate to severe' health state (direct non-medical and informal care cost)	11,814.94	-	-	-	-	Calculation**
- LTC health state (direct non-medical and informal care cost)	16,349.58	-	-	-	-	Calculation**
3. Cost of each health state (cycle 1 -35)						
3.1 Direct cost						
- 'Non to mild' health state (OP: treatment)	1,471.08	9.89	Gamma	22,118.57	0.07	stroke data*
- 'Non to mild' health state (IP: treatment)	27,595.86	492.67	Gamma	3,137.40	8.80	stroke data*
- 'Non to mild' health state (OP: out-of-pocket)	20.86	2.79	Gamma	55.70	0.37	stroke data*
- 'Non to mild' health state (IP: out-of-pocket)	313.92	22.67	Gamma	191.68	1.64	stroke data*
- 'Moderate to severe' health state (OP: treatment)	1,355.50	4.52	Gamma	89,825.32	0.02	stroke data*
- 'Moderate to severe' health state (IP: treatment)	28,753.90	232.19	Gamma	15,335.59	1.87	stroke data*
- 'Moderate to severe' health state (OP: out-of-pocket)	20.29	1.43	Gamma	201.62	0.10	stroke data*
- 'Moderate to severe' health state (IP: out-of-pocket)	349.24	14.58	Gamma	573.83	0.61	stroke data*
- LTC health state (OP: treatment)	1,528.45	7.47	Gamma	41,900.48	0.04	stroke data*
- LTC health state (IP: treatment)	36,378.53	480.59	Gamma	5,729.84	6.35	stroke data*
- LTC health state (OP: out-of-pocket)	17.81	1.88	Gamma	89.92	0.20	stroke data*
- LTC health state (IP: out-of-pocket)	443.16	28.09	Gamma	248.91	1.78	stroke data*
3.2 Direct non-medical costs						
'Non to mild' health state (OP attendance)	3.47	0.07	Gamma	2,419.29	0.0014	stroke data*
'Non to mild' health state (IP admissions)	2.04	0.02	Gamma	6,999.33	0.0003	stroke data*
'Non to mild' health state (LOS day per 1 admission)	5.47	0.06	Gamma	8,627.71	0.0006	stroke data*
'Moderate to severe' health state (OP attendance)	2.82	0.03	Gamma	11,911.92	0.0002	stroke data*
'Moderate to severe' health state (IP admissions)	2.00	0.01	Gamma	43,269.58	0.00005	stroke data*
'Moderate to severe' health state (LOS day per 1 admission)	5.76	0.03	Gamma	39,455.22	0.0001	stroke data*
LTC health state (OP attendance)	3.32	0.05	Gamma	3,731.72	0.0009	stroke data*
LTC health state (IP admissions)	2.06	0.01	Gamma	20,674.30	0.0001	stroke data*
LTC health state (LOS day per 1 admission)	7.40	0.07	Gamma	12,607.16	0.0006	stroke data*

Parameter	Point estimate	SE	Probability distribution	alpha	beta	Reference
- 'Non to mild' health state (direct non-medical and informal care cost)	12,936.22	-	-	-	-	Calculation**
- 'Moderate to severe' health state (direct non-medical and informal care cost)	12,566.78	-	-	-	-	Calculation**
- LTC health state (direct non-medical and informal care cost)	16,099.72	-	-	-	-	Calculation**
Health Utilities						
Utility of 'Non to mild' health state	0.81	0.084	Beta	16.93	4.10	[62]
Utility of 'Moderate to severe' health state	0.58	0.072	Beta	26.87	19.86	[62]
Utility of LTC health state	0.41	0.178	Beta	2.71	3.90	[62]
Others						
Discounting rate for costs per year	0.03	-	-	-	-	[190]
Discounting rate for outcomes per year	0.03	-	-	-	-	[190]

*Data from national stroke administration data in Chapter 3; **From cost measurements section

5.4.6 Model assumptions

This study simulates patient experience after the 6 months rehabilitation period. Stroke survivors were assumed to remain alive until entering the Markov model. Certain assumptions from Allen et al[207] were modified to reflect the new Thai rehabilitation guidelines such as using BI scores to assess functional ability at 6 months instead of mRS scales. The risk of death, costs and utilities were estimated over the remaining years conditional on the health state.

In terms of effectiveness of the new policy, as there was a limited data on inpatient-based rehabilitation services in Thailand, some parameters were derived from Allen's model[207] which conducted the home rehabilitation intervention. Although these parameters might not specifically to the effectiveness of inpatients rehabilitation, it could be used because the effectiveness of home-based rehabilitation could be non-inferior to the inpatient-based rehabilitation relating to the functional recovery for activities of daily living and HRQoL[210, 258, 277]. The rehabilitation therapy effect was assumed to be maintained for one year after the rehabilitation programme finished. Therefore, the treatment effect of rehabilitation was applied to cycles 0 and 1 only. This means that patients who received rehabilitation would remain in the same health state for one year (cycle 1) and then potentially transition to other health states from year 2 onwards. Because there was no treatment effect beyond 6 months, probabilities of transitioning between health states beyond 6 months are assumed to be equivalent between intervention and comparator group. Moreover, as this model did not include any other interventions apart from rehabilitation therapy, patients in a more severe health state were assumed to be unable to move to a better health state. For instance, patients, who were in the 'moderate to severe' health state after rehabilitation were unable to move to the 'non to mild' state.

In terms of cost measurements, costs related to rehabilitation during six months was retrieved from Srisubut et al[62] which conducted in the community hospitals that has been being a lead role model for other hospitals. Thus, this cost was assumed to reflect the comprehensive cost components for the new rehabilitation intervention. With respect to costs of each health state, due to a limitation on costs according to severity, this thesis used LOS to assume costs of each health state based on a domestic study[131] and the average LOS from stroke national administrative data (Chapter 3). Furthermore, this study assumed there was only one carer per patient and a full day of support was assumed. This was counted as one-working day to calculate informal care costs, based on IMC guidelines suggesting that patients should have at least one carer providing 24-hour care. Other assumptions included that both patient and carer travelled to hospital together based on one round trip per admission. Additional food costs of three meals per day were only considered for the carer, with no additional costs of accommodation during hospitalisation.

5.4.7 Sensitivity analyses

Sensitivity analyses were carried out to examine the uncertainty of specific parameters and their impact on cost-effectiveness results. Typically, one-way sensitivity analysis (OWSA), considering both health care provider and societal perspectives, is used and parameters were varied by using upper and lower values of 95% confidence intervals (95%CI)[265].

Probabilistic sensitivity analysis (PSA) was conducted to assess the uncertainty surrounding the input parameters which was derived randomly from each distribution specific to the characteristics of parameters. Monte Carlo simulation with 1,000 iterations was employed to generate a range of plausible lifetime costs, health outcomes (both LYs and QALYs), and ICERs.

A cost-effectiveness plane was generated to demonstrate the difference in effectiveness (increment between intervention and usual care) per patient (horizontal axis) and the difference in cost per patient (vertical axis). Further, a cost-effectiveness acceptability curve (CEAC) was generated to illustrate the likelihood of the intervention being cost-effective at certain WTP thresholds.

5.4.8 Scenario analysis

This study conducted threshold analysis to explore variations in the results that could occur as a result of changing assumptions in the base-case analysis. Two alternative scenarios were used to explore variations in key assumptions.

First scenario

Due to a lack of the rehabilitation effectiveness difference both between intervention and usual care groups and between health states, it is expected that patients with ‘moderate to severe’ functional ability benefited more than those with ‘non to mild’ functional ability[259]. Also, it has been believed that patients with a higher BI score at admission (less severe) had less change in BI score between admission and discharge due to a ceiling effect[277, 278], while patients in the LTC health state are less likely to be able to improve their BI score until being able to change their health states. Thus, it was assumed that benefits of intensive inpatient rehabilitation would improve health outcomes and would enable patients to transition from the ‘moderate to severe’ health state to ‘non to mild’ health state.

Second scenario

It has been reported that inpatient rehabilitation could not only incur higher service costs than in other settings (outpatient or home health care), but also incur higher costs for patients. Because Srisubut et al[62] included costs of staff training and costs of health information system management for rehabilitation programme, which related directly to health care cost, in part of direct non-medical costs instead where a breakdown cost was not provided. Thus, it cannot be able to separate costs of staff training and health information system management from direct non-medical cost of rehabilitation programme. Therefore, this scenario aimed to test the assumption that the direct non-medical cost of rehabilitation programme was varied at least 20% (e.g. from to 47,302 to 59,127 Baht).

5.4.9 Analytical framework of the value of implementation analysis

The value of implementation can be measured as either net monetary benefit (NMB) or net health benefit (NHB). These denote the additional value, in terms of money or health, to the government of a therapy associated with the new health technology[255]. A calculation of NMB is presented in Equation (20) and NHB is presented in Equation (21).

$$\text{If ICER} = \frac{\Delta \text{Costs}}{\Delta \text{QALY}} \leq \lambda$$

The net gain to the government in terms of money
Net monetary benefit (NMB) =
(ΔQALY x λ) - ΔCosts **Equation (20)**

$$\text{NMB} = (\Delta \text{QALY} \times \lambda) - \Delta \text{Costs}$$

The net gain to the government in terms of health
Net health benefit (NHB) =

$$\text{NHB} = \Delta \text{QALY} - \frac{\Delta \text{Costs}}{\lambda}$$

Equation (21)

where:
λ = Willingness To Pay threshold

The value of implementation can be estimated from two approaches. The first one is '***the expected value of <u>perfect</u> implementation***' and the second one is '***the expected value of <u>actual</u> implementation***'.

The expected value of perfect implementation, representing the maximum that can be gained from achieving implementation of the new health technology, can be estimated from the difference between '*the expected value of a decision that is implemented perfectly (100% implementation)*' and '*that with implementation at its current value of implementation'*. The current value of implementation means the current utilisation rate that patients who are already receiving the new health technology without implementation of new health technology.

In some circumstances, the implementation of new health technology might not achieve perfect implementation. It is vital to value the actual increase in implementation rate that can be attributed to the implementation rate. In this case, the expected value of actual implementation, representing value gains to the government as a result of the increase in utilisation rate of the new health technology by the implementation, can be estimated. It can be calculated from the difference between '*the total value of patients receiving the technology following the implementation*' and '*the current value of patients receiving the technology without the new health technology initiative*'.

Finally, the value of the implementation of the new health technology is calculated as the difference in the expected value of perfect implementation (or expected value of actual implementation) and the cost of the implementation activity (Figure 5-2).

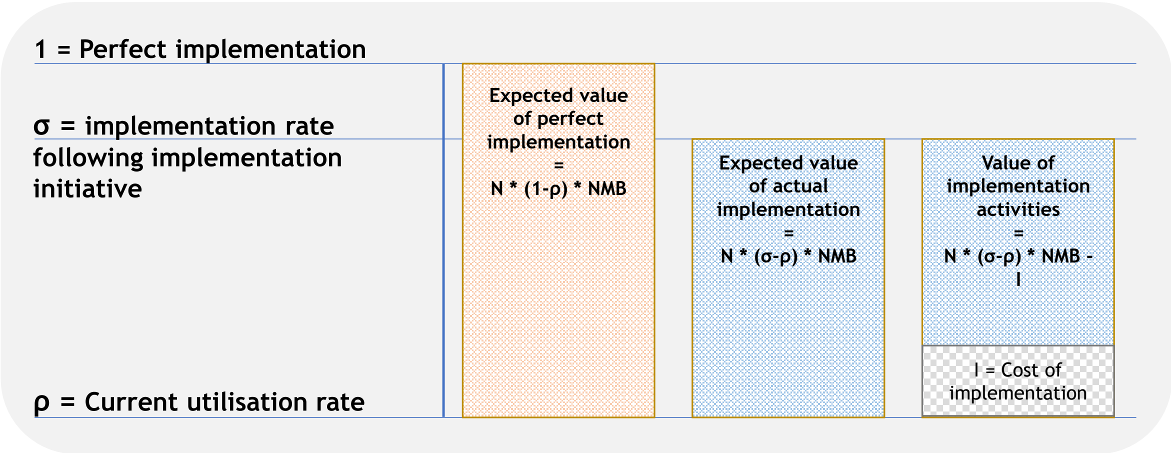

Figure 5-2 Components of value of implementation of new health technology initiative (Adapted from Whyte S et al.[279])
N = total patient population eligible for new health technology, σ = implementation rate following new health technology initiative (ranging from $0 \le \sigma \le 1$), ρ = current implementation/utilisation rate of patients already receiving new technology initiative (ranging from $0 \le \rho \le 1$), NMB: net monetary benefit, I = costs of implementation initiative

The potential of implementation of the new rehabilitation policy in this thesis can be measured by estimating the number of eligible patients per year (N) and the current implementation rate (ρ) based on the national stroke data analysed in Chapter 3. The implementation rate following implementation of new rehabilitation policy (σ) was at perfect implementation (100%). While the net benefit value can be derived from the rehabilitation economic model for one person for a given WTP threshold. Therefore, the remaining information for measurement of the value of implementation of new rehabilitation policy was costs of implementation of new rehabilitation policy (I) itself.

Costs of implementation of new rehabilitation policy (I) were calculated based on recommendations from the new rehabilitation guidelines (IMC guidelines 2019) which suggest that the levels of improvement in activities of daily living differ by type of hospital[51]. The national KPIs for IMC focus on mid-level and first-level referral hospitals and their improvement of IMC beds or IMC wards (Table 5-2).

Table 5-2 Characteristics of IMC bed and IMC ward

recommendation from IMC guideline	IMC bed (Less intensive programme)	IMC ward (Intensive programme)
Number of rehabilitation bed	at least two beds per hospital	at least six beds per hospital
Health workforce	1. General practice (GP) or family medicine (FM) 2. Nurses (5-day training nurse) 3. Physiotherapist	1. GP or FM or rehabilitation doctor 2. Nurses (4-month training nurse) 3. Physiotherapist 4. Occupational therapists (if any)
National key performance indicators fiscal year 2021[43]	Percentage of middle- and first-level referral hospitals providing IMC bed or IMC ward Goal: 80%	Percentage of provinces being able to provide IMC bed at least 1 hospital per province Goal: 40%

This study evaluated a five-year programme of investment in health policy as the period of time should be related to the service plan strategy. Costs of implementing new rehabilitation policy were calculated based on health workforce only, assuming that these hospitals have not bought any new equipment, but would just re-allocate their equipment to facilitate implementation. Thus, only additional training requirements for doctors, nurses, physiotherapist and occupational therapists were included as per recommendation in the new rehabilitation guidelines and MOPH inspection report[43, 51] (Appendix 33).

5.5 Results

5.5.1 Base case analysis

The incorporation of the intensive inpatient-based rehabilitation programme into the current practice including follow-up until 6 months compared to usual care was cost-saving for a provider perspective (Table 5-3), as it led to a reduction in per patient cost but an increase in QALYs over a lifetime horizon. The average lifetime cost was 127,798 Baht for the new rehabilitation therapy and 144,352 Baht for the current rehabilitation therapy. From both perspectives, QALY gains were 2.537 and 2.412 for the new rehabilitation therapy and current rehabilitation therapy, respectively. Thus, the intensive inpatient-based rehabilitation programme was determined to be dominant (more effective and less costly). However, from a societal perspective, the incremental cost was 30,769 Baht, with an ICER of 246,207 Baht per QALY gained which was not cost-effective at a WTP threshold of 160,000 Baht

Table 5-3 Results for the cost-utility analysis

	Usual care	IMC	Incremental
Base case analysis			
a) Provider perspective			
Total cost (Baht)	144,352	127,798	-16,554
Life years	4.267	4.405	0.108
QALYs	2.412	2.537	0.125
ICER (Baht/QALY gained)			**cost-saving**
NMB			**36,549**
b) Societal perspective			
Total cost (Baht)	201,899	232,668	30,769
Life years	4.267	4.405	0.108
QALYs	2.412	2.537	0.125
ICER (Baht/QALY gained)			**246,207**
NMB			**-10,774**
Probabilistic sensitivity analysis			
a) Provider perspective			
Cost (THB)	145,222	128,747	-16,474
Life years	4.34	4.44	0.106
QALYs	2.46	2.59	0.123
ICER (THB/QALY gained)			**cost-saving**
NMB			**36,080**
b) Societal perspective			
Cost (THB)	202,961	233,556	30,594
Life years	4.33	4.43	0.101
QALYs	2.45	2.56	0.114
ICER (THB/QALY gained)			**269,139**
NMB			**-12,406**

WTP = 160,000 THB (3,721 GBP), Exchange rate: 43THB = 1 GBP at 2022

5.5.2 Sensitivity analysis

Probabilistic sensitivity analysis (PSA)

PSA for both provider and societal perspective showed similar results as shown in the base-case analysis (Table 5-3).

The cost-effectiveness plane shows results from PSA with 1,000 iterations, recording the difference in cost and effectiveness. Figure 5-3 presents the cost-effectiveness plane from a provider and Figure 5-4 from a societal perspective. For both analyses uncertainty is driven by QALYs.

Cost-effectiveness acceptability curves (CEAC) from provider and societal perspective are presented in Figure 5-5 and Figure 5-6, respectively. From a provider perspective, at the Thai WTP threshold (160,000 Baht/QALY), the probability of the new rehabilitation programme being cost-effective, compared to usual care, was around 95%. In contrast, from a societal perspective, at the Thai WTP threshold, the new rehabilitation programme was not cost-effective with the probability of being cost-effective being under 30%. When increasing the WTP threshold to over 300,000 Baht per QALY gained, the new rehabilitation programme would start being cost-effective.

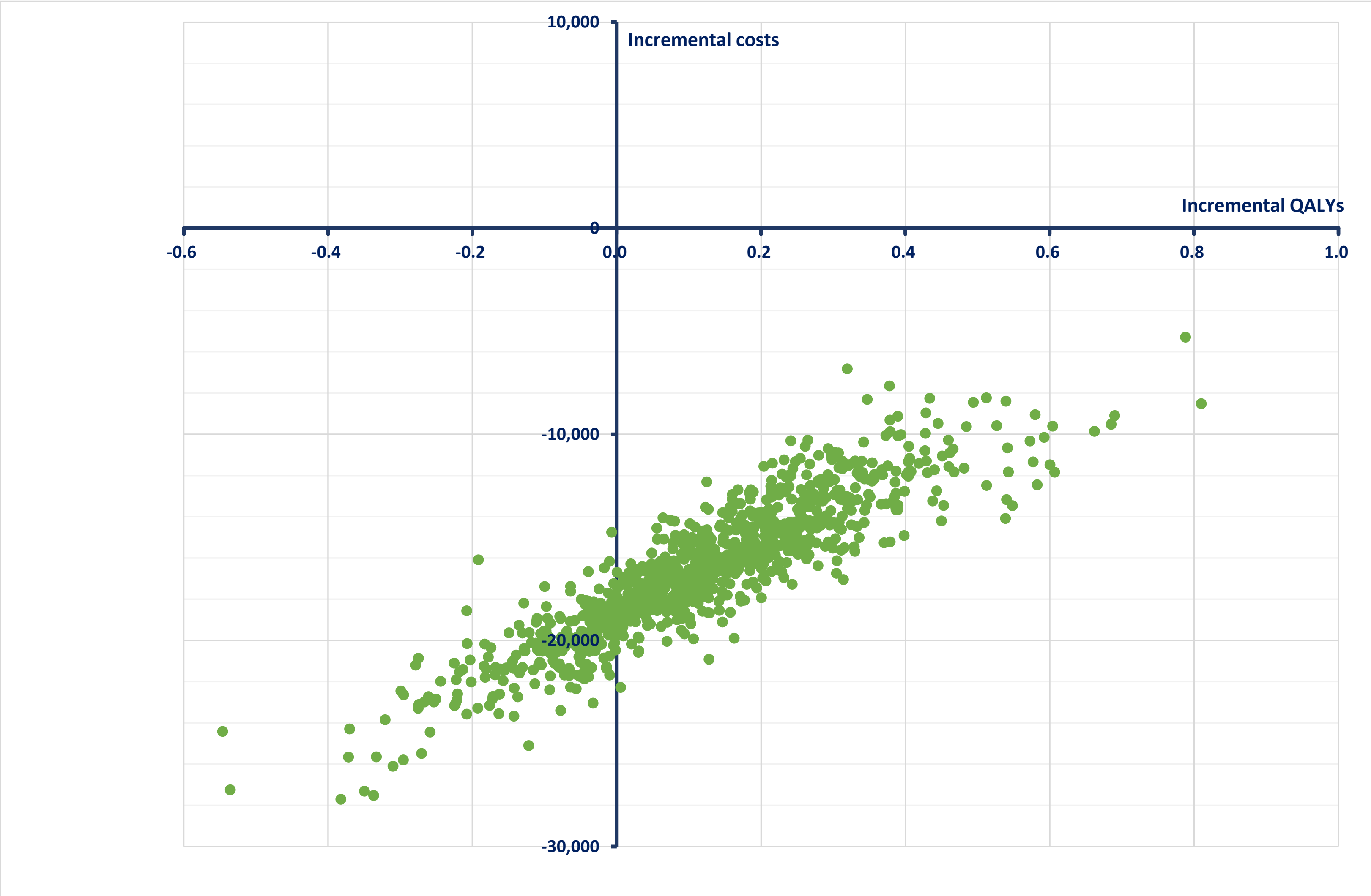

Figure 5-3 Cost-effectiveness plane from provider perspective

(Y-axis: Unit = Baht)

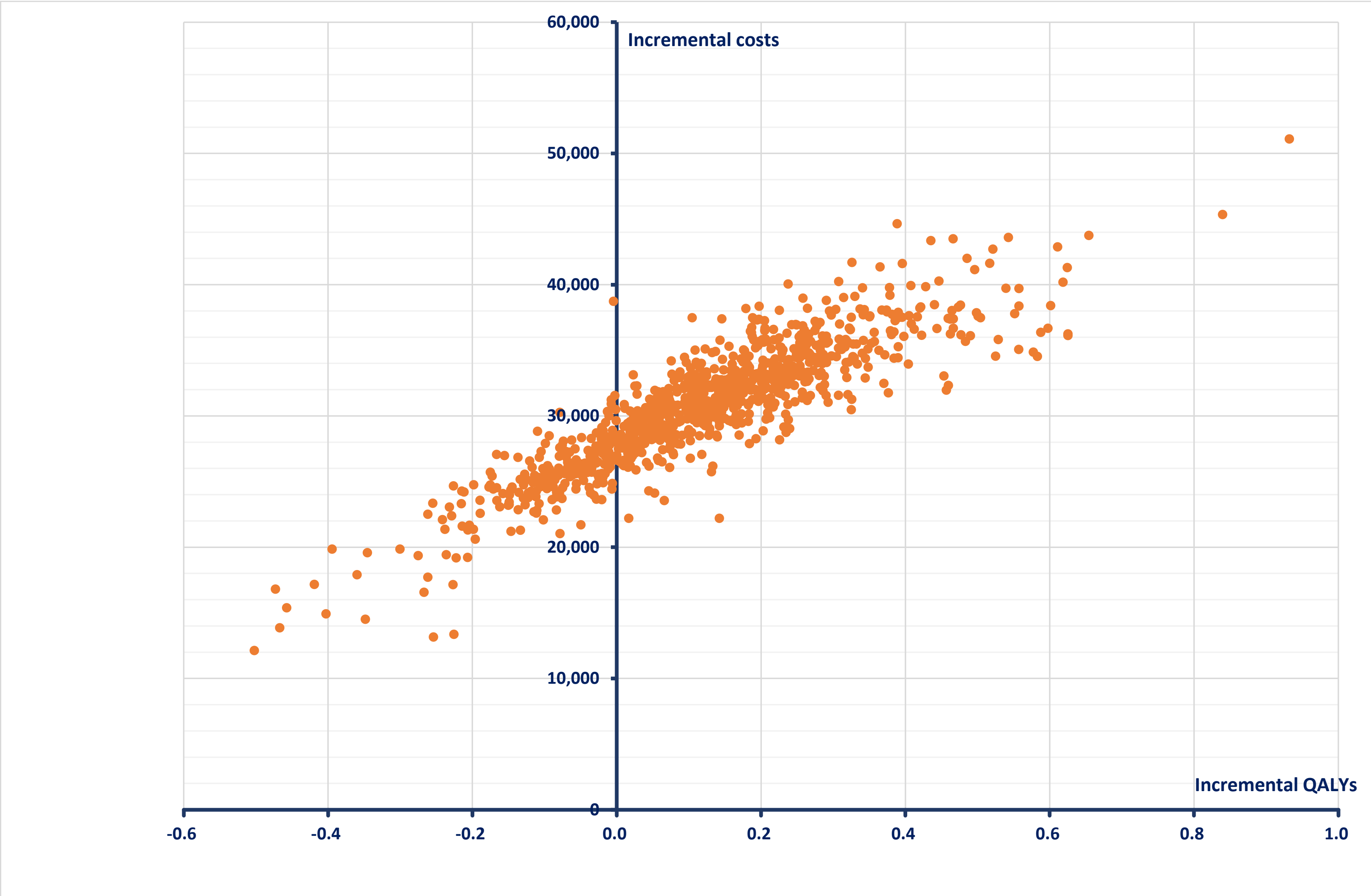

Figure 5-4 Cost-effectiveness plane from societal perspective

(Y-axis: Unit = Baht)

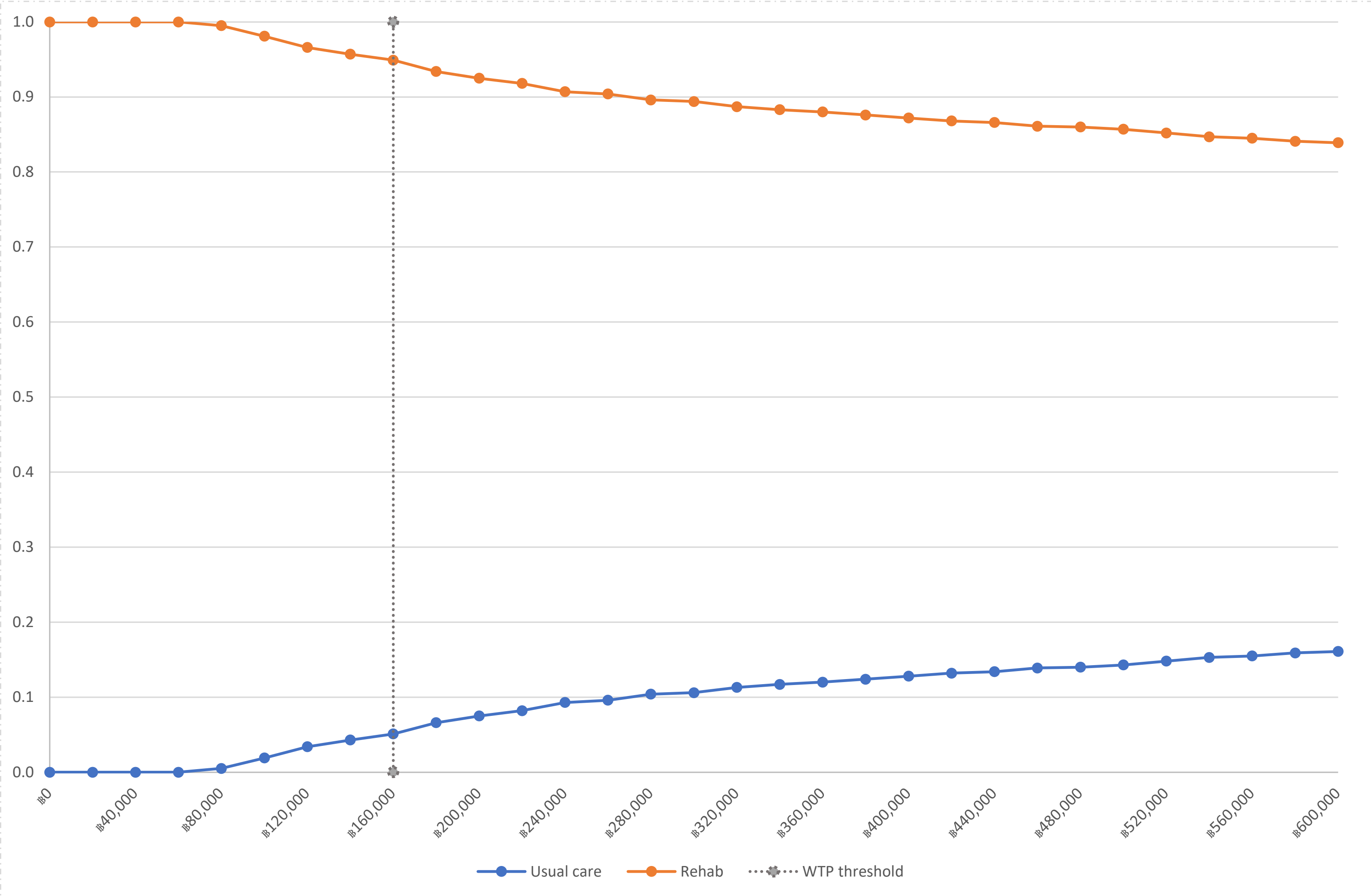

Figure 5-5 Cost-effectiveness acceptability curve from provider perspective

X-axis: Willingness to pay (Baht), Y-axis: Probability of being cost-effective

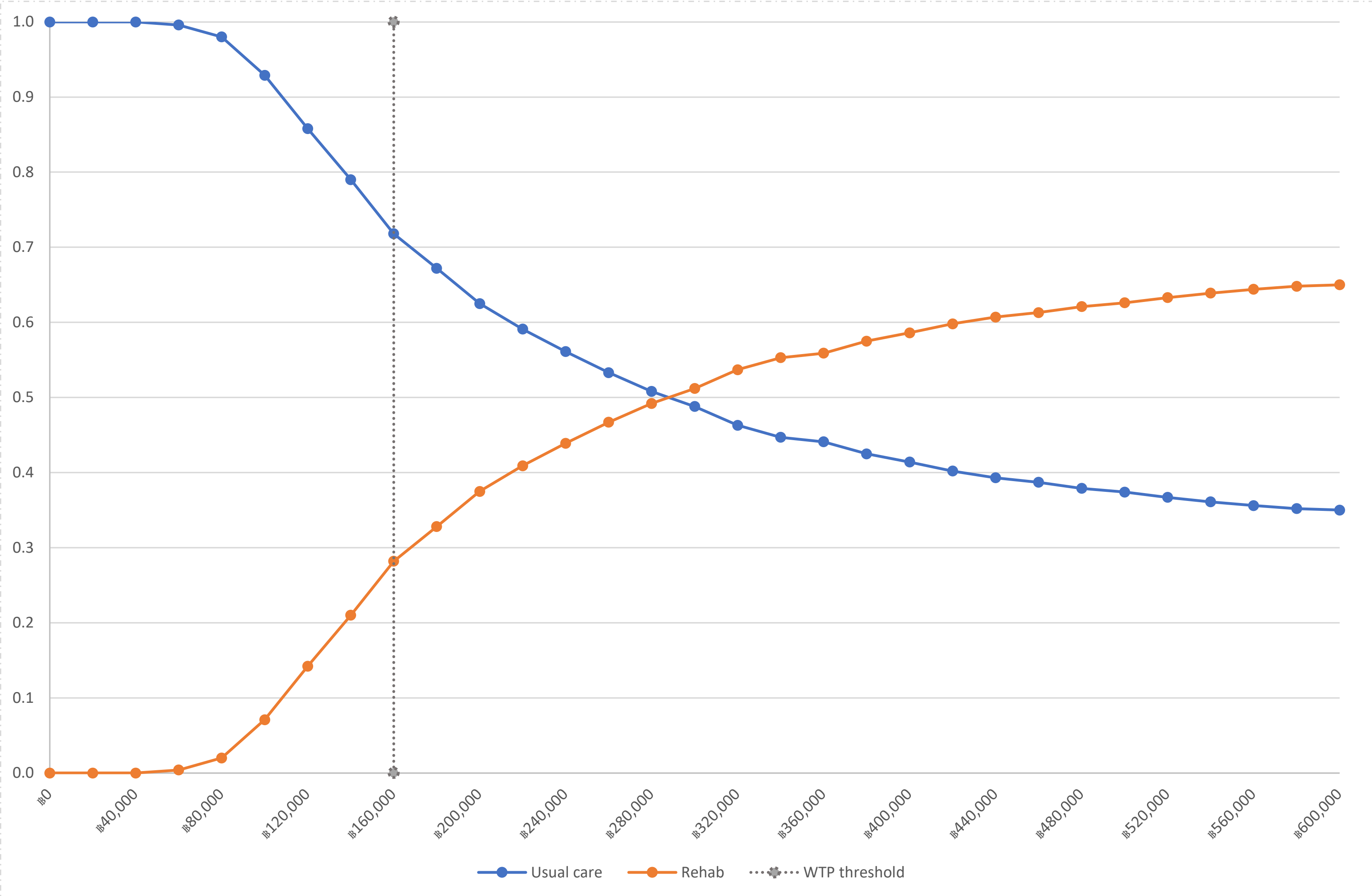

Figure 5-6 Cost-effectiveness acceptability curve from societal perspective
X-axis: Willingness to pay (Baht), Y-axis: Probability of being cost-effective

<u>One-way sensitivity analyses (OWSA)</u>

For almost all cases explored in the OWSA using a provider perspective (Figure 5-7), intensive inpatient rehabilitation was cost saving compared to usual care. Results were most sensitive to changes in the following parameters:

- transition probability from 'non to mild' to 'moderate to severe' health state
- transition probability from 'moderate to severe' to ‘LTC’ health state
- utility of 'non to mild' health state
- varying direct medical cost of rehabilitation programme by ±20%

However, these parameters had no impact on the ICER and the new rehabilitation programme remained cost-saving compared to usual care.

When considering a societal perspective (Figure 5-8), the most influential parameters were:

- transition probability from 'non to mild' to 'moderate to severe' health state
- transition probability from 'moderate to severe' to ‘LTC’ health state
- utility of 'non to mild' health state

Notably, apart from the scenario analysis, varying the direct non-medical cost of rehabilitation intervention by ±20% was found to have meaningful impact on results. Although, it showed high uncertainty, the new rehabilitation programme would be cost-effective if using the lowest value of non-medical cost of rehabilitation parameter (range: 47,302 - 70,953; ICER: 151,583 - 340,832; %change: -38% to 38%).

Full results of OWSA, parameters, ranges and percent change are shown in Appendix 32.

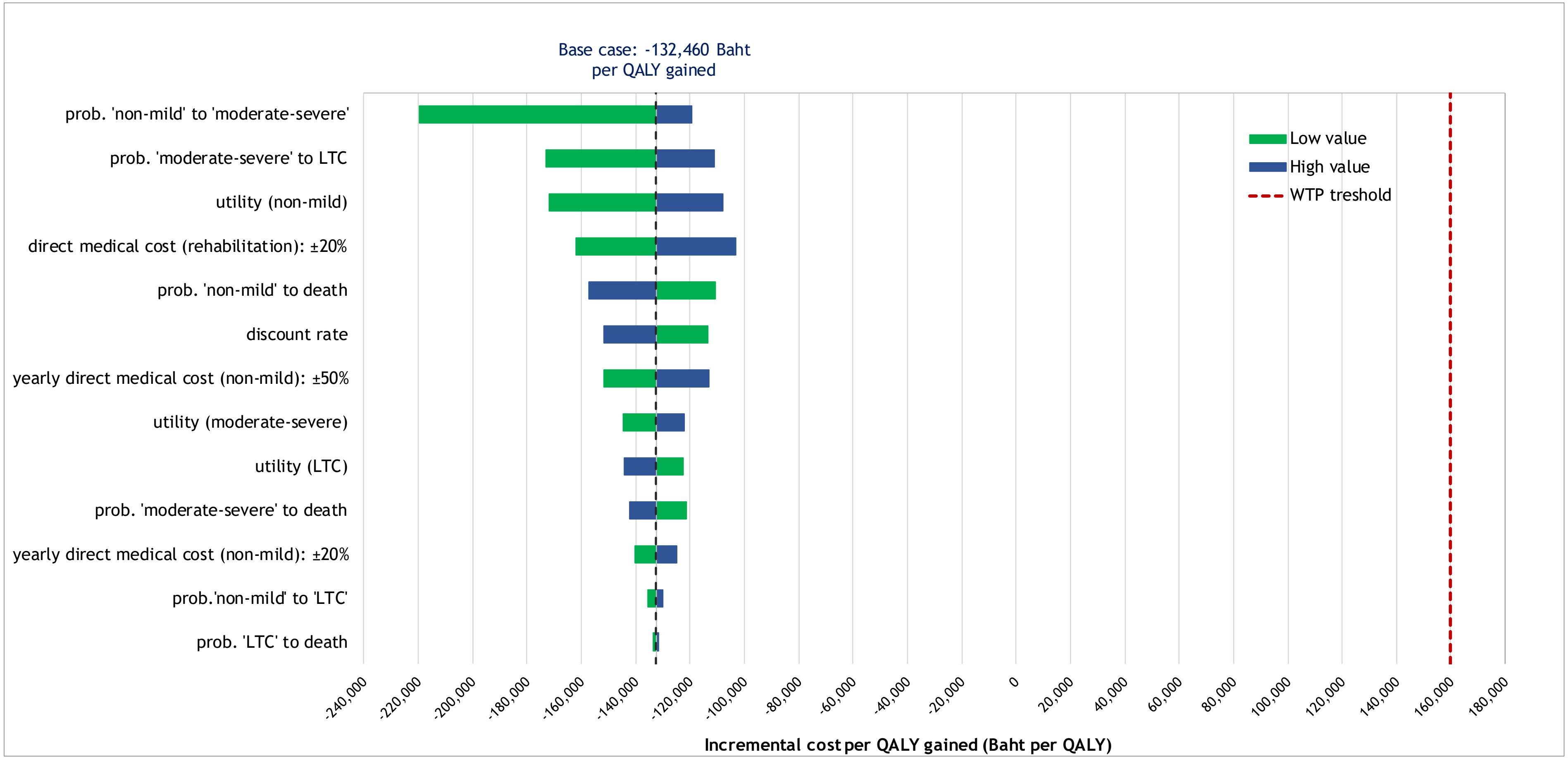

Figure 5-7 One-way sensitivity analyses considering provider perspective

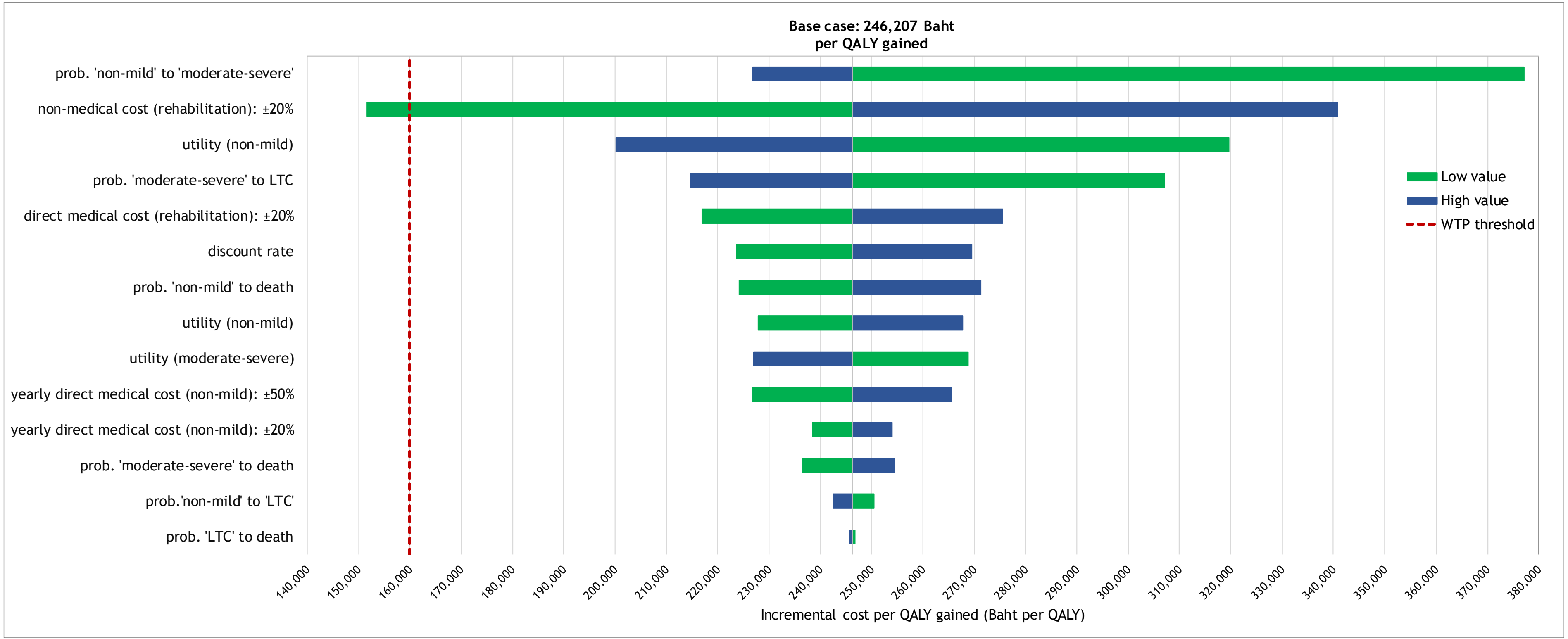

Figure 5-8 One-way sensitivity analyses considering societal perspective

5.5.3 Results from scenario analyses

The results from both scenarios present in Table 5-4.

For the first scenario, the proportion of patients in the 'non to mild' health state was assumed to be higher through a reduction in the proportion of people in the 'moderate to severe' health state while the proportion of patients in the 'LTC' health state remained unchanged. The number of patients in the 'non to mild' health state were varied from 12 patients - as a base case (equal to a probability of 0.240) until the calculated ICER was below the WTP threshold of 160,000 Baht (societal perspective). When the number of patients in the 'non to mild' state increased by 5 patients (17 patients - equal to a probability of 0.34), the new rehabilitation programme could be considered as being cost-effective at an ICER of 142,677 Baht.

The second scenario tested the reduction of direct non-medical costs of rehabilitation by 20%. Both deterministic analysis and PSA results showed the new rehabilitation services was cost-effective from a societal perspective. Because direct non-medical costs were not related to provider perspective results are not presented here.

Table 5-4 Results from scenario analysis

Deterministic	**Usual care**	**IMC**	**Incremental**
First scenario			
a) Provider perspective			
Total cost (Baht)	144,351	129,601	**-14,751**
Life years	4.297	4.474	**0.177**
QALYs	2.412	2.647	**0.235**
ICER (Baht/QALY gained)			**cost-saving**
NMB			**52,282**
b) Societal perspective			
Total cost (Baht)	201,898.71	235,366.48	**33,468**
Life years	4.297	4.474	**0.177**
QALYs	2.412	2.647	**0.235**
ICER (Baht/QALY gained)			**142,677**
NMB			**4,063**

Deterministic	Usual care	IMC	Incremental
Second scenario			
a) Societal perspective			
Total cost (Baht)	201,899	220,842	**18,944**
Life years	4.297	4.405	**0.108**
QALYs	2.412	2.537	**0.125**
ICER (Baht/QALY gained)			**151,583**
NMB			**1,052**

5.5.4 Results of the value of implementation analysis

To estimate the value of implementation of the new rehabilitation implementation, it is important to calculate the total cost of new rehabilitation implementation (I). See Appendix 33 for a full information of the implementation cost of the rehabilitation programme calculation. The total cost of new rehabilitation implementation (I) was 505,380,500 Baht over five years. The total costs for the first year was 8,516,500 Baht while total costs for the next four years were 496,864,000 Baht. The highest cost component was the cost related to physiotherapist training (54% in first year and 62% in the next four years).

The estimation of the value of implementation of the new rehabilitation programme (see Figure 5-2) was performed based on (a) base-case analysis, (b) increasing in probability of patients transitioning from 'moderate to severe' health state to 'non to mild' health state (scenario 1) and (c) a reduction of non-medical cost of 20% (scenario 2). The results of the value of implementation analysis are presented in Table 5-5.

Table 5-5 The estimation of the value of implementation of the new rehabilitation programme

Value of implementation	Provider perspective	Societal perspective
Base case analysis		
expected value of perfect implementation (per person)	23,359	NA
expected value of perfect implementation: minimum of QALY gained that the benefits exceed its implementation cost	0 QALY*	NA
expected value of actual implementation: achievable rehabilitation implementation with benefits exceed its implementation cost	≥37%	NA

Value of implementation	Provider perspective	Societal perspective
Scenario1: increasing in probability of patients transitioning from 'moderate to severe' health state to 'non to mild' health state		
expected value of perfect implementation (per person)	34,057	1,269
expected value of perfect implementation: minimum of QALY gained that the benefits exceed its implementation cost	0 QALY**	≥0.223 QALY
expected value of actual implementation: achievable rehabilitation implementation with benefits exceed its implementation cost	≥35%	≥69%
Scenario2: a reduction of non-medical cost of 20%		
expected value of perfect implementation (per person)	NA	1,231
expected value of perfect implementation: minimum of QALY gained that the benefits exceed its implementation cost	NA	≥0.114 QALY
expected value of actual implementation: achievable rehabilitation implementation with benefits exceed its implementation cost	NA	≥69%

Current value of technology given current utilisation and eligible patients (eligible patients=338,176 ,current utilisation=32%)
*at zero QALY, the expected value of perfect implementation yielded 3.3 billion Baht or 9,762 Baht per person
**at zero QALY, the expected value of perfect implementation yielded 2.9 billion Baht or 8,536 Baht per person

(a) Base-case analysis

To estimate the value of perfect implementation as the NMB from the new rehabilitation programme implementation was parameterised with respective values.

Expected value of perfect implementation activities (= N(1-ρ)*NMB – I)*

= [338,176 * (1-0.32) * ((0.125 x 160,000) – (-16,554))] – 505,380,500

= 7,899,487,097 Baht

From a provider perspective (Table 5-5), the expected value of perfect implementation of the new rehabilitation programme (with a current level of implementation at 32%) presented as NMB was 7.9 billion Baht over five years or 23,359 Baht per eligible person. The benefit of implementing the new rehabilitation programme exceed its implementation cost. This presents the maximum amount that the Thai

MOPH could invest in implementing the new rehabilitation programme while still accruing value from the rehabilitation intervention itself.

Although the QALY from the economic model showed that the QALY gained from the new rehabilitation policy was 0.132, it is important to assess their value for money in terms of the minimum of QALY gained at which benefits exceed the cost for perfect implementation, given the current level of implementation. Based on the expected value of perfect implementation, it was found that even if incremental QALY gained was zero QALY, the expected value of perfect implementation still exceeded costs, in NMB terms, which yielded 3.3 billion Baht over a five-year period or 9,762 Baht per person. This means that benefit of implementing rehabilitation is expected to be greater than its cost although the QALY from rehabilitation intervention and usual care were equal. This could be because the new rehabilitation programme was dominant (cost-saving) in a provider perspective.

Expected value of actual implementation activities (= N(σ-ρ)*NMB - I)*

= [338,176 * (actual implementation rate following new health technology initiative - 0.32) * ((0.125 x 160,000) – (-16,554))] – 505,380,500

As mentioned, in real-world practice, the actual level of implementation could be lower than the initially expected perfect implementation. The value of implementation analysis to examine the extent to which a max level of implementation that benefits would still exceed costs of its implementation was also carried out.

In provider perspective, the findings showed that if the Thai MOPH or health care providers can increase the rate of rehabilitation implementation (from current level = 32%) to be at least 37% over 5 years, as long as the implementation costs were less than 505,380,500 Baht, the benefits of implementing the rehabilitation programme exceeded its costs. Below this point, i.e. increased the new rehabilitation implementation from 32% to 36%, the cost of implementing stroke rehabilitation into routine practices is expected to be greater than the benefit, in NMB terms, which means that the new rehabilitation implementation is not worth implementing.

However, results from a societal perspective indicated the new rehabilitation programme was not cost-effective; therefore, the value of implementation was not performed.

(b) increasing in probability of patients transitioning from 'moderate to severe' health state to 'non to mild' health state (scenario 1)

The value of implementation based on the first scenario analysis was undertaken. The first scenario (Table 5-4) examined the effectiveness of the implementation rehabilitation intervention which assumed to increase proportion of patients who improved in the functional ability by 10% (5 patients increased: from 12 to 17 patients in 'non to mild' health state).

Provider perspective

the expected value of perfect implementation (= N(1-ρ)*NMB - I)*

= [338,176 * (1-0.32) * ((0.235 x 160,000) – (-14,751))] – 505,380,500

= 11,517,360,930 Baht

In a provider perspective, with the current level of implementation at 32%, the expected value of perfect implementation was 11.5 billion Baht over a five-year period or 34,057 Baht per person.

When considering the minimum of QALY gained, that the benefits still exceed the implementation cost, at the zero QALY, the expected value of perfect implementation was 2.8 billion Baht over a five-year period or 8,536 Baht per person. To put it another way, despite the zero QALY, benefits out-weigh implementation costs.

The 'break-even' value of the minimum implementation activity point was estimated at approximately 35% implementation. The rehabilitation implementation cost was expected to be greater than its benefits if implementing below this rate.

Societal perspective

the expected value of perfect implementation (= N(1-ρ)*NMB - I)*

= [338,176 * (1-0.32) * ((0.235 x 160,000) – 33,468)] – 505,380,500

= 429,051,559 Baht

In terms of a societal perspective, the expected value of perfect implementation to the Thai MOPH was only 429 million Baht or 1,269 Baht per person. Further analysis on the minimum QALY gained found that at least 0.223 QALY per patient, benefits out-weigh implementation costs. For determining whether the minimum level of implementation that would need to be achieved, it was found to be at least 69% should be implemented so that benefits would exceed implementation costs. Below this implementation rate, the implementation of rehabilitation would not be worthwhile.

(c) a reduction of non-medical cost of 20% (scenario 2)

The second scenario examined a reduction in the non-medical cost of 20%. After a reduction of non-medical cost of 20% in the deterministic sensitivity analysis, the ICERs was lower than the WTP threshold indicating that the new rehabilitation was cost-effective compared to usual care. However, when conducting the PSA, it appears that a reduction of non-medical cost of 20% was not cost-effective under the Thai WTP threshold. On the contrary, the new rehabilitation was being cost-effective if non-medical cost was decreased for 25%. This was due to the uncertainty of parameters used in the model. Therefore, to estimate the value of implementation of this scenario, the 25% non-medical cost reduction was used instead of 20%.

It should be noted that only results from societal perspective were presented in this section as these costs are not associated with a provider perspective.

the expected value of perfect implementation (= N(1-ρ)*NMB - I)*

= [338,176 * (1-0.32) * ((0.125 x 160,000) – 15,987)] – 505,380,500

= 416,367,050 Baht

At the current level of the new rehabilitation implementation in Thailand, the expected value of perfect implementation was 416 million Baht or 1,231 Baht per person, as the NMB to the Thai MOPH, over the five-year period.

Furthermore, benefits from the new rehabilitation policy out-weigh implementation costs if the minimum QALY gain was at least 0.114 per patient. It also found that at the implementation rate at least 69%, benefits exceed implementation costs and as such the new rehabilitation implementation is of value to the Thai MOPH.

5.6 Discussion

In a resource-limited country such as Thailand, there was only one national study[62] evaluating the cost-effectiveness of new rehabilitation policy implementation. However, this study has several limitations such as, small sample size and short time horizon analysis. It is important to consider long-term outcomes using a lifetime horizon to estimate the value of implementation as net monetary benefit from implementation of new rehabilitation programme because the long-term outcomes are applicable to chronic health conditions which estimated costs and effects could be affected by their consequences of health condition[280].

5.6.1 Key findings

Economic evaluation

This chapter presented the economic evaluation of new rehabilitation therapy policy compared to current rehabilitation therapy in Thailand. At the base-case analysis, from provider perspective, the new rehabilitation therapy was considered cost-saving compared to the current rehabilitation therapy at a 160,000 Baht WTP threshold. In contrast, from a societal perspective, the new rehabilitation therapy was unlikely to be cost-effective which was consistent with recent Thai economic evaluation study[62]. However, this results are different with other studies that classified stroke patients based on severity[42, 207]. However, these studies mainly focused on the home-based or community-based rehabilitation compared to hospital-based rehabilitation. Oppositely, the Thai MOPH recommends the inpatient-based rehabilitation. The inconsistency of results could be due to the differences in interventions and cost components. Hospital-based rehabilitation might be partly driven by the assumption of higher non-medical care costs than other types of rehabilitation and might be associated with productivity cost of carer. Furthermore, this could be due to a trivial differences in effectiveness of rehabilitation between the two treatments from Srisubut's study as mentioned earlier that the outpatient-based rehabilitation program as a comparator may not be generalisable to standard care being implemented due to more frequent visits than usual practices. Thus, this could be contributed to the underestimate of the real effectiveness value of the new rehabilitation policy. Another possible explanation for the negligible difference between the proportion of patient who improved from rehabilitation compared to usual care might be that the neurological recovery after stroke might exhibit a nonlinear, logarithmic pattern[50, 281]. Based on a literature review, it could be due to the floor and ceiling effects[277, 278], thus, the mean BI score improvement might not be represented that the patient can move from more severe to less severe health state even though the BI scores increase[256, 259, 276].

In terms of the different results between two perspectives in this chapter, one possible implication here is that while inpatient rehabilitation post-stroke might generate savings or minimising of hospital cost to health care providers[180], it may also pose a financial strain on patients' out-of-pocket costs[243]. Also, it can be seen from Candio et al[42] that there was 24 countries showing the cost-saving results when conducting a healthcare payer perspective but only 21 countries in a societal perspective.

There is also considerable uncertainty surrounding the results. The key parameters in this thesis are mainly driven by transition probability, utility and direct non-medical cost of rehabilitation. However, the uncertainty of transition probabilities and utility did not change the main results. In terms of direct non-medical cost of rehabilitation, when costs bound to patients were reduced at least 20%, it turned the ICER around to be lower than the WTP threshold or being cost-effective. This could confirm the explanation about costs of rehabilitation were put to patient. Thus, policymakers should consider the resource allocation as well as the reformation of rehabilitation service provision to reduce cost bound by patients.

The value of implementation

The value of implementation approach can be used to inform the Thai policy makers regarding the value to the health service of implementing rehabilitation into clinical practice and the optimum implementation levels that needs to be achieved vis-à-vis maintain the cost-effectiveness of a new health technology. The findings showed that these could be an example providing an informative demonstration to estimate the perfect and actual values of the new intervention implementation which could be used to improve the uptake or utilisation and the level of investment in the new interventions. As can be seen from the findings, the value of implementation, with the current level of implementation at 32%, appears to be worth in investment. Besides, the perfect implementation could be ideal. Based on the base-case, if the rate of implementation was greater than 37% from a provider perspective the new rehabilitation intervention was likely providing additional value, in NMB terms, to the Thai MOPH. While in the scenario analysis, if the rate of implementation was greater than 35% from a provider perspective and at least 69% from a societal perspective, the new rehabilitation intervention was likely providing additional value, in NMB terms, to the Thai MOPH. However, robust data on costs and effectiveness of the new rehabilitation implementation should be collected to for more comprehensive evaluation. In this regard, the follow-up research collecting of the BI scores of stroke patients during six months after inpatient-base rehabilitation and at certain time point, e.g. every year, five years, should be conducted.

It should be noted that implementation costs in this thesis did not take account for the capital costs of health care facilities as a result of having re-organised and invested in infrastructure. For instance, ward area or building, beds, and medical devices. Thus, uncertainty remains over the costs of implementing rehabilitation into routine clinical practice conditions in Thai context[255].

Based on the literature, there was limited evidence on value of implementation in stroke and rehabilitation but found a number of studies evaluating the value of implementation which mostly are focused on variations in clinical practice and improvement of effective and cost-effective health technologies implementation[253, 266, 282]. Additionally, the value of implementation framework can be applied to other economic evaluation studies which can help to inform policy decision-making to assess the value of implementation of other health technologies in terms of resource allocation or the impact of capacity constraints which impact the number of eligible patients who are in need of health intervention[283].

5.6.2 Strength and limitations

This is the first study, in Thailand, addressing new rehabilitation services policy in long-term health outcomes for post-stroke patients. The value of implementation framework was extended in this thesis to demonstrate the changes in level of implementation to evaluate the value to the Thai MOPH. In this thesis a five-year period was used as a short-term goal and investment. This could be added to the economic evaluation study to inform the policy decisions to invest on new intervention appropriately. However, the limitations of available data were a major limitation. As mentioned above, there was a limited study in Thai setting that reported the effectiveness of the new rehabilitation intervention patients who reach a goal set by MOPH including the effectiveness of rehabilitation interventions classifying based on functional ability.

In terms of the methodological challenges, this thesis underlines a comparability of cost estimates. Cost data in Chapter 3 was not available in order to obtain costs regarding to each health state; thus, costs according to severity of each health state were assumed based on the average LOS at incident admission[131]. Therefore, cost measurement methods can considerably affect the cost estimates of health state. In addition, costs in this thesis could be underestimated due to shorter LOS than some countries[258, 277, 284, 285] and could limited to comparable to other studies.

5.6.3 Policy recommendations

The findings in this chapter indicate that the new rehabilitation policy was cost-saving in provider perspective. In societal perspective, the new rehabilitation intervention is unlikely to be cost-effective; however, the new rehabilitation intervention would be cost-effective in the case of an increase in proportion of patient who improved from rehabilitation programme or a reduction in non-medical and informal care costs. Therefore, resources allocation of rehabilitation interventions should be considered to inform the policy decision. Furthermore, the value of implementation in this chapter provides the case study which can be used to consider level of implementation of healthcare services compare the implementation costs and the benefits of investment in the new intervention for improving the level of implementation of the cost-effective healthcare technologies. Furthermore, the individual-level data with BI outcome should be recorded at the national level to monitor and evaluate this new policy in the future.

5.7 Conclusion

At the current level of rehabilitation implementation, rehabilitation intervention is likely to be cost-saving in provider perspective while is unlikely to be cost-effective in societal perspective. The most influential parameter was the direct non-medical costs of the IMC rehabilitation programme, including productivity loss/informal care costs borne by the carer. This parameter was driving the change of results from being not cost-effective to being a cost-effective intervention, when moving from a provider perspective to a societal perspective. Furthermore, improvements in the proportion of patient who improved in functional ability at least 10% or a reduction in non-medical costs at least 25% yielded cost-effective results.

At the expected value of perfect implementation showed the net monetary benefit from new rehabilitation policy to the Thai MOPH for 7.9 billion Baht over five years or 23,359 Baht per stroke person. These information can also be used to inform policy decisions in relation to what levels of rehabilitation implementation do we need to reach in order to maintain the cost-effectiveness of rehabilitation programme and improve health outcomes of stroke patients in Thailand.

Chapter 6 Discussion

In Chapter 1, the challenges of stroke treatment and rehabilitation therapy were introduced. Although, in 2018, the overall stroke death rate, and death rates for ischaemic and haemorrhagic stroke were deemed to have improved as evidenced by being lower than the national KPIs, it is generally recognised that these vary greatly between health regions. Thus, the Thai MOPH developed a new set of KPIs for stroke service delivery through the service plan strategy 2018-2022 according to hospital level as well as evaluating the service improvement by health region. Hospitals in the same health region have to work together to achieve the goals under the concept of a seamless health service network, self-contain and referral hospital cascade. Low utilisation rates of rehabilitation services are also observed. Even though the Thai MOPH had published rehabilitation guidelines[25], these were not well implemented by healthcare professionals. This was due to limitations in health workforce[19, 45], limited resources and infrastructure in provincial and rural areas[33, 52], limited stroke rehabilitation services in several regions[41], and low access to rehabilitation services[45]. In 2019, the new strategy for rehabilitation services 'Intermediate care (IMC)' guidelines[51] was endorsed to address these difficulties. This new initiative has not been evaluated in terms of cost-effectiveness and value of implementation.

Therefore, this thesis addressed the gaps in evidence. The overarching aim of this thesis was to evaluate the implications of the endorsement of the new rehabilitation policy for stroke patients and to estimate cost-effectiveness and value of implementation of this new rehabilitation strategy. The following research questions were investigated:

Research question 1: What are the differences in services available in healthcare facilities for stroke care across different hospital levels in Thailand?

Research question 2: To what extent does the stroke service plan improvement affect health resource utilisation, cost and health outcomes of stroke patients and does it differ across stroke subtypes?

Research question 3: What is the existing evidence in terms of economic evaluation for stroke rehabilitation services and how could those evidence be used to inform an evaluation of the new rehabilitation guidelines in Thailand?

Research question 4: Is adopting the new rehabilitation service policy cost-effective and what is the potential value of implementation of the new rehabilitation service policy for future eligible stroke cohorts?

The next sections provide a discussion of the main findings in the context of potential policy implications. Furthermore, areas of future research are also discussed.

6.1 Main findings

6.1.1 The availability of stroke services and hospital facilities at different hospital levels in Thailand

Results from Chapter 2 identified challenges that rehabilitation services in Thailand face. Although this thesis focused on rehabilitation implementation policy, some of the findings are likely to be related to the upstream processing of service provision. The results from the survey in Chapter 2 showed that healthcare providers had capacity to setup SUs which was achieved fully (100%) in advanced-level and standard-level hospitals including essential supportive components. However, capacity issues remained, particularly at mid-level hospitals. The most important challenges included the available specialties, which differed between hospital levels, in particular the scarcity of neurologists in rural areas[27, 53]. Rehabilitation physicians were available in all advanced-level and standard-level hospitals, but only in 50% of mid-level hospitals. Therefore, well-trained non-neurologists can play a key role in stroke treatment[27] under supervision of a neurologist from advanced-level or standard-level hospitals[94].

Not all hospitals performed assessment of clinical scores on discharge. However, IMC guidelines, focussing on the recovery phase, recommended to measure the need for rehabilitation using BI scores before discharge from hospital. This could affect health outcome assessments in the post-acute period.

Besides, there was considerable variation in the proportion of stroke patients receiving rehabilitation. Some challenges still remain to improve quality of care, such as stroke centre certification, health information systems, in particular monitoring systems for clinical measurements and health outcome assessments in the recovery phase (BI score), for continuity of care inter-hospital between health regions and at national level.

Data linkage and health record systems for clinical or health outcomes in order to follow-up and monitor health outcomes of patients should be developed between hospitals and at national levels. Lastly, the stroke organisational survey should be reviewed and updated regularly in the MOPH annual reports and audit systems. The ability to track changes over time in stroke service quality should be the cornerstone of stroke provision.

6.1.2 Stroke resource utilisation, costs and all-cause mortality in Thailand

Chapter 3 provided information from a demand side. This chapter aimed to examine the extent to which the stroke service plan improvement affected health resource utilisation, cost and health outcomes of stroke patients and whether this differed by stroke subtype.

A low percentage (32%) of stroke survivors received rehabilitation services with the majority being patients with ischaemic stroke. This is comparable with a previous international observational study by Langhorne et al. (2018)[60], which indicated that around 31% of participants in LMICs received post-discharge rehabilitation, while this was 92% in high-income countries. This is also consistent with a Thai study from 2015[45], trying to develop a new inpatient-based rehabilitation service for stroke patients offered within this first week; three days a week after stable clinical outcomes. The author suggested a low level of rehabilitation services offered. The reason could be related to the reimbursement system which is based on the DRG system that does not take account of inpatient-based rehabilitation services. As health care financing and reimbursement are vital to health care providers, this could affect the quality of care and accessibility to health care services[286].

This is in accord with a recent study[65], that investigated the early phase of the IMC policy in 17 hospitals across all regions of Thailand during 2019-2020. Their evidence indicates that, due to DRG-based payments, medical expenses reimbursed from NHSO was only 74% of medical costs in advanced-level and standard-level hospitals, and 64% in community hospitals. This is an important issue for policy makers and health care purchasers for further consideration of offering incentives or adequate reimbursement of rehabilitation services to hospitals.

Other reasons of low percentage of stroke patients accessed rehabilitation services could be the inadequacy of district-level staffing for rehabilitation[8] and patient awareness towards the importance of rehabilitation and transportation problems[8]. The latter can be explained that although healthcare staff regularly referred patients back to a hospital close to where they lived, some stroke patients may experience an inconvenience to attend rehabilitation therapy at hospital. For example, an limitation of the affordability of transportation costs[8].

Results from this thesis also highlight that patients who received rehabilitation during their incident admission incurred lower mean annual medical cost which tended to decrease by approximately 3,800 Baht (£88) per patient. It could be implied that an initial higher investment in rehabilitation services could have the potential to lead to lower future costs and have positive effects on reducing dependency and increasing activities of daily living[176].

Receiving rehabilitation was associated with a 15% decrease in the risk of mortality with patients with haemorrhagic stroke receiving rehabilitation had the lowest mortality risk compared to patients with other subtypes. It could be argued that providing rehabilitation at the incident admission could not only save medical costs but reduce risk of mortality. These results corroborate the findings of previous work which showed the benefit of early rehabilitation after stroke in the short and long-term[26, 174, 176].

It is interesting to note that large variations in mortality risk between health regions were observed, indicating that living in other geographic areas than Bangkok was associated with a higher risk of mortality. As quality of care may have an effect on stroke survival, the inequality in stroke care between health regions could be attributed to the differences in stroke management systems in each health region.

This is the first time that recent Thai national administrative data, from the NHSO information systems which contains medical records from contracted health service providers across Thailand and represents 75% the Thai population[8], was used to provide a national-level assessment. The data used in this thesis were retrieved between 2015 and 2020 which aligns with the service plan strategy 2018 - 2022. The analyses in this thesis demonstrate the usefulness of routine data as it enables a comprehensive assessment of services provided for and health outcomes of stroke patients, providing more robust data than studies undertaken in a single setting[185, 186].

Real-world data (RWD) offers great potential for evidence-based decision making around rehabilitation services. Unlike RCT data, RWD are observational in nature and can be highly complex[185]. However, as these data have not been collected to answer specific clinical or research questions, they can lack information on clinical outcomes or could be incomplete. Appropriate data management and analyses are required to address some of these issues. The national administrative data used in this thesis did not contain information on functional ability outcomes, specifically the BI score. However, the NHSO has recently started a value-based programme including the recording of BI scores aiming at a reimbursement system towards new rehabilitation services provided under the IMC policy[51]. This could provide opportunities for health care delivery improvement, in particular focusing on effectiveness, QoL as well as value for money to the Thai MOPH of the new rehabilitation policy implementation in Thailand.

Findings from this chapter provide an important contribution to understanding patient characteristics, differences in resource utilisation and costs as well as all-cause mortality. This is an intriguing one which could be explored along with the new rehabilitation policy which has been endorsed in

2019. Findings corroborate the findings of previous work in light of the low accessibility of rehabilitation services while the new policy recommended that health care providers, in particular mid-level hospitals, should improve and provide an intensive inpatient rehabilitation programme for 14 days with follow up for six months to eligible stroke patients[6].

6.1.3 Methodological approaches to assess cost-effectiveness of stroke rehabilitation

The third research question was addressed in Chapter 4 based on work in Chapters 2 and 3. IMC guidelines for stroke rehabilitation had been endorsed in 2019, and it was recommended that patients should receive rehabilitation services based on severity levels assessed using the BI score. Only one national publication conducted an economic evaluation of this new rehabilitation policy and only considered short-term impacts on health outcomes. The findings can be categorised into four different areas: (i) improvement of rehabilitation services, (ii) improvement of function/mobility or strength, (iii) improvement of communication skills and (iv) other rehabilitation-related services.

The majority of rehabilitation interventions were targeted at improvement of rehabilitation services, but most studies relied on RCT data with a short time horizon. The majority of new rehabilitation interventions/services were likely to be cost-saving or cost-effective. However, it was found that there were different approaches used for performing model-based economic evaluation of stroke rehabilitation. This may be related to different study purposes or objectives of the researcher or healthcare decision-maker to compare rehabilitation interventions within a country-specific context[243]. In terms of quality assessments, the reviewed studies were generally of good quality allowing and identification of the most suitable economic model to assess rehabilitation services.

Only seven studies used economic models to assess cost-effectiveness of rehabilitation interventions. However, these studies were moderately heterogeneous in terms of model structure, time horizon, methods for cost measurements, assumptions, and methods to assess uncertainty. It is worth highlighting that these studies mainly considered direct medical costs, especially costs related to the new intervention, but barely considered overhead costs of interventions or costs of lost productivity including informal care. A possible explanation for this exclusion might be that most stroke patients were elderly and the authors considered that productivity loss might be negligible compared to costs of implementing new interventions. This could introduce bias to the cost-effectiveness results as costs might be underestimated and could affect ICER results[244].

Only one study by Allen et al[207] evaluated rehabilitation programme with the differences in functional ability status in stroke patients. This model evaluated outcomes over a long-term time horizon and appeared to be inclusive of all the relevant health states similar to the recommendations in the new Thai rehabilitation guidelines. Thus, the model from Allen et al[207] was identified as the most suitable model which can be applied and adopted to the Thai rehabilitation economic model. Moreover, the quality assessment also showed highly warranted in both the CHEERS and the Philips checklists.

In conclusion, it is important to bear in mind that the systematic review in this thesis reviewed studies over the past 10 years as it was hypothesised that these studies should best reflect up-to-date practices in delivering stroke rehabilitation services as well as the effects of treatments. Second, due to variability in reporting the type of interventions between studies, cost components, and outcome measures, a comparison between studies was difficult and can only be described in a narrative way. Furthermore, most of the studies were carried out in developed countries with differences in several economic evaluation components. This can be seen in Candio’s study[42] who compared home-based rehabilitation and conventional hospital-based rehabilitation in European areas. The findings indicated that, of 32 European countries, home-based rehabilitation was found to be cost-saving in 24 countries and cost-effective in the remaining eight countries. Thus far, the thesis has argued that it is important to conduct an economic evaluation within a specific context. A suitable and practical economic evaluation of rehabilitation provision should be applied for Thai health care system.

6.1.4 Economic evaluation and value of implementation of the new rehabilitation service policy in Thailand

Based on the lessons learned from previous chapters, a context-specific economic evaluation of the new rehabilitation policy was presented in Chapter 5, aimed at meeting the following objectives: (i) to develop a rehabilitation model for post-stroke care which can be used for the economic evaluation of the new rehabilitation service policy in Thailand, and (ii) to examine the potential value of implementation of the new rehabilitation service policy.

The findings showed that inpatient rehabilitation was cost-saving from a provider perspective. This is consistent with findings of other studies that evaluated the cost-effectiveness of rehabilitation programmes (Chapter 4). In contrast, the rehabilitation service was not cost-effective when adopting a societal perspective. Only when direct non-medical costs were reduced by 20% in sensitivity analyses, the intervention was found to be cost-effective at a WTP threshold of 160,000 Baht. It seems possible that the inpatient rehabilitation intervention might help to save money for the health care system. Conversely, it is possible that it may add financial strain to patients' out-of-pocket costs such as costs related to informal care or direct non-medical costs[243]. In terms of sensitivity analyses using a provider perspective, varying parameters had no impact on the ICER and the new rehabilitation programme remained cost-saving compared to usual care. When considering a societal perspective, the most influential parameters were the transition probability from 'non to mild' to 'moderate to severe' health state, transition probability from 'moderate to severe' to 'LTC' health state, and the utility assigned to the 'non to mild' health state. In scenario analysis, the first scenario revealed that if the proportion of patients in the 'non-to-mild' health state increased by 10%, the new rehabilitation programme was cost-effective. Likewise, the second scenario, reducing the non-medical costs by at least 20% resulted in the new rehabilitation programme being cost-effective.

The expected value of perfect implementation based on the provider perspective, as a base-case scenario, showed that at the current level of rehabilitation implementation (32%), the benefits of the new rehabilitation policy exceeded its cost of implementation which means that the new rehabilitation programme would be worth implementing. The expected value of perfect implementation as the NMB from the new rehabilitation policy is approximately 23,359 Baht per person or 7.9 billion Baht over five years. This represents the maximum amount that the Thai MOPH could invest in implementing the rehabilitation programme while still accruing value from the intervention itself. Perfect implementation at 100% rarely seems feasible/realistic. If rehabilitation can be offered to at least 37% of eligible patients over five years, the benefits of the new rehabilitation policy would exceed its costs as long as the implementation costs are less than 505,380,500 Baht over five years (or < 101 million Baht per year).

From a societal perspective, the expected value of perfect implementation to the Thai MOPH was 1,269 Baht per person or 429 million Baht over five years. If non-medical costs were reduced by 25%, the benefits exceeded the implementation costs. When considering the actual level of implementation from a societal perspective the level of implementation that would need to be achieved, was found to be at least 69% of eligible patients over 5 years, so that benefits to the Thai MOPH would exceed implementation costs, meaning the programme would be worth implementing.

This is the first study to estimate the potential cost-effectiveness and the value of implementation of rehabilitation in a Thai setting. This thesis carefully considered all available information and was conducted based on the best available evidence relating to the new rehabilitation guidelines for Thailand. The evidence from this study suggests that input parameters used to perform cost-effectiveness analysis were crucial due to a lack of national studies reporting the proportion of patients who improved in each health state following a new rehabilitation policy.

It should be noted that, it could be an underestimation of the effectiveness of the new rehabilitation policy implementation observed in the national study[62]. Moreover, there were also limits of effectiveness estimates of rehabilitation categorised according to disability levels. For example, most studies, evaluating rehabilitation effectiveness, reported results in form of overall mean BI score increase[256, 259, 276], standardised mean difference (SMD)[258] but had no effectiveness data separated by disability level. Although, the rehabilitation model classified by individual functional ability levels would be data-demanding and may need country-specific data, the availability of data regarding the effectiveness of the rehabilitation programme for stroke patients categorised according to functional ability levels would allow for a more accurate comparative effectiveness analysis of new rehabilitation policy versus usual rehabilitation therapy in real life clinical practices.

6.2 Contribution to knowledge

This thesis made a number of contributions to the development of rehabilitation services in Thailand.

Firstly, this thesis considered the supply-side perspective in terms of the availability of stroke services and healthcare facilities across different hospital levels (Chapter 2). Little is known about the national situation of stroke services and how local practitioners adapted their services or clinical practice to respond to the MOPH policy. This was examined quite thoroughly via the survey presented in Chapter 2.

Secondly, healthcare resource utilisation, costs and all-cause mortality related to stroke were estimated in Chapter 3. The current stroke treatments are likely to be acceptable as can be seen from the survival analyses. Nevertheless, the percentage of patients accessing rehabilitation therapy was found to be low and there were differences in services provided between health regions.

Thirdly, there were limited economic models that evaluated rehabilitation services with considering long-term outcomes and the effectiveness of rehabilitation therapy in terms of BI scores based on functional ability status. This study summarised and synthesised findings from published economic models to identify the most suitable model that can be applied and adopted in a Thai setting.

Lastly, this thesis is the first study that evaluated real-world routine practice using national-level data. This study also evaluated the cost-effectiveness and value of implementation of the new rehabilitation policy in a Thai setting (Chapter 5).

From a methodological aspect, this thesis can serve as an exemplar for informing health policy decisions as well as researchers interested in stroke care provision. In this thesis, evidence from real-world data was combined with evidence from literature using robust research methods such as the two-part models to handle the zero-inflated data in the national administrative data. Parametric survival analysis was used to explore the relationship between service utilisation and mortality risk for stroke patients. A critical appraisal of research studies through a systematic review was carried out to inform model-based CUA and value of implementation analysis, which can determine the maximum return on investment in implementing new health technologies and inform resource allocation decisions.

To summarise, there are five key contributions from this thesis:

1) Findings from the national stroke survey in Chapter 2 indicate that setting up a stroke unit, as a national goal, was achieved fully (100%) in advanced-level and standard-level referral hospitals including key essential supportive components. Hence, stroke care from a provider perspective is likely to have shown improvement in service delivery, achieving the goals set by the Thai MOPH. Surprisingly, the potential to provide stroke services was also found in mid-level hospitals although improvements still need to be made in areas of health workforce.

2) Findings from the analyses of national administrative data in Chapter 3 reveal a low percentage of patients accessing rehabilitation services following their first stroke. However, patients receiving rehabilitation at the incident stroke admission incurred lower annual costs and had a lower risk of mortality compared with patients not receiving rehabilitation. This result is important to ensure the standard of care. In addition, this study can demonstrate the usefulness of using real-world clinical practice data from the national healthcare administrative data set in which research results are considered generalisable.

Nevertheless, difficulties in retrieving data and the lack of disease-specific health outcome measures should be addressed in order to increase the usefulness of these data.

3) Based on the systematic review of economic evaluations of rehabilitation services (Chapter 4), a limited number of studies employed an economic model to assess cost-effectiveness of rehabilitation therapy. Unfortunately, most of these studies were carried out in developed countries, highlighting the need of a context-specific economic evaluation for a Thai setting. Approximately half of all reviewed studies concluded that rehabilitation interventions represent good value for money.

4) Findings from the model-based economic evaluation (Chapter 5) demonstrated that the new rehabilitation policy is cost-saving from a provider perspective, but not cost-effective from a societal perspective. It seems possible that the new policy shifts the cost burden to patients caused by a requirement of a 24-hour caregiver for each stroke patient. As shown in the scenario analysis, when considering a reduction in direct non-medical costs, results changed considerably and were found to be cost-effective at the WTP threshold of 160,000 Baht.

5) The value of implementation analysis presented in this thesis indicates that there was a monetary benefit to MOPH from the implementation of the new rehabilitation policy. However, the intervention does not need to be perfectly implemented. At the base-case analysis, the implementation level of 37%, the population net monetary benefits obtained from this new rehabilitation policy exceeded the cost of implementation. This means the implementation of the rehabilitation programme would be worthwhile if it could maintain implementation costs to be less than 505 million Baht over five years.

6.3 Limitations

This thesis is an example of utilising several research methods to answer research questions in real-world settings. A variety of analysis techniques and analysis tools were used to address possible limitations in this thesis.

In Chapter 2, despite a low response rate for the survey, almost all geographical areas of Thailand are represented. Additionally, the survey did not cover all hospital types such as the Bangkok area and university hospitals which mostly serve as excellence centres. This will have led to limitations in terms of comparability between health regions. Lastly, the investigation of the care map of IMC was not performed since the new IMC guideline and new rehabilitation policy have just been endorsed in 2019[51].

In Chapter 3, although NHSO data are accessible for research purposes, the data sets are stored in a format that makes utilising the data difficult and time-consuming. Moreover, cause of death and disease-specific health outcomes, e.g. BI score, could not be obtained. Therefore, the functional ability levels or competing risks could not be considered. Other limitations include the lack of some important information that were not made available by NHSO, such as date of birth, medicines, and whether a stroke unit was available.

In Chapter 4, limited information was found on the effectiveness of rehabilitation therapy in terms of BI score, which could be associated with categories on functional ability.

Lastly, as discussed in section 6.1.4, results need to be interpreted with caution and further research will be needed to reduce the level of uncertainty around the ICER. Further, this analysis did not take into account private rehabilitation centres which could be utilised by some patients. Moreover, there were difficulties in capturing costs and outcomes at the national level due to the lack of registry and data records at national organisations such as MOPH, and NHSO.

6.4 Policy recommendations for improving stroke services in Thailand

Over the past few decades, it is becoming progressively imperative that real-world data provide insights into what happens in current clinical practice and real-world evidence is beneficial to inform policy makers on the levels of current provision of healthcare services. It also helps to accelerate the development of new policies and approval of new health technologies or interventions[287].

Findings from this thesis can support policy decision-making with reference to stroke service provision and value of implementation. This thesis exhibited that there has been a substantial improvement in stroke treatment, in particular for the acute-stroke phase. It is worth noting that this might not be sufficient though to provide benefit to the community of all patients with stroke. For instance, Gilligan et al[288], assessed different interventions in stroke acute care that provided the most potential benefits. The authors revealed that although thrombolysis was recognised as one of the most effective interventions for the acute-phase of stroke, the greatest potential benefits to the community was found to be the stroke unit care and management (from intensive care to rehabilitation unit). Although, rehabilitation therapy might provide a smaller gain for an individual patient with stroke, it might be able to contributed to potentially greater benefits to the community compared to some acute-care interventions when we extrapolate the benefits to the entire population of stroke patients. This could be because of the proportion of patients who would be eligible for rehabilitation compared to those receiving particular interventions in acute care. Thus, the overall potential benefits to the community, as a whole, would be greater than some stroke acute-care interventions.

The following section presents key policy recommendations which could facilitate the improvement of service delivery, especially the new rehabilitation policy. Other issues such as a priority, feasibility, budget, ethical, and equity prior to suggesting new policy recommendations also need to be considered.

1) The Thai MOPH should conduct a regular organisational survey as well as improve health information systems, especially the linkage between hospitals for continuous monitoring and evaluation of service provision and health care facilities to ensure adequate capacity and standard of care. An extension of certification, currently in place for stroke units, to also apply to rehabilitation/IMC centres or institutions, could be a further consideration to be included as KPI for a minimum level of

implementation.

2) This thesis illustrated differences in the risk of mortality between stroke subtypes. Additionally, findings revealed that, on average, stroke patients were younger in Thailand than in developed countries such as the UK[289], Canada[207], Europe[42]. Overall, the mean age of patients with stroke in LMICs was lower than in developed countries[290] irrespective of stroke subtype, gender. This information could be used to better tailor stroke care and rehabilitation provision for stroke subtypes or by age group.

3) The development of national health information systems or a national registry in order to measure activities of daily living in stroke patients, both in the acute- and post-acute phase, and monitoring health outcomes of stroke patients is imperative. This should be taken into account by policy makers, especially MOPH and all health insurance scheme organisations. Regular evaluation and monitoring of national health care data aligns with the service plan strategy 2018 – 2022 and provides an important contribution to understanding patient characteristics, differences in resource utilisation and costs as well as survival probability of stroke patients. The work carried out in Chapter 3 can be used as a guide for further evaluation of the performance of the new policy implementation under the service plan strategy.

4) Currently, functional ability outcomes have been recorded at the hospital level, while NHSO has started a vertical programme recently[291, 292] to reimburse rehabilitation services provided under the intermediate care policy. This could provide room for focusing on effectiveness, QoL according to functional ability levels and stroke subgroups. The economic evaluation and the value of new health technology implementation in Thailand could be further used to inform Thai policymakers, such as the MOPH, health care purchasers and health system researchers, to allocate health care resources effectively.

5) Findings revealed that the new rehabilitation policy was cost-saving from a provider perspective but it was not cost-effective when adopting a societal perspective at the Thai willingness to pay threshold at 160,000

Thai Baht. However, several studies suggested that home-based or community-based rehabilitation showed various benefits. These included not only a reduction in costs but also a reduction in the burden that is placed on carers[46]. Results from the systematic review also suggest that home-based or community-based rehabilitation programmes could be the most cost-effective model of care[180, 293]. Hence, these can increase local access for patients and reduce transportation costs to centre-based rehabilitation. Policymakers and stakeholders should consider innovative approaches and a shift towards providing rehabilitation services in more remote settings.

6) Improvements in service provision to reduce inequality of health opportunity in non-Bangkok areas are essential[294, 295]. When re-designing policies to reduce health inequalities in areas outside Bangkok, national and regional health care administrative organisations, such as MOPH and health care purchasers, should focus, for example, on better distribution of health workforce[245, 296].

6.5 Areas for Further Research

The key areas for future research are listed below, in order of priority. In Chapter 3, the analysis was reliant on data that had already been collected in the claims data of the NHSO. However, there is still a need to improve the cost measurements, accounting for the cost data related to the new rehabilitation programme. Therefore, further studies should explore using actual costs from each hospital. Further, data on BI score should be collected routinely to allow an investigation of changes in the score.

The systematic review revealed that most studies were carried out in developed countries, not necessarily reflecting issue in LMICs. Future studies should consider their own context of relevant alternative intervention options and data that reflects the practical context for decision makers.

Future economic evaluations of rehabilitation services should also focus on the economic impact of productivity loss such as presenteeism, or productivity loss of carers. These costs might place huge financial constraints on patients and families when taking a societal perspective[190, 246-248]. Neglecting costs due to lost productivity including informal care could introduce bias to the cost-effectiveness results as costs might be underestimated and could bias ICER results[244].

The economic model in this thesis was constructed to evaluate the cost-effectiveness of a new rehabilitation intervention which aimed to improve individual functional ability. However, it would be noteworthy to apply the model for an evaluation of rehabilitation according to the types of rehabilitation coupled with a subgroup analysis of patients according to their functional ability, to explore the extent to which the rehabilitation option could maximise health outcomes. This would be useful to inform decision making on resource allocation because other settings such as in developed countries mostly provided a home-based or community-based rehabilitation programme, while the Thai MOPH has suggested to provide inpatient-based rehabilitation. Hence, the inpatient based programme would need to be better justified, given that other countries seem to be offering different types of rehabilitation services.

6.6 Conclusions

This thesis was able to demonstrate the value of employing real world data to generate evidence for Thai decision makers. Using a case study of endorsing a new rehabilitation policy for stroke patients, results are presented on cost-effectiveness and value of implementation in terms of net monetary benefit to the Thai MOPH.

Results suggest that improvements in health care facilities that need to complement health care workforce still need to be made for stroke care. Mortality rates from real-word data showed a decreasing trend and receiving rehabilitation was associated with a decrease in the risk of mortality and costs; although, low accessibility to rehabilitation was observed.

Using a societal perspective, the new rehabilitation policy in Thailand is currently not cost-effective. This suggests that the Thai MOPH should collaborate with all health insurance schemes, as health purchasers, in order to enhance the provision of stroke care, especially in the remote settings. This should be aimed at either the effectiveness of or the costs related to the rehabilitation programme. Importantly, supportive systems, especially health information systems and linkage between health care facilities/organisations, is vital to ensure continuity of care along the stroke care pathway.

Reference

1. Tangcharoensathien V, Limwattananon S, Patcharanarumol W, Thammatacharee J, Jongudomsuk P, Sirilak S. Achieving universal health coverage goals in Thailand: the vital role of strategic purchasing. Health Policy and Planning. 2014;30(9):1152-61.
2. Pianghatai Ingun, Chirod Narkpaichit, Prasit Boongerd. Thailand health information system improvement through universal health coverage implementation. Journal of the Thai Medical Informatics Association. 2015;2:137-47.
3. Khampang R, Tantivess S, Teerawattananon Y, Chootipongchaivat S, Pattanapesaj J, Butchon R, et al. Pay-for-performance in resource-constrained settings: Lessons learned from Thailand?s Quality and Outcomes Framework [version 1; peer review: 1 approved, 1 approved with reservations]. F1000Research. 2016;5(2700).
4. Viroj NaRanong, Anchana NaRanong, Sornchai Treamworakul, Sasiwooth Wongmonta. Universal health coverage schemes in Thailand 2002-2003. Bangkok: Thailand Development Research Institute; 2005.
5. Patcharanarumol W, Panichkriangkrai W, Sommanuttaweechai A, Hanson K, Wanwong Y, Tangcharoensathien V. Strategic purchasing and health system efficiency: A comparison of two financing schemes in Thailand. PLOS ONE. 2018;13(4):e0195179.
6. Bureau of Health Administration. Service plan strategy 2018 - 2022. Nonthaburi: Office of the Permanent Secretary, Ministry of Public Health; 2016.
7. Japan International Cooperation Agency (JICA) Research Institute, Saitama University and Thammasat University. Case studies of social infrastructure demand estimates in Indonesia and Thailand 2018. Available from: https://www.jica.go.jp/jica-ri/publication/booksandreports/20180831_02.html.
8. Jongudomsuk P, Srithamrongsawat S, Patcharanarumol W, Limwattananon S, Pannarunothai S, Vapatanavong P, et al. The Kingdom of Thailand Health System Review. Vol.5 No.5. Manila: World Health Organization, Regional Office for the Western Pacific. 2015.
9. Strategy and Planning Division. Public health resource 2018. Nonthaburi, Thailand: Permanent Secretary Offices, Ministry of Public Health, Thailand; 2018.
10. Donkor ES. Stroke in the 21st Century: A Snapshot of the Burden, Epidemiology, and Quality of Life. Stroke Research and Treatment. 2018;2018:3238165.
11. Boden-Albala B, Appleton N, Schram B. Chapter 1 - Stroke Epidemiology and Prevention. In: Wilson R, Raghavan P, editors. Stroke Rehabilitation: Elsevier; 2019. p. 1-21.
12. Yiengprugsawan V, Healy J, Kendig H. Health system responses to population ageing and noncommunicable diseases in Asia. Comparative Country Studies, Volume 2, Number 2, 2016 ed. New Delhi: World Health Organization. Regional Office for South-East Asia; 2016.
13. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. Lancet. 2010;376(9735):112-23.
14. Johnson CO, Nguyen M, Roth GA, Nichols E, Alam T, Abate D, et al. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet Neurology. 2019;18(5):439-58.

15. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1204-22.
16. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. Lancet. 2016;388(10046):761-75.
17. Hanchaiphiboolkul S, Poungvarin N, Nidhinandana S, Suwanwela NC, Puthkhao P, Towanabut S, et al. Prevalence of stroke and stroke risk factors in Thailand: Thai Epidemiologic Stroke (TES) Study. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2011;94(4):427-36.
18. Kongbunkiat K, Kasemsap N, Thepsuthammarat K, Tiamkao S, Sawanyawisuth K. National data on stroke outcomes in Thailand. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2015;22(3):493-7.
19. Suwanwela NC. Stroke Epidemiology in Thailand. J Stroke. 2014;16(1):1-7.
20. Burden of Disease Research Program. Burden of diseases and injuries of Thai population in 2014. Nonthaburi: International Health Policy Program; 2017.
21. Strategy and Planning Division. Public health statistics 2021. Nonthaburi: Ministry of Public Health; 2021. 156 p.
22. Pornpatr A. Dharmasaroja, Disya Ratanakorn, Samart Nidhinandana, Sirintara Singhara Na Ayudhaya, Anchalee Churojana, Sureerat Suwatcharangkoon, et al. Thai guidelines of endovascular treatment in patients with acute ischemic stroke. J Thai Stroke Soc. 2016;15 (Suppl 1):S9-S27.
23. Prasat Neurological Institute. Clinical Practice Guidelines for Ischemic Stroke. 32 ed. Bangkok2012. 55 p.
24. Prasat Neurological Institute. Clinical Practice Guidelines for Hemorrhagic Stroke. Bangkok: Tanapress; 2012. 72 p.
25. Prasat Neurological Institute. Clinical Practice Guidelines for Stroke Rehabilitation. 3 ed. Bangkok: Tanapress; 2016. 138 p.
26. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2018;49(3):e46-e99.
27. Suwanwela NC, Chutinet A, Kijpaisalratana N. Thrombolytic Treatment in Thailand. Journal of Stroke Medicine. 2018;1(1):41-4.
28. Wongwiangjunt S, Kommoltri C, Poungvarin N, Nilanont Y. Stroke awareness and factors influencing hospital arrival time: a prospective observational study. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2015;98(3):260-4.
29. Muengtaweepongsa S, Hunghok W, Harnirattisai T. Poor recognition of prompted treatment seeking even with good knowledge of stroke warning signs contribute to delayed arrival of acute ischemic stroke patients in Thailand. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2014;23(5):498-52.
30. Bureau of inspection and evaluation. Results of inspection and evaluation fiscal year 2018: first round Nonthaburi: The Office of Permanent Secretary, Ministry of Public Health; 2018 [
31. Saengsuwan J, Suangpho P. Self-perceived and Actual Risk of Further Stroke in Patients with Recurrent Stroke or Recurrent Transient Ischemic Attack

in Thailand. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2019;28(3):632-9.
32. Kijpaisalratana N, Chutinet A, Akarathanawat W, Vongvasinkul P, Suwanwela NC. Outcomes of thrombolytic therapy in acute ischemic stroke: mothership, drip-and-ship, and ship-and-drip paradigms. BMC neurology. 2020;20(1):45.
33. Tiamkao S. Development of the stroke service system in the 7th health zone (Roi et, Khon kaen, Maha sarakham and Kalasin province). Journal of the Medical Association of Thailand. 2019;18(1):25-41.
34. Lambrinos A, Schaink AK, Dhalla I, Krings T, Casaubon LK, Sikich N, et al. Mechanical Thrombectomy in Acute Ischemic Stroke: A Systematic Review. Can J Neurol Sci. 2016;43(4):455-60.
35. Tan C-C, Wang H-F, Ji J-L, Tan M-S, Tan L, Yu J-T. Endovascular Treatment Versus Intravenous Thrombolysis for Acute Ischemic Stroke: a Quantitative Review and Meta-Analysis of 21 Randomized Trials. Molecular Neurobiology. 2017;54(2):1369-78.
36. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2021;52(7):e364-e467.
37. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2019;50(12):e344-e418.
38. Wu X, Khunte M, Gandhi D, Sanelli P, Forman HP, Malhotra A. A systematic review of cost-effectiveness analyses on endovascular thrombectomy in ischemic stroke patients. Eur Radiol. 2022;32(6):3757-66.
39. De Rubeis G, Fabiano S, Bertaccini L, Wlderk A, Pezzella FR, Anticoli S, et al. Is Mechanical Thrombectomy or Thrombolysis Universally Cost-Effective? A Systematic Review of the Literature. World Neurosurg. 2023;169:e29-e39.
40. Dharmasaroja P, Ratanakorn D, Nidhinandana S, Singhara Na Ayudhaya S, et al. 2019 Thai guidelines of endovascular treatment in patients with acute ischemic stroke. J Thai Stroke Soc. 2019;18(2):52-75.
41. National Health Security Office. Annual report 2018. Bangkok. 2018.
42. Candio P, Violato M, Luengo-Fernandez R, Leal J. Cost-effectiveness of home-based stroke rehabilitation across Europe: A modelling study. Health Policy. 2022;126(3):183-9.
43. Bureau of inspection and evaluation. Results of inspection and evaluation fiscal year 2021 (second round): Intermediate Care Nonthaburi: The Office of Permanent Secretary, Ministry of Public Health; 2021 [
44. Langhorne P, Ramachandra S. Organized inpatient (Stroke Unit) care for Stroke. Stroke. 2020;51(12):e349-e50.
45. Khiaocharoen O., Pannarunothai S., Riewpaiboon W., Zungsontiporn C. Rehabilitation service development for sub-acute and non-acute patients under the universal coverage scheme in Thailand. Journal of Health Science. 2015;24(3):493-509.
46. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, et al. Guidelines for Adult Stroke Rehabilitation and Recovery. Stroke. 2016;47(6):e98-e169.
47. Bowker LK, Price JD, Smith SC, editors. Chapter 4 Rehabilitation2006.

48. Lee KB, Lim SH, Kim KH, Kim KJ, Kim YR, Chang WN, et al. Six-month functional recovery of stroke patients: a multi-time-point study. International Journal of Rehabilitation Research. 2015;38(2):173-80.
49. Yagi M, Yasunaga H, Matsui H, Morita K, Fushimi K, Fujimoto M, et al. Impact of Rehabilitation on Outcomes in Patients With Ischemic Stroke. Stroke. 2017;48(3):740-6.
50. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. Lancet. 2011;377(9778):1693-702.
51. Intermediate care service plan board. Guideline for intermediate care (Service Plan). Health Administration Division, Ministry of Public Health, Thailand: Born To Be Publishing; 2019. 72 p.
52. Rajborirug K, Tumviriyakul H, Suwanno J. Effects of Stroke Unit Care in Acute Ischemic Stroke Patient Ineligible for Thrombolytic Treatment. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2017;100(4):410-7.
53. Thira Woratanarat, Patarawan Woratanarat, Charupa Lekthipa. Primary health care systems (PRIMASYS): case study from Thailand. Geneva: World Health Organization; 2017. 36 p.
54. Khiaocharoen O, Pannarunothai S, Riewpaiboon W, Ingsrisawang L, Teerawattananon Y. Economic Evaluation of Rehabilitation Services for Inpatients with Stroke in Thailand: A Prospective Cohort Study. Value in Health Regional Issues. 2012;1(1):29-35.
55. Bureau of inspection and evaluation. Results of second round inspection and evaluation fiscal year 2020 Nonthaburi: The Office of Permanent Secretary, Ministry of Public Health; 2021 [
56. Bureau of inspection and evaluation. Results of inspection and evaluation fiscal year 2018: second round Nonthaburi: The Office of Permanent Secretary, Ministry of Public Health; 2018 [
57. Limwattananon Chulaporn, Tiamkoa Somsak, Chonsophon Suratchada, Waleekhachonloet On-anong, Rattanachotpanit Thananan. Differences in stroke care and outcomes across health insurance schemes: a quantitative analysis. Nonthaburi: Health Insurance System Research Office; 2014.
58. Limwattananon S. Acute myocardial infarction, AMI and Ischemic and hemorrhagic strockes. Health Insurance System Research Office; 2012.
59. Vongmongkol V, Tangcharoensthien V, Greetong T, Mcneil E, Chongsuvivatwong V. Trend in recombinant tissue plasminogen activator (rtPA) use for ischemic stroke in Thailand: geographic inequality, cost of treatment and impact on 30-day case fatality rate. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2018;101(7):875-81.
60. Langhorne P, O'Donnell MJ, Chin SL, Zhang H, Xavier D, Avezum A, et al. Practice patterns and outcomes after stroke across countries at different economic levels (INTERSTROKE): an international observational study. The Lancet. 2018;391(10134):2019-27.
61. Charoensuk V., Kongsin S., Jiamton S., Yuadyoung M. Cost-effectiveness analysis of rehabilitation services For stroke patients in Pranangklao hospital, Fiscal year 2011-2012. Journal of Health Science. 2015;24(3):563-73.
62. Srisubat A, O-charot L, Loharjun B, Siriwatvejakul U, Kuptniratsaikul V, Opachalermphan S. Cost-effectiveness of intermediate care (inpatient) in post-acute stroke compared with out-patient rehabilitation program. Journal of the Department of Medical Services. 2019;44(5):167-73.
63. Worakijthamrongchai T, Thawornchaisit P, Kongsin S. Cost-utility analysis of mechanical thrombectomy for acute ischemic stroke. Journal of Health Systems Research. 2022;16(4):472-87.

64. Hankey GJ, Jamrozik K, Broadhurst RJ, Forbes S, Anderson CS. Long-Term Disability After First-Ever Stroke and Related Prognostic Factors in the Perth Community Stroke Study, 1989–1990. Stroke. 2002;33(4):1034-40.
65. Chuenklin T., Rungnoei N., Naphas K, Benjaporn S, Khotthong K, Girdwichai W, et al. An Assessment on the Ministry of Public Health's Intermediate Care Policy: A Quantitative Analysis. Journal of Health Systems Research. 2021;15(2):183-99.
66. Kaeowichian N, Suthamchai B, Chuenklin T, Rungnoei N, Girdwichai W, Pannarunothai S. Intermediate Care Policy in Thailand: What Should be Done? Journal of Health Science. 2021;30(5):894 - 906.
67. Aljunid SM, Srithamrongsawat S, Chen W, Bae SJ, Pwu R-F, Ikeda S, et al. Health-Care Data Collecting, Sharing, and Using in Thailand, China Mainland, South Korea, Taiwan, Japan, and Malaysia. Value in Health. 2012;15(1, Supplement):S132-S8.
68. National Health Security Office. Annual report 2003. Bangkok. 2004. 71 p.
69. National Health Security Office. Annual report 2004. Bangkok. 2004. 38 p.
70. Milea D, Azmi S, Reginald P, Verpillat P, Francois C. A review of accessibility of administrative healthcare databases in the Asia-Pacific region. Journal of Market Access & Health Policy. 2015;3(1):28076.
71. Ingun P, Narkpaichit C, Laowahutanon T, Rekakanakul R, Pusamang A, Kesthom K. Integrated National Health Information System of HIV/AIDS in Thailand: Case of NAP application. Journal of the Thai Medical Informatics Association. 2015;2:131-36.
72. Tiamkao S, Pranboon S, Thepsuthammarat K, Sawanyawisuth K. Status epilepticus in the elderly patients: A national data study in Thailand. Journal of the neurological sciences. 2017;372:501-5.
73. Butsing N, Mawn BE, Suwannapong N, Tipayamongkholgul M. Long-term survival of stroke patients in Thailand. The Southeast Asian Journal of Tropical Medicine and Public Health. 2018;49(2):322-30.
74. Limwattananon C, Jaratpatthararoj J, Thungthong J, Limwattananon P, Kitkhuandee A. Access to reperfusion therapy and mortality outcomes in patients with ST-segment elevation myocardial infarction under universal health coverage in Thailand. BMC Cardiovascular Disorders. 2020;20(1):121.
75. Sobhonslidsuk A, Poovorawan K, Soonthornworasiri N, Pan-Ngum W, Phaosawasdi K. The incidence, presentation, outcomes, risk of mortality and economic data of drug-induced liver injury from a national database in Thailand: a population-base study. BMC gastroenterology. 2016;16(1):135.
76. Pattanaprateep O, Chuansumrit A, Kongsakon R. Cost-Utility Analysis of Home-Based Care for Treatment of Thai Hemophilia A and B. Value in Health Regional Issues. 2014;3:73-8.
77. Poovorawan K, Treeprasertsuk S, Thepsuthammarat K, Wilairatana P, Kitsahawong B, Phaosawasdi K. The burden of cirrhosis and impact of universal coverage public health care system in Thailand: Nationwide study. Annals of hepatology. 2015;14(6):862-8.
78. Wood AD, Mannu GS, Clark AB, Tiamkao S, Kongbunkiat K, Bettencourt-Silva JH, et al. Rheumatic Mitral Valve Disease Is Associated With Worse Outcomes in Stroke. Stroke. 2016;47(11):2695-701.
79. Veerasarn K, Veerasarn V. Treatment of Brain Tumors in Thailand from 2005 to 2014: Data from the National Health Security Office. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2016;99 Suppl 3:S74-81.
80. Treeprasertsuk S, Poovorawan K, Soonthornworasiri N, Chaiteerakij R, Thanapirom K, Mairiang P, et al. A significant cancer burden and high mortality

of intrahepatic cholangiocarcinoma in Thailand: a nationwide database study. BMC gastroenterology. 2017;17(1):3.
81. Sirikarn P, Pattanittum P, Tiamkao S. One- to 10-year Status Epilepticus Mortality (SEM) score after 30 days of hospital discharge: development and validation using competing risks analysis. BMC neurology. 2019;19(1):307.
82. Barlas RS, Clark AB, Bettencourt-Silva JH, Sawanyawisuth K, Kongbunkiat K, Kasemsap N, et al. Pneumonia and Risk of Serious Adverse Outcomes in Hospitalized Strokes in Thailand. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2019;28(6):1448-54.
83. Thammatacharee N, Suphanchaimat R. Long-Term Projections of Patients Undertaking Renal Replacement Therapy Under the Universal Coverage Scheme in Thailand. Risk Manag Healthc Policy. 2020;13:27-34.
84. Cumming K, Tiamkao S, Kongbunkiat K, Clark AB, Bettencourt-Silva JH, Sawanyawisuth K, et al. Impact of HIV on inpatient mortality and complications in stroke in Thailand: a National Database Study. Epidemiology and infection. 2017;145(6):1285-91.
85. Bureau of inspection and evaluation. Results of inspection and evaluation fiscal year 2019. Nonthaburi: Ministry of Public Health; 2019.
86. Dharmasaroja P. Stroke network [Editorial]. J Thai Stroke Soc. 2015;14(1):2.
87. Prasat Neurological Institute, Department of Medical Services. Standard Stroke Center. Bangkok: Ministry of Public Health, Thailand; 2018. 54 p.
88. Dwyer M, Peterson GM, Gall S, Francis K, Ford KM. Health care providers' perceptions of factors that influence the provision of acute stroke care in urban and rural settings: A qualitative study. SAGE open medicine. 2020;8.
89. Witthayapipopsakul W, Cetthakrikul N, Suphanchaimat R, Noree T, Sawaengdee K. Equity of health workforce distribution in Thailand: an implication of concentration index. Risk Manag Healthc Policy. 2019;12:13-22.
90. NHS National Services Scotland. Scottish Stroke Care Audit, 2011 National Report: Scottish Stroke Improvement Programme Report-2019. Edinburgh 2019.
91. Ringelstein E, Busse O, Ritter M. Current concepts of stroke units in Germany and Europe. Schweizer archiv fur Neurologie und Psychiatrie. 2011;162(4):155-60.
92. Langhorne P, Pollock A, in Conjunction with The Stroke Unit Trialists' Collaboration. What are the components of effective stroke unit care? Age and Ageing. 2002;31(5):365-71.
93. Rac VE, Sahakyan Y, Fan I, Ieraci L, Hall R, Kelloway L, et al. The characteristics of stroke units in Ontario: a pan-provincial survey. BMC health services research. 2017;17(1):154.
94. Tiamkao S, Ienghong K, Cheung LW, Celebi I, Suzuki T, Apiratwarakul K. Stroke Incidence, Rate of Thrombolytic Therapy, Mortality in Thailand from 2009 to 2021. Open Access Macedonian Journal of Medical Sciences. 2022;10(E):110-5.
95. Stolz E, Hamann GF, Kaps M, Misselwitz B. Regional differences in acute stroke admission and thrombolysis rates in the German federal state of Hesse. Dtsch Arztebl Int. 2011;108(36):607-11.
96. Addo J, Bhalla A, Crichton S, Rudd AG, McKevitt C, Wolfe CDA. Provision of acute stroke care and associated factors in a multiethnic population: prospective study with the South London Stroke Register. BMJ. 2011;342:d744.
97. Quain Debbie A, Parsons MW, Loudfoot AR, Spratt NJ, Evans MK, Russell ML, et al. Improving access to acute stroke therapies: a controlled trial of organised pre-hospital and emergency care. Medical Journal of Australia. 2008;189(8):429-33.

98. Bureau of inspection and evaluation. Results of inspection and evaluation fiscal year 2020. Nonthaburi: Ministry of Public Health; 2020.
99. Lau F, Kuziemsky C, editors. Handbook of eHealth Evaluation: An Evidence-based Approach [Internet]. Victoria (BC): University of Victoria; 2017. Available from: https://www.ncbi.nlm.nih.gov/books/NBK481590/.
100. Bowling A, Ebooks Corporation L. Research methods in health: investigating health and health services. Fourth ed. Maidenhead, Berkshire: Open University Press; 2014.
101. Chinchai P, Sirisatayawong P, Jindakum N. Community Integration and Quality of Life: Stroke Survivors as Recipients of Rehabilitation by Village Health Volunteers (VHVs) in Thailand. Occup Ther Health Care. 2020;34(3):277-90.
102. Samuthpongtorn C, Jereerat T, Suwanwela NC. Stroke risk factors, subtypes and outcome in elderly Thai patients. BMC neurology. 2021;21(1):322.
103. Saokaew S, Sugimoto T, Kamae I, Pratoomsoot C, Chaiyakunapruk N. Healthcare Databases in Thailand and Japan: Potential Sources for Health Technology Assessment Research. PLOS ONE. 2015;10(11):e0141993.
104. National Health Security Office. Annual report 2008. Bangkok. 2009. 40 p.
105. National Health Security Office. The management of provider payments in the universal coverage scheme (UCS) in Thailand. Bangkok 2019.
106. National Health Security Office. Audit system for the universal coverage scheme (UCS) in Thailand. Available from: https://eng.nhso.go.th/assets/portals/1/files/9%20UCS%20AUDIT%20System%20INFOGRAPHIC.pdf.
107. Paoin W. Development of ICD-10 Thai Modification in Thailand. Meeting of WHO Collaborating Centres for the Family of the International Classification: Document C406. Geneva, Switzerland: the World Health Organization; 2006 [cited May 9, 2022]. Available from: https://apps.who.int/classifications/apps/icd/meetings/2006meeting/WHOFIC2006 - C406 - Development of ICD-10 Thai Modification in Thailand.pdf.
108. Marcelo AB, Pascual KC, Udayasankaran JG, Allaudin FS, Kijsanayotin B. Chapter 17 - A framework for regional health information systems interoperability: The Asia eHealth Information Network (AeHIN) experience. In: Hovenga E, Grain H, editors. Roadmap to Successful Digital Health Ecosystems: Academic Press; 2022. p. 399-414.
109. Jakob R. Disease Classification. In: Quah SR, editor. International Encyclopedia of Public Health (Second Edition). Oxford: Academic Press; 2017. p. 332-7.
110. Belotti F, Deb P, Manning WG, Norton EC. Twopm: Two-Part Models. The Stata Journal. 2015;15(1):3-20.
111. Charlson M, Pompei P, Alfa KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. Journal of chronic diseases. 1987;40 5:373-83.
112. Thai Casemix Centre, Thai Health Information Standards Development Center, Health Systems Research Institute. The unit cost per disease phase 1 (Third year). Bangkok: Thai Casemix Centre; 2020.
113. National Health Security Office. Annual report 2019. Bangkok. 2020. 235 p.
114. National Health Security Office. Annual Report 2020. Bangkok: Sahamitr Printing & Publishing Company Limited; 2021. 260 p.
115. Khiaocharoen O, Zungsontiporn C, Cheyprasert S, Pannarunothai S. Relative Weight for Thai Diagnosis Related Groups Version 6.2. Journal of Health Science. 2019;28(3):518-32.

116. Khiaocharoen O, Zungsontiporn C, Cheyprasert S, Pannarunothai S. Relative Weight Adjustment by Length of Stay for Thai Diagnosis Related Groups, Version 6.2. Journal of Health Science. 2021;30(1):151-61.
117. Information Service Division Scotland. ISD Scotland Data Dictionary. Edinburgh: Public Health Scotland; [cited Jan 5, 2022]. Available from: https://www.ndc.scot.nhs.uk/Dictionary-A-Z/Definitions/index.asp?Search=C&ID=170&Title=Continuous%20Inpatient%20Stay.
118. Mihaylova B, Briggs A, O'Hagan A, Thompson SG. Review of statistical methods for analysing healthcare resources and costs. Health Econ. 2011;20(8):897-916.
119. Manning WG, Basu A, Mullahy J. Generalized modeling approaches to risk adjustment of skewed outcomes data. J Health Econ. 2005;24(3):465-88.
120. Clarke P, Gray A, Legood R, Briggs A, Holman R. The impact of diabetes-related complications on healthcare costs: results from the United Kingdom Prospective Diabetes Study (UKPDS Study No. 65). Diabet Med. 2003;20(6):442-50.
121. Yousufuddin M, Moriarty JP, Lackore KA, Zhu Y, Peters JL, Doyle T, et al. Initial and subsequent 3-year cost after hospitalization for first acute ischemic stroke and intracerebral hemorrhage. Journal of the neurological sciences. 2020;419:117181.
122. Diehr P, Yanez D, Ash A, Hornbrook M, Lin DY. Methods for analyzing health care utilization and costs. Annu Rev Public Health. 1999;20:125-44.
123. Kirkwood BR, Sterne JAC, Ebooks Corporation L. Essential medical statistics, 2nd Edition. 2nd ed. Malden, MA: Blackwell Science; 2003.
124. Duan N. Smearing Estimate: A Nonparametric Retransformation Method. Journal of the American Statistical Association. 1983;78(383):605-10.
125. Barber J, Thompson S. Multiple regression of cost data: use of generalised linear models. J Health Serv Res Policy. 2004;9(4):197-204.
126. Glick HA, Doshi JA, Sonnad SS. Economic Evaluation in Clinical Trials, 2nd Edition. Australian and New Zealand journal of public health. 2015;39 6:594.
127. Polsky D, Glick H. Costing and cost analysis in randomized controlled trials: caveat emptor. Pharmacoeconomics. 2009;27(3):179-88.
128. Pagano E, Petrelli A, Picariello R, Merletti F, Gnavi R, Bruno G. Is the choice of the statistical model relevant in the cost estimation of patients with chronic diseases? An empirical approach by the Piedmont Diabetes Registry. BMC health services research. 2015;15(1):582.
129. Klieštik T, Kočišová K, Mišanková M. Logit and Probit Model used for Prediction of Financial Health of Company. Procedia Economics and Finance. 2015;23:850-5.
130. Harrell FE. Regression modeling strategies : with applications to linear models, logistic and ordinal regression, and survival analysis. 2015.
131. Khiaocharoen O, Pannarunothai S, Zungsontiporn C. Cost of acute and sub-acute care for stroke patients. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2012;95(10):1266-77.
132. Sribundit N, Riewpaiboon A, Chaikledkaew U, Stewart JF, Tantirittisak T, Hanchaipiboolkul S, editors. Cost of acute care for ischemic stroke in Thailand.2017.
133. Ma Z, Deng G, Meng Z, Wu H. Hospitalization Expenditures and Out-Of-Pocket Expenses in Patients With Stroke in Northeast China, 2015–2017: A Pooled Cross-Sectional Study. Frontiers in Pharmacology. 2021;11(2455).

134. Girotra T, Lekoubou A, Bishu KG, Ovbiagele B. A contemporary and comprehensive analysis of the costs of stroke in the United States. Journal of the neurological sciences. 2020;410:116643.
135. Stahmeyer JT, Stubenrauch S, Geyer S, Weissenborn K, Eberhard S. The Frequency and Timing of Recurrent Stroke: An Analysis of Routine Health Insurance Data. Dtsch Arztebl Int. 2019;116(42):711-7.
136. Skajaa N, Adelborg K, Horváth-Puhó E, Rothman KJ, Henderson VW, Thygesen LC, et al. Risks of Stroke Recurrence and Mortality After First and Recurrent Strokes in Denmark: A Nationwide Registry Study. Neurology. 2021:10.1212/WNL.0000000000013118.
137. Coull AJ, Rothwell PM. Underestimation of the Early Risk of Recurrent Stroke. Stroke. 2004;35(8):1925-9.
138. Mohan KM, Crichton SL, Grieve AP, Rudd AG, Wolfe CDA, Heuschmann PU. Frequency and predictors for the risk of stroke recurrence up to 10 years after stroke: the South London Stroke Register. Journal of Neurology, Neurosurgery & Psychiatry. 2009;80(9):1012-8.
139. Han J, Mao W, Ni J, Wu Y, Liu J, Bai L, et al. Rate and Determinants of Recurrence at 1 Year and 5 Years After Stroke in a Low-Income Population in Rural China. Front Neurol. 2020;11:2.
140. Lewsey J, Jhund PS, Gillies M, Chalmers JWT, Redpath A, Briggs A, et al. Temporal trends in hospitalisation for stroke recurrence following incident hospitalisation for stroke in Scotland. BMC Medicine. 2010;8(1):23.
141. Kleinbaum DG, Klein M. Survival Analysis A Self-Learning Text, Third Edition. 3rd ed. 2012. ed. New York, NY: Springer New York; 2012.
142. Latimer NR. Survival Analysis for Economic Evaluations Alongside Clinical Trials—Extrapolation with Patient-Level Data:Inconsistencies, Limitations, and a Practical Guide. Medical Decision Making. 2013;33(6):743-54.
143. Gray A, Clarke PM, Wolstenholme JL, Wordsworth S. Applied Methods of Cost-effectiveness Analysis in Healthcare: Oxford University Press; 2010.
144. Burden of Disease Research Program Thailand. Health Adjusted Life Expectancy: HALE. Nonthaburi: International Health Policy Program; 2017.
145. Venketasubramanian N, Yin A. Hospital costs for stroke care in Singapore. Cerebrovasc Dis. 2000;10(4):320-6.
146. Dodel RC, Haacke C, Zamzow K, Paweilik S, Spottke A, Rethfeldt M, et al. Resource utilization and costs of stroke unit care in Germany. Value Health. 2004;7(2):144-52.
147. Zhang H, Yin Y, Zhang C, Zhang D. Costs of hospitalization for stroke from two urban health insurance claims data in Guangzhou City, southern China. BMC health services research. 2019;19(1):671.
148. Christensen MC, Previgliano I, Capparelli FJ, Lerman D, Lee WC, Wainsztein NA. Acute treatment costs of intracerebral hemorrhage and ischemic stroke in Argentina. Acta Neurol Scand. 2009;119(4):246-53.
149. Kaur P, Kwatra G, Kaur R, Pandian JD. Cost of stroke in low and middle income countries: a systematic review. Int J Stroke. 2014;9(6):678-82.
150. Yoneda Y, Okuda S, Hamada R, Toyota A, Gotoh J, Watanabe M, et al. Hospital cost of ischemic stroke and intracerebral hemorrhage in Japanese stroke centers. Health Policy. 2005;73(2):202-11.
151. Barber SL, Lorenzoni L, Ong P. Price setting and price regulation in health care: lessons for advancing universal health coverage. Geneva: World Health Organization; 2019 2019.
152. Kammuang-lue P, Kovindha A. A 3-year retrospective study on total admission charge of spinal cord injured patients with pressure ulcer at

rehabilitation ward, Maharaj Nakorn Chiang Mai Hospital. J Thai Rehabli Med. 2012;22:58-63.
153. Harnphadungkit K, Puprasert C. Hospital charges and diagnosis related groups (DRGs) payment of inpatients at rehabilitation ward, Siriraj hospital. J Thai Rehabil Med. 2016;26(3):111-18.
154. Subacute rehabilitation committee. Subacute rehabilitation and lesson learned. Nonthaburi2016.
155. Venketasubramanian N, Yoon BW, Pandian J, Navarro JC. Stroke Epidemiology in South, East, and South-East Asia: A Review. J Stroke. 2017;19(3):286-94.
156. Cha Y-J. The Economic Burden of Stroke Based on South Korea's National Health Insurance Claims Database. International Journal of Health Policy and Management. 2018;7(10):904-9.
157. Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RAL, McNeil JJ, et al. Lifetime cost of stroke subtypes in Australia. Stroke. 2003;34(10):2502-7.
158. Andersen KK, Olsen TS, Dehlendorff C, Kammersgaard LP. Hemorrhagic and Ischemic Strokes Compared. Stroke. 2009;40(6):2068-72.
159. Salvadori E, Papi G, Insalata G, Rinnoci V, Donnini I, Martini M, et al. Comparison between Ischemic and Hemorrhagic Strokes in Functional Outcome at Discharge from an Intensive Rehabilitation Hospital. Diagnostics (Basel). 2020;11(1).
160. Perna R, Temple J. Rehabilitation Outcomes: Ischemic versus Hemorrhagic Strokes. Behavioural Neurology. 2015;2015:891651.
161. Chiu D, Peterson L, Elkind MSV, Rosand J, Gerber LM, Silverstein MD. Comparison of outcomes after intracerebral hemorrhage and ischemic stroke. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2010;19(3):225-9.
162. Zhang J, Song S, Zhao Y, Ma G, Jin Y, Zheng ZJ. Economic burden of comorbid chronic conditions among survivors of stroke in China: 10-year longitudinal study. BMC health services research. 2021;21(1):978.
163. Ofori-Asenso R, Zomer E, Chin KL, Si S, Markey P, Tacey M, et al. Effect of Comorbidity Assessed by the Charlson Comorbidity Index on the Length of Stay, Costs and Mortality among Older Adults Hospitalised for Acute Stroke. Int J Environ Res Public Health. 2018;15(11).
164. Ding R, Zhu D, Ma Y, Shi X, He P. Comparison of health service use and costs in stroke with and without comorbidities: a cross-sectional analysis using China urban medical claims data. BMJ Open. 2020;10(12):e037032.
165. Barber M, Roditi G, Stott DJ, Langhorne P. Poor outcome in primary intracerebral haemorrhage: results of a matched comparison. Postgraduate Medical Journal. 2004;80(940):89-92.
166. Chaikledkaew U, Pongchareonsuk P, Chaiyakunapruk N, Ongphiphadhanakul B. Factors Affecting Health-Care Costs and Hospitalizations among Diabetic Patients in Thai Public Hospitals. Value in Health. 2008;11:S69-S74.
167. Zhang J, Wang Y, Wang G-N, Sun H, Sun T, Shi J-Q, et al. Clinical factors in patients with ischemic versus hemorrhagic stroke in East China. World J Emerg Med. 2011;2(1):18-23.
168. Ojaghihaghighi S, Vahdati SS, Mikaeilpour A, Ramouz A. Comparison of neurological clinical manifestation in patients with hemorrhagic and ischemic stroke. World J Emerg Med. 2017;8(1):34-8.
169. Toyoda K, Yoshimura S, Nakai M, Koga M, Sasahara Y, Sonoda K, et al. Twenty-Year Change in Severity and Outcome of Ischemic and Hemorrhagic Strokes. JAMA Neurology. 2022;79(1):61-9.

170. Guo Y, Wang H, Tao T, Tian Y, Wang Y, Chen Y, et al. Determinants and Time Trends for Ischaemic and Haemorrhagic Stroke in a Large Chinese Population. PLOS ONE. 2016;11(9):e0163171.
171. Tiamkao S. Development of the stroke service system in the 7th Health Zone (Roi Et, Khon Kaen, Maha Sarakham and Kalasin province). Journal of Thai Stroke Society. 2019;18(1):25-41.
172. Dehlendorff C, Andersen KK, Olsen TS. Sex Disparities in Stroke: Women Have More Severe Strokes but Better Survival Than Men. J Am Heart Assoc. 2015;4(7):e001967.
173. Sun Y, Lee SH, Heng BH, Chin VS. 5-year survival and rehospitalization due to stroke recurrence among patients with hemorrhagic or ischemic strokes in Singapore. BMC neurology. 2013;13(1):133.
174. Coleman ER, Moudgal R, Lang K, Hyacinth HI, Awosika OO, Kissela BM, et al. Early Rehabilitation After Stroke: a Narrative Review. Current Atherosclerosis Reports. 2017;19(12):59.
175. Momosaki R, Yasunaga H, Kakuda W, Matsui H, Fushimi K, Abo M. Very Early versus Delayed Rehabilitation for Acute Ischemic Stroke Patients with Intravenous Recombinant Tissue Plasminogen Activator: A Nationwide Retrospective Cohort Study. Cerebrovascular Diseases. 2016;42(1-2):41-8.
176. Wang W, Wei M, Cheng Y, Zhao H, Du H, Hou W, et al. Safety and Efficacy of Early Rehabilitation After Stroke Using Mechanical Thrombectomy: A Pilot Randomized Controlled Trial. Frontiers in Neurology. 2022;13.
177. Legg LA, Lewis SR, Schofield-Robinson OJ, Drummond A, Langhorne P. Occupational Therapy for Adults With Problems in Activities of Daily Living After Stroke. Stroke. 2017;48(11):e321-e2.
178. Boesen F, Nørgaard M, Trénel P, Rasmussen PV, Petersen T, Løvendahl B, et al. Longer term effectiveness of inpatient multidisciplinary rehabilitation on health-related quality of life in MS patients: a pragmatic randomized controlled trial - The Danish MS Hospitals Rehabilitation Study. Mult Scler. 2018;24(3):340-9.
179. Hopman WM, Verner J. Quality of Life During and After Inpatient Stroke Rehabilitation. Stroke. 2003;34(3):801-5.
180. Brusco NK, Taylor NF, Watts JJ, Shields N. Economic evaluation of adult rehabilitation: a systematic review and meta-analysis of randomized controlled trials in a variety of settings. Arch Phys Med Rehabil. 2014;95(1):94-116.e4.
181. Slot KB, Berge E, Dorman P, Lewis S, Dennis M, Sandercock P. Impact of functional status at six months on long term survival in patients with ischaemic stroke: prospective cohort studies. Bmj. 2008;336(7640):376-9.
182. Norrving B, Barrick J, Davalos A, Dichgans M, Cordonnier C, Guekht A, et al. Action Plan for Stroke in Europe 2018–2030. European Stroke Journal. 2018;3(4):309-36.
183. Reiwpaiboon A. Standard Cost Lists for Health Economic Evaluation in Thailand. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2014;97:S127-34.
184. Riewpaiboon A. Measurement of costs for health economic evaluation. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2014;97 Suppl 5:S17-26.
185. Liu F, Demosthenes P. Real-world data: a brief review of the methods, applications, challenges and opportunities. BMC Medical Research Methodology. 2022;22(1):287.
186. Ung D, Kim J, Thrift AG, Cadilhac DA, Andrew NE, Sundararajan V, et al. Promising Use of Big Data to Increase the Efficiency and Comprehensiveness of Stroke Outcomes Research. Stroke. 2019;50(5):1302-9.

187. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009;62(10):1006-12.
188. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of Clinical Epidemiology. 2009;62(10):e1-e34.
189. Schardt C, Adams MB, Owens T, Keitz S, Fontelo P. Utilization of the PICO framework to improve searching PubMed for clinical questions. BMC Medical Informatics and Decision Making. 2007;7.
190. Chaikledkaew U, Kittrongsiri K. Guidelines for health technology assessment in Thailand (Second edition) - the development process. Journal of Medical Association of Thailand. 2014;97(Suppl.5).
191. Wijnen B, Van Mastrigt G, Redekop WK, Majoie H, De Kinderen R, Evers S. How to prepare a systematic review of economic evaluations for informing evidence-based healthcare decisions: data extraction, risk of bias, and transferability (part 3/3). Expert review of pharmacoeconomics & outcomes research. 2016;16(6):723-32.
192. Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ,. Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022): Cochrane; 2022. Available from: www.training.cochrane.org/handbook.
193. Ramsey SD, Willke RJ, Glick H, Reed SD, Augustovski F, Jonsson B, et al. Cost-Effectiveness Analysis Alongside Clinical Trials II—An ISPOR Good Research Practices Task Force Report. Value in Health. 2015;18(2):161-72.
194. Evers SM, Hiligsmann M, Adarkwah CC. Risk of bias in trial-based economic evaluations: identification of sources and bias-reducing strategies. Psychology & health. 2015;30(1):52-71.
195. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. BMJ. 1996;313(7052):275-83.
196. Chiou C-F, Hay JW, Wallace JF, Bloom BS, Neumann PJ, Sullivan SD, et al. Development and Validation of a Grading System for the Quality of Cost-Effectiveness Studies. Medical Care. 2003;41(1):32-44.
197. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. Value in Health. 2013;16(2):231-50.
198. Min C, Xue M, Haotian F, Jialian L, Lingli Z. An overview of the characteristics and quality assessment criteria in systematic review of pharmacoeconomics. PLOS ONE. 2021;16(2):e0246080.
199. Philips Z, Bojke L, Sculpher M, Claxton K, Golder S. Good practice guidelines for decision-analytic modelling in health technology assessment: a review and consolidation of quality assessment. Pharmacoeconomics. 2006;24(4):355-71.
200. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. International journal of technology assessment in health care. 2005;21(2):240-5.
201. Langer A. A framework for assessing Health Economic Evaluation (HEE) quality appraisal instruments. BMC health services research. 2012;12(1):253.
202. Palmer R, Enderby P, Cooper C, Latimer N, Julious S, Paterson G, et al. Computer therapy compared with usual care for people with long-standing

aphasia poststroke: A pilot randomized controlled trial. Stroke. 2012;43(7):1904-11.
203. Sampson C, James M, Whitehead P, Drummond A. An introduction to economic evaluation in occupational therapy: cost-effectiveness of pre-discharge home visits after stroke (HOVIS). British Journal of Occupational Therapy. 2014;77(7):330-5.
204. Forster A, Young J, Chapman K, Nixon J, Patel A, Holloway I, et al. Cluster Randomized Controlled Trial: Clinical and Cost-Effectiveness of a System of Longer-Term Stroke Care. Stroke. 2015;46(8):2212-9.
205. Sackley CM, Walker MF, Burton CR, Watkins CL, Mant J, Roalfe AK, et al. An occupational therapy intervention for residents with stroke-related disabilities in UK care homes (OTCH): Cluster randomised controlled trial with economic evaluation. Health Technology Assessment. 2016;20(15):1-137.
206. Rodgers H, Howel D, Bhattarai N, Cant R, Drummond A, Ford GA, et al. Evaluation of an extended stroke rehabilitation service (EXTRAS) a randomized controlled trial and economic analysis. Stroke. 2019;50(12):3561-8.
207. Allen L, John-Baptiste A, Meyer M, Richardson M, Speechley M, Ure D, et al. Assessing the impact of a home-based stroke rehabilitation programme: a cost-effectiveness study. Disability and rehabilitation. 2019;41(17):2060-5.
208. Tam A, Mac S, Isaranuwatchai W, Bayley M. Cost-effectiveness of a high-intensity rapid access outpatient stroke rehabilitation program. International journal of rehabilitation research. 2019;Internationale Zeitschrift fur Rehabilitationsforschung. Revue internationale de recherches de readaptation. 42(1):56-62.
209. Chen CM, Yang YH, Lee M, Chen KH, Huang SS. Economic evaluation of transferring first-stroke survivors to rehabilitation wards: A 10-year longitudinal, population-based study. Topics in Stroke Rehabilitation. 2020;27(1):8-14.
210. Tung YJ, Lin WC, Lee LF, Lin HM, Ho CH, Chou W. Comparison of Cost-Effectiveness between Inpatient and Home-Based Post-Acute Care Models for Stroke Rehabilitation in Taiwan. Int J Environ Res Public Health. 2021;18(8).
211. Gao L, Sheppard L, Wu O, Churilov L, Mohebbi M, Collier J, et al. Economic evaluation of a phase III international randomised controlled trial of very early mobilisation after stroke (AVERT). BMJ Open. 2019;9 (5) (no pagination)(e026230).
212. van Mastrigt GAPG, van Eeden M, van Heugten CM, Tielemans N, Schepers VPM, Evers SMAA. A trial-based economic evaluation of the Restore4Stroke self-management intervention compared to an education-based intervention for stroke patients and their partners. BMC health services research. 2020;20(1):294.
213. Louw Q, Twizeyemariya A, Grimmer K, Leibbrandt D. Estimating the costs and benefits of stroke rehabilitation in South Africa. Journal of Evaluation in Clinical Practice. 2020;26(4):1181-7.
214. Llorens R, Noe E, Colomer C, Alcaniz M. Effectiveness, usability, and cost-benefit of a virtual reality-based telerehabilitation program for balance recovery after stroke: A randomized controlled trial. Archives of Physical Medicine and Rehabilitation. 2015;96(3):418-25.e2.
215. Abdul Aziz AF, Mohd Nordin NA, Muhd Nur A, Sulong S, Aljunid SM. The integrated care pathway for managing post stroke patients (iCaPPS(©)) in public primary care Healthcentres in Malaysia: impact on quality adjusted life years (QALYs) and cost effectiveness analysis. BMC geriatrics. 2020;20(1):70.
216. Nagayama H, Tomori K, Ohno K, Takahashi K, Nagatani R, Izumi R, et al. Cost effectiveness of the occupation-based approach for subacute stroke

patients: Result of a randomized controlled trial. Topics in Stroke Rehabilitation. 2017;24(5):337-44.
217. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes, 4rd Edition. Oxford: Oxford University Press; 2015.
218. Taylor P, Humphreys L, Swain I. The long-term cost-effectiveness of the use of Functional Electrical Stimulation for the correction of dropped foot due to upper motor neuron lesion. Journal of Rehabilitation Medicine. 2013;45(2):154-60.
219. Logan PA, Armstrong S, Avery TJ, Barer D, Barton GR, Darby J, et al. Rehabilitation aimed at improving outdoor mobility for people after stroke: a multicentre randomised controlled study (the Getting out of the House Study). Health technology assessment (Winchester, England). 2014;18(29):vii-viii, 1-113.
220. Adie K, Schofield C, Berrow M, Wingham J, Humfryes J, Pritchard C, et al. Does the use of Nintendo Wii SportsTM improve arm function? Trial of WiiTM in Stroke: a randomized controlled trial and economics analysis. Clinical rehabilitation. 2017;31(2):173-85.
221. Collins M, Clifton E, Wijck FV, Mead GE. Cost-effectiveness of physical fitness training for stroke survivors. The journal of the Royal College of Physicians of Edinburgh. 2018;48(1):62-8.
222. Fernandez-Garcia C, Ternent L, Homer TM, Rodgers H, Bosomworth H, Shaw L, et al. Economic evaluation of robot-assisted training versus an enhanced upper limb therapy programme or usual care for patients with moderate or severe upper limb functional limitation due to stroke: results from the RATULS randomised controlled trial. BMJ Open. 2021;11(5):e042081.
223. Wagner TH, Lo AC, Peduzzi P, Bravata DM, Huang GD, Krebs HI, et al. An economic analysis of robot-assisted therapy for long-term upper-limb impairment after stroke. Stroke. 2011;42(9):2630-2.
224. Hornby TG, Rafferty MR, Pinto D, French D, Jordan N. Cost-Effectiveness of High-intensity Training vs Conventional Therapy for Individuals With Subacute Stroke. Arch Phys Med Rehabil. 2022;103(7s):S197-s204.
225. Chan B. Effect of increased intensity of physiotherapy on patient outcomes after stroke: An economic literature review and cost-effectiveness analysis. Ontario Health Technology Assessment Series. 2015;15(7).
226. Christie LJ, Fearn N, McCluskey A, Lovarini M, Rendell R, Pearce A. Cost-Effectiveness of Constraint-Induced Movement Therapy Implementation in Neurorehabilitation: The ACTIveARM Project. PharmacoEconomics - Open. 2022;6(3):437-50.
227. Geng R, Zhang J, Lv F, Sun Q. Cost-effectiveness analysis of reformative bobath rehabilitation versus traditional rehabilitation in post-stroke syndrome. International Journal of Clinical and Experimental Medicine. 2018;11(11):12246-52.
228. Bowen A, Hesketh A, Patchick E, Young A, Davies L, Vail A, et al. Clinical effectiveness, cost-effectiveness and service users' perceptions of early, well-resourced communication therapy following a stroke: A randomised controlled trial (the ACT noW study). Health Technology Assessment. 2012;16(26):1-159.
229. Latimer NR, Dixon S, Palmer R. Cost-utility of self-managed computer therapy for people with aphasia. International journal of technology assessment in health care. 2013;29(4):402-9.
230. Latimer NR, Bhadhuri A, Alshreef AO, Palmer R, Cross E, Dimairo M, et al. Self-managed, computerised word finding therapy as an add-on to usual care for chronic aphasia post-stroke: An economic evaluation. Clinical rehabilitation. 2020:269215520975348.

231. Humphreys I, Thomas S, Phillips C, Lincoln N. Cost analysis of the Communication and Low Mood (CALM) randomised trial of behavioural therapy for stroke patients with aphasia. Clinical Rehabilitation. 2014:epub.
232. van Eeden M, Kootker JA, Evers SM, van Heugten CM, Geurts AC, van Mastrigt GA. An economic evaluation of an augmented cognitive behavioural intervention vs. computerized cognitive training for post-stroke depressive symptoms. BMC neurology. 2015;15:266.
233. Forster A, Dickerson J, Young J, Patel A, Kalra L, Nixon J, et al. A structured training programme for caregivers of inpatients after stroke (TRACS): A cluster randomised controlled trial and cost-effectiveness analysis. The Lancet. 2013;382(9910):2069-76.
234. Angerova Y, Marsalek P, Chmelova I, Gueye T, Uherek S, Briza J, et al. Cost and cost-effectiveness of early inpatient rehabilitation after stroke varies with initial disability: the Czech Republic perspective. International journal of rehabilitation research. 2020;Internationale Zeitschrift fur Rehabilitationsforschung. Revue internationale de recherches de readaptation. 43(4):376-82.
235. Luengo-Fernandez R, Gray AM, Bull L, Welch S, Cuthbertson F, Rothwell PM, et al. Quality of life after TIA and stroke. Ten-year results of the Oxford Vascular Study. 2013;81(18):1588-95.
236. Pickard AS, Johnson JA, Feeny DH. Responsiveness of generic health-related quality of life measures in stroke. Qual Life Res. 2005;14(1):207-19.
237. Conner-Spady B, Suarez-Almazor ME. Variation in the estimation of quality-adjusted life-years by different preference-based instruments. Med Care. 2003;41(7):791-801.
238. Huppertz-Hauss G, Aas E, Lie Høivik M, Langholz E, Odes S, Småstuen M, et al. Comparison of the Multiattribute Utility Instruments EQ-5D and SF-6D in a Europe-Wide Population-Based Cohort of Patients with Inflammatory Bowel Disease 10 Years after Diagnosis. Gastroenterol Res Pract. 2016;2016:5023973.
239. Leung YY, Png ME, Wee HL, Thumboo J. Comparison of EuroQol-5D and short form-6D utility scores in multiethnic Asian patients with psoriatic arthritis: a cross-sectional study. J Rheumatol. 2013;40(6):859-65.
240. Sørensen J, Linde L, Ostergaard M, Hetland ML. Quality-adjusted life expectancies in patients with rheumatoid arthritis--comparison of index scores from EQ-5D, 15D, and SF-6D. Value Health. 2012;15(2):334-9.
241. Yang F, Lau T, Lee E, Vathsala A, Chia KS, Luo N. Comparison of the preference-based EQ-5D-5L and SF-6D in patients with end-stage renal disease (ESRD). Eur J Health Econ. 2015;16(9):1019-26.
242. Salaffi F, Carotti M, Ciapetti A, Gasparini S, Grassi W. A comparison of utility measurement using EQ-5D and SF-6D preference-based generic instruments in patients with rheumatoid arthritis. Clin Exp Rheumatol. 2011;29(4):661-71.
243. Tummers JF, Schrijvers AJ, Visser-Meily JM. Economic evidence on integrated care for stroke patients; a systematic review. International journal of integrated care. 2012;12:e193.
244. Lu ZK, Xiong X, Lee T, Wu J, Yuan J, Jiang B. Big Data and Real-World Data based Cost-Effectiveness Studies and Decision-making Models: A Systematic Review and Analysis. Front Pharmacol. 2021;12:700012.
245. Bernhardt J, Urimubenshi G, Gandhi DBC, Eng JJ. Stroke rehabilitation in low-income and middle-income countries: a call to action. Lancet. 2020;396(10260):1452-62.

246. Guidelines for the economic evaluation of health technologies: Canada. 4th ed. Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH); 2017.
247. Daccache C, Rizk R, Dahham J, Evers SMAA, Hiligsmann M, Karam R. Economic evaluation guidelines in low- and middle-income countries: a systematic review. International journal of technology assessment in health care. 2022;38(1):e1.
248. National Institute for Health and Care Excellence (NICE). NICE health technology evaluations: the manual2022 Feb 24, 2022 [cited Feb 24, 2022]. Available from: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation.
249. Sritipsukho P, Riewpaiboon A, Chaiyawat P, Kulkantrakorn K. Cost-effectiveness analysis of home rehabilitation programs for Thai stroke patients. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2010;93 Suppl 7:S262-70.
250. Guideline Development Working Group. Guideline for health technology assessment in Thailand updated edition: 2019. Nonthaburi: Health Systems Research Institute; 2021.
251. Baghbanian A, Merlin T, Carter D, Wang S. Methods for the health technology assessment of complex interventions: a protocol for a scoping review. BMJ Open. 2020;10(11):e039263.
252. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. Bmj. 2021;374:n2061.
253. Hoomans T, Fenwick EA, Palmer S, Claxton K. Value of information and value of implementation: application of an analytic framework to inform resource allocation decisions in metastatic hormone-refractory prostate cancer. Value Health. 2009;12(2):315-24.
254. Fenwick E, Claxton K, Sculpher M. The value of implementation and the value of information: combined and uneven development. Med Decis Making. 2008;28(1):21-32.
255. Walker SM, Faria R, Palmer SJ, Sculpher M. Getting cost-effective technologies into practice: the value of implementation: Policy Research Unit in Economic Evaluation of Health and Care Interventions (EEPRU); 2014.
256. Kuptniratsaikul V, Wattanapan P, Wathanadilokul U, Sukonthamarn K, Lukkanapichonchut P, Ingkasuthi K, et al. The Effectiveness and Efficiency of Inpatient Rehabilitation Services in Thailand: A Prospective Multicenter Study. Rehabilitation Process and Outcome. 2016;5:RPO.S34816.
257. McGlinchey MP, James J, McKevitt C, Douiri A, Sackley C. The effect of rehabilitation interventions on physical function and immobility-related complications in severe stroke: a systematic review. BMJ Open. 2020;10(2):e033642.
258. Zhang WW, Speare S, Churilov L, Thuy M, Donnan G, Bernhardt J. Stroke rehabilitation in China: a systematic review and meta-analysis. International Journal of Stroke. 2014;9(4):494-502.
259. Wattanapan P, Lukkanapichonchut P, Massakulpan P, Suethanapornkul S, Kuptniratsaikul V. Effectiveness of Stroke Rehabilitation Compared between Intensive and Nonintensive Rehabilitation Protocol: A Multicenter Study. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2020;29(6):104809.
260. Chaiyawat P, Kulkantrakorn K. Randomized controlled trial of home rehabilitation for patients with ischemic stroke: impact upon disability and elderly depression. Psychogeriatrics. 2012;12(3):193-9.

261. Briggs A, Claxton K, Sculpher M. Decision modelling for health economic evaluation: Oxford University Press; 2006.
262. Tilling C, Krol M, Tsuchiya A, Brazier J, Exel J, Brouwer W. Does the EQ-5D reflect lost earnings? Pharmacoeconomics. 2012;30(1):47-61.
263. Drummond MF, O'Brien BJ, Torrance GW, Stoddart GL. Methods for the Economic Evaluation of Health Care Programmes. Oxford: Oxford University Press; 1997.
264. Health Intervention and Technology Assessment Program, International Health Policy Program, Thai Health Promotion Foundation, Health Systems Research Institute. Guidelines for health technology assessment in Thailand (First Edition). Journal of Medical Association of Thailand. 2008;91(Suppl. 2).
265. Gray AM, Clarke PM, Wolstenholme JL, Wordsworth, Sarah. Applied Methods of Cost-effectiveness Analysis in Healthcare. United Kingdom: Oxford University Press; 2010.
266. Faria R, Walker S, Whyte S, Dixon S, Palmer S, Sculpher M. How to Invest in Getting Cost-effective Technologies into Practice? A Framework for Value of Implementation Analysis Applied to Novel Oral Anticoagulants. Med Decis Making. 2017;37(2):148-61.
267. Bureau of inspection and evaluation. Results of inspection and evaluation fiscal year 2022 (second round): Intermediate Care Nonthaburi: The Office of Permanent Secretary, Ministry of Public Health; 2022 [
268. Rungnoei N, Chuenklin T, Kaeowichian N, Suthamchai B, Girdwichai W, Pannarunothai S. Success of intermediate care implementation according to the Ministry of Public Health's policy. Journal of Health Systems Research. 2021;15(1):81-101.
269. World Health Organization. Life tables by country: Thailand. Geneva. 2020 [updated Dec 6, 2020; cited June 08, 2022]. Available from: https://apps.who.int/gho/data/?theme=main&vid=61640.
270. Permsuwan U, Guntawongwan K, Buddhawongsa P. Handling time in economic evaluation studies. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2014;97 Suppl 5:S50-8.
271. Claxton K, Walker S, Palmer S, Sculpher M. Appropriate Perspectives for Health Care Decisions. Centre for Health Economics, University of York; 2010.
272. Bureau of Trade and Economic Indices. Report for Consumer Price Index of Thailand base year 2019: Ministry of Commerce; 2022 [cited Sep 15, 2022]. Available from: http://www.indexpr.moc.go.th/price_present/TableIndexG_region.asp?table_name=cpig_index_country&province_code=5&type_code=g&check_f=i&year_base=2562&nyear=2565.
273. Office of the National Economic and Social Development Council. National income of Thailand 2020, chain volume measures. Bangkok; 2021.
274. Thavorncharoensap M. Measurement of utility. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2014;97 Suppl 5:S43-9.
275. Briggs AH, Ades AE, Price MJ. Probabilistic sensitivity analysis for decision trees with multiple branches: use of the Dirichlet distribution in a Bayesian framework. Med Decis Making. 2003;23(4):341-50.
276. Kuptniratsaikul V, Kovindha A, Piravej K, Dajpratham P. First-Year Outcomes after Stroke Rehabilitation: A Multicenter Study in Thailand. ISRN Rehabilitation. 2013;2013:595318.
277. Canadian Partnership for Stroke Recover. Evidence-Based Review of Stroke Rehabilitation. 2013.
278. Quinn TJ, Langhorne P, Stott DJ. Barthel Index for Stroke Trials. Stroke. 2011;42(4):1146-51.

279. Whyte S, Dixon S, Faria R, Walker S, Palmer S, Sculpher M, et al. Estimating the Cost-Effectiveness of Implementation: Is Sufficient Evidence Available? Value Health. 2016;19(2):138-44.
280. O'Mahony JF, Newall AT, van Rosmalen J. Dealing with Time in Health Economic Evaluation: Methodological Issues and Recommendations for Practice. PharmacoEconomics. 2015;33(12):1255-68.
281. Kwakkel G, Kollen B, Twisk J. Impact of Time on Improvement of Outcome After Stroke. Stroke. 2006;37(9):2348-53.
282. Heggie R, Wu O, White P, Ford GA, Wardlaw J, Brown MM, et al. Mechanical thrombectomy in patients with acute ischemic stroke: A cost-effectiveness and value of implementation analysis. Int J Stroke. 2020;15(8):881-98.
283. Wright SJ, Newman WG, Payne K. Quantifying the Impact of Capacity Constraints in Economic Evaluations: An Application in Precision Medicine. Med Decis Making. 2022;42(4):538-53.
284. Hebert D, Lindsay MP, McIntyre A, Kirton A, Rumney PG, Bagg S, et al. Canadian stroke best practice recommendations: Stroke rehabilitation practice guidelines, update 2015. International Journal of Stroke. 2016;11(4):459-84.
285. Kang J-H, Bae H-J, Choi Y-A, Lee SH, Shin HI. Length of Hospital Stay After Stroke: A Korean Nationwide Study. Ann Rehabil Med. 2016;40(4):675-81.
286. OECD, Organization WH. Case-based Payment Systems for Hospital Funding in Asia2015.
287. Chodankar D. Introduction to real-world evidence studies. Perspect Clin Res. 2021;12(3):171-4.
288. Gilligan AK, Thrift AG, Sturm JW, Dewey HM, Macdonell RAL, Donnan GA. Stroke Units, Tissue Plasminogen Activator, Aspirin and Neuroprotection: Which Stroke Intervention Could Provide the Greatest Community Benefit? Cerebrovascular Diseases. 2005;20(4):239-44.
289. Akyea RK, Vinogradova Y, Qureshi N, Patel RS, Kontopantelis E, Ntaios G, et al. Sex, Age, and Socioeconomic Differences in Nonfatal Stroke Incidence and Subsequent Major Adverse Outcomes. Stroke. 2021;52(2):396-405.
290. Rahbar MH, Medrano M, Diaz-Garelli F, Gonzalez Villaman C, Saroukhani S, Kim S, et al. Younger age of stroke in low-middle income countries is related to healthcare access and quality. Annals of Clinical and Translational Neurology. 2022;9(3):415-27.
291. National Health Security Office. Guideline for National Health Security Office fund management fiscal year 2021. Nonthaburi: Sahamitr printing and publishing Co. Ltd.; 2020 [cited 2023 Mar 5,]. Available from: https://www.nhso.go.th/storage/files/shares/PDF/fund_man01.pdf.
292. National Health Security Office. Criteria and conditions for claiming health service expenses 2022 [cited Mar 5, 2023. Available from: http://pbhd.moph.go.th/nhso/รวมหลักเกณฑ์และเงื่อนไขบริการสปสช.2566.pdf.
293. Hillier S, Inglis-Jassiem G. Rehabilitation for community-dwelling people with stroke: home or centre based? A systematic review. Int J Stroke. 2010;5(3):178-86.
294. Woodward A, Kawachi I. Why reduce health inequalities? Journal of Epidemiology and Community Health. 2000;54(12):923-9.
295. Chainarong Sungchang. Health inequality analysis and social determinants within urban area. Journal of Health Science. 2020;29(5):772-82.
296. Pittman P, Chen C, Erikson C, Salsberg E, Luo Q, Vichare A, et al. Health workforce for health equity. Med Care. 2021;59(Suppl 5):S405-s8.

297. Doran CM. Critique of an economic evaluation using the drummond checklist. Applied Health Economics and Health Policy. 2010;8(6):357-9.
298. Yong YV, Shafie AA. Economic evaluation of enhanced asthma management: a systematic review. Pharm Pract (Granada). 2014;12(4):493.
299. van Mastrigt GA, Hiligsmann M, Arts JJ, Broos PH, Kleijnen J, Evers SM, et al. How to prepare a systematic review of economic evaluations for informing evidence-based healthcare decisions: a five-step approach (part 1/3). Expert review of pharmacoeconomics & outcomes research. 2016;16(6):689-704.
300. Luhnen M, Prediger B, Neugebauer EAM, Mathes T. Systematic reviews of economic evaluations in health technology assessment: a review of characteristics and applied methods. International journal of technology assessment in health care. 2018;34(6):537-46.
301. Walker DG, Wilson RF, Sharma R, Bridges J, Niessen L, Bass EB, et al. AHRQ Methods for Effective Health Care. Best Practices for Conducting Economic Evaluations in Health Care: A Systematic Review of Quality Assessment Tools. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012.
302. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. BMJ : British Medical Journal. 2013;346:f1049.
303. Schünemann HJ HJ, Vist GE, Glasziou P, Akl EA, Skoetz N, Guyatt GH. Chapter 14: Completing ‘Summary of findings’ tables and grading the certainty of the evidence. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.1 (updated September 2020). Cochrane, 2020. Available from www.training.cochrane.org/handbook2020.
304. Brunetti M, Shemilt I, Pregno S, Vale L, Oxman AD, Lord J, et al. GRADE guidelines: 10. Considering resource use and rating the quality of economic evidence. J Clin Epidemiol. 2013;66(2):140-50.
305. Sirindhorn National Medical Rehabilitation Institute. Program of nursing specialty in rehabilitation nursing. Nonthaburi. 2021 [cited August 15, 2022]. Available from: https://www.snmri.go.th/2022/08/หลักสูตรการพยาบาลเฉพาะ/.
306. Rangsit University, Sirindhorn National Medical Rehabilitation Institute. Program of Physical Therapy (Rehabilitation in Intermediate Care). Pathum Thani. 2022 [cited August 15, 2022]. Available from: https://cyberuonline.rsu.ac.th/2022/08/02/ptimc/.

Appendices

Appendix 1 The developed questionnaires adapted from the INTERSTROKE study

HiTAP HeHTa Questionnaire ID: ☐☐☐☐☐

Stroke service questionnaire

We would like to collect the description of the type of service and care that the majority of stroke patients will receive at your centre. Please put **X** mark in the box ☐ in front of the statement and/or fill in the blank truthfully. If there is no service available, please enter/fill 0.

A. Hospital Characteristics		
A1	Province	
A2	Hospital name	
A3	Hospital level	☐ A ☐ S ☐ M1 ☐ Other (specify) ....
A4	Area health	
A5	How many beds are in your hospital?	In total ☐ In medicine departments (i.e. non-surgery) ☐ Dedicated for stroke patients ☐
A6	How many physicians are in your hospital?	In total ☐ General practice ☐ Internal medicine ☐ Neurologist ☐ Certificate in Fellowship Training in Stroke ☐ Surgeon ☐ Neurosurgeon ☐ Emergency medicine ☐ Radiologist/ Interventional radiologist ☐ Rehabilitation physician ☐ Family medicine ☐ Other (specify) ____________________
A7	On average, how many stroke patients are admitted to your hospital each year?	In total (ICD10: I60-I69) ☐ Ischemic stroke (ICD10: I63) ☐ Haemorrhagic stroke (ICD10: I60-I62) ☐ Unspecified stroke (ICD10: I64-I69) ☐
A8	On average, how many stroke patients are transferred to other hospitals each year?	In total (ICD10: I60-I69) ☐ Ischemic stroke (ICD10: I63) ☐ Haemorrhagic stroke (ICD10: I60-I62) ☐ Unspecified stroke (ICD10: I64-I69) ☐
A9	What number of stroke patients are usually in your hospital at any one time?	Approximate number (cases) ☐

A. Hospital Characteristics			
A10	Which of the following departments are usually involved in providing care for stroke patients during their acute illness? (Tick all that apply)	General (internal) medicine Neurology Surgery Rehabilitation General practice / Family medicine Nursing Pharmacy Other (specify) ___	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
A11	What proportion of stroke patients are looked after by a specialist doctor training in stroke?	approximate proportion (%)	☐
A12	Does your hospital have your own stroke registry?	☐ Yes ☐ No	
A13	Does your hospital have any network with other hospitals and which hospital is the main hub?	☐ Yes, having stroke fast track — Hospital hub name: ___ ☐ Yes, having referral system — Hospital hub name: ___	☐ No ☐ No

B. Healthcare service funding					
B1	What proportion (%) of source of fund for stroke services?	**Services**	**Government funding**	**Private funding**	**Other (specify)**
		Medical services			
		Medicine (i.e. rt-PA drug)			
		Investigation (i.e. CT scanning, MRI, lab test)			
		Rehabilitation programme			
		Material and equipment			
		Education programme			
		Other (specify) ___			
B2	Which items would the patient have to pay for?	☐ Medical services ☐ Medicines ☐ Medical equipment ☐ Other (specify) ___	☐ Investigations (e.g. CT scanning, MRI) ☐ Therapy (e.g. physiotherapy) ☐ None of the above/Free-of-charge		

C. Stroke unit services				
C1	Does your hospital have a Stroke Unit/corner?	Stroke Unit Stroke corner	☐ Yes (Go to C2) ☐ Yes (Go to C2)	☐ No (Go to C7) ☐ No (Go to C7)
C2	How many beds are in your stroke unit/corner?	Number of beds in stroke unit Number of beds in stroke corner		☐ ☐
C3	What proportion (%) of stroke patients are usually admitted to stroke unit/corner?	approximate proportion (%)		☐

C. Stroke unit services		
C4	Which of these features describe your stroke unit?	☐ Discrete ward area for stroke patients ☐ Physicians and/or nurses whose work is mainly managing stroke patients ☐ Multidisciplinary team with main responsibility in managing stroke patients ☐ Special education programmes provided for stroke unit staff ☐ Information and education for stroke patients and their families or caregivers ☐ Written standard protocols for stroke management (i.e. a written management care plan) ☐ Other (specify) ______________
C5	Does your hospital receive a stroke centre certification?	☐ Yes ☐ No
C6	Which of the following staffs and number of staff are usually involved in providing care for stroke patients in stroke unit?	

Type of staff	Approx. number of staffs in stroke unit	Number of part-time staffs	Number of full-time staffs
General practice			
Internal medicine			
Neurology			
Certificate in fellowship training in stroke			
Surgery			
Neurosurgery			
Emergency medicine			
Radiology/ Interventional radiology			
Rehabilitation physician			
Family medicine			
Nurse			
Pharmacist			
Physiotherapist			
Occupational therapist			
Speech-Language therapist			
Psychologist			
Social worker			
Other (specify) ______________			

C. Stroke unit services		
C7	Do you have a multidisciplinary team (medical, nursing, pharmacy, therapy staff) who meet on a regular basis to plan patient management?	☐ Yes, meeting once per day ☐ Yes, meeting once per week ☐ Yes, meeting less than once per week (specify) ____ ☐ No multidisciplinary team
C8	After initial acute treatment, where do patients usually receive continuing rehabilitation in hospital?	☐ Yes, in general medical or neurology wards ☐ Yes, in the stroke unit ☐ Yes, transfer to another hospitals (higher level) ☐ Yes, transfer to another hospitals (lower level) ☐ No continuing rehabilitation available ☐ Other (specify) ____
C9	If patients require ongoing rehabilitation at the time of discharge from hospital, who usually delivers care to these patients and how are they funded?	(see table below)
C10	Are the patient or family members / care givers usually educated in rehabilitation?	☐ Yes ☐ No (Go to D1)
C11	Who usually educates patient or family members / care givers in rehabilitation?	☐ Doctors ☐ Nurses ☐ Physiotherapists ☐ Occupational therapists ☐ Psychologists ☐ Speech therapists ☐ Village Health Volunteer ☐ Other (specify) ____

C9:

Staff	Government funded	Privately funded	Other (specify)
Doctors			
Nurses			
Physiotherapists			
Occupational therapists			
Speech therapists			
Psychologists			
Village Health Volunteer			
Family members	---------		
Other (specify) ____			

D. Other facilities and services		
D1	Do you have a written guidance for stroke management (i.e. a written management care plan) for hospital staffs?	☐ Yes ☐ No (Go to D4)
D2	Which of the topics are included in your guidance?	Please list any items/topics included in your hospital protocols *(e.g. assessment of swallowing impairment, early mobilisation, prevention of complications)*

	D. Other facilities and services	
D3	Can you provide written copies of the guidance if requested?	☐ Yes ☐ No
D4	Which and when of these clinical assessment scores does your hospital uses for evaluating stroke patients? And where do you record these data (i.e. electronic database, OPD card)?	(see table below)
D5	Which and when of these laboratory investigations does your hospital uses for investigating stroke patients? And where do you record these data (i.e. electronic database, OPD card)?	(see table below)
D6	Which of these medications are provided and what proportion (%) of stroke patients are usually received each drug?	(see table below)
D7	If you have a rt-PA drug, which route of rt-PA is prescribed?	☐ Intravenous ☐ Intra-arterial ☐ Other (specify) ____________
D8	Which investigations and what proportion (%) of stroke patients are usually received within 24 hours after admission in your hospital?	(see table below)

D4:

Admission	Discharge	Recorded location	Clinical assessment
			Glasgow coma scales
			Barthel Index
			modified Rankin Score
			National Institutes of Health Stroke Scale
			Swallowing impairment
			Level of consciousness
			Malnutrition
			Other (specify) ____________

D5:

Admission	Discharge	Recorded location	Laboratory
			Blood sugar
			HbA1C
			CBC
			INR
			Creatinine
			EGFR
			Total cholesterol
			LDL
			HDL
			Triglyceride
			Other (specify) ____________

D6:

Medications	Approximate proportion (%)
Recombinant tissue plasminogen activator (rt-PA)	
Antiplatelet (i.e. aspirin, ticlopidine, clopidogrel, aspirin + dipyridamole)	
Anticoagulant (i.e. warfarin, dabigatran, apixaban, rivaroxaban)	

D8:

Investigations	Approximate proportion (%)
Elektrokardiogram (EKG) monitor	
Computerized Tomography (CT) brain	
Magnetic Resonance Imaging (MRI)/Angiography (MRA)	
Carotid Doppler ultrasound	
Other (specify) ____________	

D. Other facilities and services		
D9	Does your hospital can perform an endovascular treatment (thrombectomy) in acute stroke?	☐ Yes ☐ No
D10	Do you have a prevention of complications written plans/protocols?	☐ Yes ☐ No

E. Post-stroke care			
E1	Does your hospital have a post-rehabilitation unit?	☐ Yes ☐ No	
E2	Which type of medical rehabilitation services are provided and what proportion of stroke patients are received this service?	**Rehabilitation services**	**approximate proportion (%)**
		Acute/Inpatient rehabilitation	
		Outpatient rehabilitation	
		Post-acute rehabilitation	
		Home-based rehabilitation	
		Community-based rehabilitation	
		Others (specify) ___________________________	
E3	Do you have a follow-up system after patient discharge from hospital?	☐ Yes ☐ No	
E4	Which type of home health care services are provided for stroke patients?	☐ GP / Internal medicine ☐ Family medicine ☐ Rehabilitation physician ☐ Pharmacist ☐ Physiotherapist ☐ Speech-language pathologist ☐ Village Health Volunteer ☐ Thai Traditional Medicine	☐ Neurologist / Certificate in fellowship training in stroke ☐ Emergency medicine ☐ Nurse ☐ Psychologists ☐ Occupational therapist ☐ Nutritionist ☐ Social Medicine ☐ Others (specify) ___________________
E5	Does your hospital have an intermediate care service (IMC) and long-term care (LTC) service?	IMC ☐ Yes ☐ No LTC ☐ Yes ☐ No	

Further comments

....

....

....

THANK YOU VERY MUCH

Please return the questionnaire via email: 2425416K@student.gla.ac.uk

Date of completing questionnaire ___/_____/____

Appendix 2 The approved questionnaire

Ethics Committee

Institute for the Development of Human Research Protections (IHRP)

Building 8 Floor 7 Room 702 Department of Medical Science Ministry Public Health Nonthaburi Thailand 11000

Certificate of Approval

Title of Project: A comparison of current pattern of care and future development of stroke service delivery in Thailand. (Version 3/07102562)

Principal Investigator: Suthasinee Kumluang

Responsible Organization: Health Intervention and Technology Assessment Program, Ministry of Public Health.

The Ethics Committee of Institute for the Development of Human Research Protections (IHRP) had reviewed the research proposal. Concerning on scientific, ICH-GCP and ethical issues, the committee has approved for the implementation of the research study mentioned above.

Signature: ....
(Dr.Vichai Chokevivat)
Chairman

Signature: ....
(Dr.Pramote Stienrut)
Committee and Secretary

Date of Approval: October 15, 2019

HiTAP HEHTA

Version 3/07102562

รหัสแบบสอบถาม: ☐☐☐☐☐

แบบสอบถาม

การให้บริการโรคหลอดเลือดสมองของสถานพยาบาลภาครัฐ

วันที่ตอบแบบสอบถาม วันที่____เดือน__________พ.ศ. 2562

คำชี้แจง แบบสอบถามนี้เป็นส่วนหนึ่งของการศึกษาเรื่อง "การศึกษาเพื่อเปรียบเทียบรูปแบบการให้บริการดูแลผู้ป่วยโรคหลอดเลือดสมอง และการพัฒนาระบบบริการผู้ป่วยโรคหลอดเลือดสมองของประเทศไทยในอนาคต" และเป็นส่วนหนึ่งของงานวิจัยระดับปริญญาเอก ดำเนินงานโดย ภญ.สุธาสินี คำหลวง นักศึกษาระดับปริญญาเอกจากภาควิชา Health Economics and Health Technology Assessment (HEHTA), Institute of Health & Wellbeing, มหาวิทยาลัยกลาสโกว์, สกอตแลนด์ ประเทศสหราชอาณาจักร และนักวิจัยจากโครงการประเมินเทคโนโลยีและนโยบายด้านสุขภาพ (Health Intervention and Technology Assessment Program: HITAP) กระทรวงสาธารณสุข มีวัตถุประสงค์เพื่อศึกษารูปแบบการดูแลรักษา (pattern of cares) และการให้บริการโรคหลอดเลือดสมองของสถานพยาบาลภาครัฐ การสำรวจนี้รวบรวมข้อมูลจากสถานพยาบาลในระดับตติยภูมิและทุติยภูมิของกระทรวงสาธารณสุขตามกรอบของ service plan พ.ศ. 2561 - 2565 เพื่อให้ทราบภาพรวมของระบบการให้บริการสำหรับผู้ป่วยโรคหลอดเลือดสมองในปัจจุบันของประเทศไทย และหลังจากนั้นจะนำข้อมูลนี้มาสังเคราะห์ร่วมกับผลการศึกษาในส่วนของฐานข้อมูลผู้ป่วยโรคหลอดเลือดสมองในระดับประเทศ เพื่อศึกษาเปรียบเทียบรูปแบบการให้บริการดูแลรักษา ผลลัพธ์ด้านสุขภาพ และแนวทางการพัฒนาระบบการให้บริการโรคหลอดเลือดสมองที่เหมาะสมกับบริบทของระบบสุขภาพของประเทศไทยต่อไป

แบบสอบถามประกอบด้วย **ส่วนที่ 1** ข้อมูลพื้นฐานของสถานพยาบาล **ส่วนที่ 2** งบประมาณของสถานพยาบาล **ส่วนที่ 3** ข้อมูลการให้บริการหอผู้ป่วยโรคหลอดเลือดสมอง **ส่วนที่ 4** ข้อมูลการให้บริการอื่นๆ และ**ส่วนที่ 5** การบริการผู้ป่วยหลังการเกิดโรคหลอดเลือดสมอง

ผู้วิจัยหวังเป็นอย่างยิ่งว่าจะได้รับความอนุเคราะห์ข้อมูลจากท่านและขอขอบคุณมา ณ โอกาสนี้

ขอความกรุณาท่านส่งแบบสอบถามกลับทางอีเมล 2425416K@student.gla.ac.uk หรือทางไปรษณีย์ (ธุรกิจตอบรับ)

หากท่านมีคำถาม ข้อสงสัยเกี่ยวกับงานวิจัย ท่านสามารถติดต่อสอบถามนักวิจัยได้ที่

ภญ.สุธาสินี คำหลวง
โครงการประเมินเทคโนโลยีและนโยบายด้านสุขภาพ
ชั้น 6 อาคาร 6 กรมอนามัย กระทรวงสาธารณสุข ถ.ติวานนท์อ.เมือง จ.นนทบุรี 11000
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ชื่อผู้ให้ข้อมูล______________________________นามสกุล______________________________
ชื่อสถานพยาบาล____
ที่อยู่สถานพยาบาล เลขที่__________ถนน______________ตำบล______________อำเภอ______________
จังหวัด______________________________________รหัสไปรษณีย์______________________________
เบอร์โทรศัพท์____________________เบอร์มือถือ________________E-mail________________________

อนุมัติ
15 ต.ค. 2562
คณะกรรมการจริยธรรมการวิจัยในมนุษย์ฯ
สถาบันพัฒนาการคุ้มครองการวิจัยในมนุษย์ (สคม.)

Version 3/07102562

HiTAP HeHTa

รหัสแบบสอบถาม: ☐☐☐☐☐

แบบสอบถามการให้บริการโรคหลอดเลือดสมองของสถานพยาบาลภาครัฐ

คำชี้แจง

○ การเก็บข้อมูลของสถานพยาบาลภาครัฐในการศึกษานี้ เป็นการเก็บข้อมูลประเภทและชนิดของการให้บริการป้องกันและรักษาโรคหลอดเลือดสมองที่ผู้มารับบริการส่วนใหญ่ได้รับบริการ ณ สถานพยาบาลนั้นๆ

○ โปรดกาเครื่องหมาย X ในกล่อง ☐ หน้าข้อความ และ/หรือ เติมข้อความตามความเป็นจริง

○ โปรดกรอก 0 หากไม่มีการให้บริการในสถานพยาบาลของท่าน

ส่วนที่ 1 ข้อมูลพื้นฐานของสถานพยาบาล (Hospital Characteristics)			
1.1	จังหวัด		
1.2	ชื่อสถานพยาบาล		
1.3	ระดับสถานพยาบาล	☐ A ☐ S ☐ M1 ☐ M2 ☐ อื่นๆ (โปรดระบุ) ____________	
1.4	เขตสุขภาพที่		
1.5	ในสถานพยาบาลของท่าน มีจำนวนเตียงที่ให้บริการเท่าใด	จำนวนเตียงทั้งหมดของโรงพยาบาล	
		จำนวนเตียงหอผู้ป่วยทั่วไป	
		จำนวนเตียงหอผู้ป่วยโรคหลอดเลือดสมอง (stroke unit)	
1.6	ในสถานพยาบาลของท่าน มีแพทย์เป็นจำนวนเท่าใด (หน่วย: คน) * ไม่นับซ้ำ ตัวอย่างเช่น มีแพทย์ทั้งหมดจำนวน 10 คน แบ่งเป็น แพทย์อายุรกรรม 5 คน แพทย์ประสาทวิทยา 2 คน แพทย์อนุสาขาประสาทวิทยาโรคหลอดเลือดสมอง 1 คน และแพทย์ศัลยกรรม 2 คน เป็นต้น	จำนวนแพทย์ทั้งหมด	
		แพทย์เวชปฏิบัติทั่วไป	
		แพทย์อายุรกรรม	
		แพทย์ประสาทวิทยา	
		แพทย์อนุสาขาประสาทวิทยาโรคหลอดเลือดสมอง	
		แพทย์ศัลยกรรม	
		แพทย์ประสาทศัลยกรรม	
		แพทย์เวชศาสตร์ฉุกเฉิน	
		รังสีแพทย์/แพทย์รังสีร่วมรักษา	
		แพทย์เวชศาสตร์ฟื้นฟู	
		แพทย์เวชศาสตร์ครอบครัว	
		อื่นๆ (โปรดระบุ) ____________	
1.7	ในปีงบประมาณ 2561 สถานพยาบาลของท่านมีผู้ป่วยโรคหลอดเลือดสมองประเภทผู้ป่วยในเป็นจำนวนเท่าใด (หน่วย - ครั้งต่อปี)	โรคหลอดเลือดสมองทั้งหมด (ICD10: I60-I69)	
		โรคหลอดเลือดสมองตีบ/อุดตัน (ICD10: I63)	
		โรคหลอดเลือดสมองแตก (ICD10: I60-I62)	
		โรคหลอดเลือดสมองอื่นๆ (ICD10: I64-I69)	
1.8	ในปีงบประมาณ 2561 สถานพยาบาลของท่านมีผู้ป่วยโรคหลอดเลือดสมองประเภทผู้ป่วยใน และส่งต่อไปยังสถานพยาบาลอื่นเป็นจำนวนเท่าใด (หน่วย - ครั้งต่อปี)	โรคหลอดเลือดสมองทั้งหมด (ICD10: I60-I69)	
		โรคหลอดเลือดสมองตีบ/อุดตัน (ICD10: I63)	
		โรคหลอดเลือดสมองแตก (ICD10: I60-I62)	
		โรคหลอดเลือดสมองอื่นๆ (ICD10: I64-I69)	

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ส่วนที่ 1 ข้อมูลพื้นฐานของสถานพยาบาล (Hospital Characteristics)		
1.9	โดยทั่วไป สถานพยาบาลของท่านมีผู้ป่วยโรคหลอดเลือดสมองประเภทผู้ป่วยในโดยประมาณกี่คน (หน่วย - คน)	จำนวนผู้ป่วยโรคหลอดเลือดสมองประเภทผู้ป่วยใน (โดยประมาณ) ☐
1.10	แผนกใดในสถานพยาบาลของท่านที่เกี่ยวข้องในกระบวนการการดูแลรักษาผู้ป่วยโรคหลอดเลือดสมองระยะเฉียบพลัน (acute illness) * เลือกได้มากกว่า 1 ข้อ	กลุ่มงานอายุรกรรม ☐ กลุ่มงานประสาทวิทยา ☐ กลุ่มงานศัลยกรรม ☐ กลุ่มงานเวชศาสตร์ฟื้นฟู ☐ กลุ่มงานเวชปฏิบัติทั่วไป/เวชศาสตร์ครอบครัว ☐ กลุ่มงานพยาบาล ☐ กลุ่มงานเภสัชกรรม ☐ อื่นๆ (โปรดระบุ) ________________ ☐
1.11	ร้อยละของผู้ป่วยโรคหลอดเลือดสมองที่ได้รับการดูแลรักษาโดยแพทย์เฉพาะทางโรคหลอดเลือดสมอง เป็นจำนวนเท่าใด * เทียบกับผู้ป่วยโรคหลอดเลือดสมองทั้งหมด	ร้อยละ (โดยประมาณ) ☐
1.12	มีระบบการลงทะเบียนผู้ป่วยโรคหลอดเลือดสมอง (stroke registry) เป็นของสถานพยาบาลของท่านเองหรือไม่	☐ มี ☐ ไม่มี
1.13	สถานพยาบาลของท่านมีเครือข่ายกับสถานพยาบาลอื่นหรือไม่ และมีสถานพยาบาลใดเป็นแม่ข่าย	☐ มี stroke fast track ชื่อรพ.แม่ข่าย ____________ ☐ ไม่มี ☐ มีระบบรับ - ส่งต่อ ชื่อรพ.แม่ข่าย ____________ ☐ ไม่มี

ส่วนที่ 2 งบประมาณของสถานพยาบาล (Healthcare service funding)					
2.1	งบประมาณที่ใช้สำหรับการให้บริการโรคหลอดเลือดสมอง มาจากแหล่งใด และคิดเป็นร้อยละโดยประมาณเท่าใด * ระบุตัวเลข (ร้อยละ) ในช่อง ตามประเภทผู้สนับสนุนงบประมาณ	ประเภทบริการ	งบจาก ภาครัฐ	งบจาก ภาคเอกชน	อื่นๆ
		ค่าบริการทางการแพทย์			
		ค่ายา (เช่น ยา rt-PA)			
		ค่าทำหัตถการ (เช่น CT scanning, MRI, ค่าตรวจเลือด)			
		ค่าฟื้นฟูสมรรถภาพ (เช่น ค่ากายภาพบำบัด)			
		ค่าวัสดุอุปกรณ์การแพทย์			
		ค่าใช้จ่ายกิจกรรมการให้ความรู้แก่บุคลากรทางการแพทย์ ผู้ป่วยโรคหลอดเลือดสมอง และ/หรือผู้ดูแล			
		อื่นๆ (โปรดระบุ) ____________			
2.2	ในสถานพยาบาลของท่าน มีบริการใดบ้างที่ผู้ป่วยโรคหลอดเลือดสมองต้องชำระเงินเอง (เบิกจากสิทธิไม่ได้)	☐ ค่าบริการทางการแพทย์ ☐ ค่าทำหัตถการ (เช่น CT scanning, MRI) ☐ ค่ายา (เช่น ยา rt-PA) ☐ ค่าฟื้นฟูสมรรถภาพ (เช่น ค่ากายภาพบำบัด) ☐ ค่าวัสดุอุปกรณ์การแพทย์ ☐ ไม่ต้องชำระเงินเอง ☐ อื่นๆ (โปรดระบุ) ________________			

ส่วนที่ 3 ข้อมูลการให้บริการหอผู้ป่วยโรคหลอดเลือดสมอง (Stroke unit services)		
3.1	สถานพยาบาลของท่านมีหอผู้ป่วยโรคหลอดเลือดสมอง (stroke unit/corner) หรือไม่	☐ มี stroke unit ☐ ไม่มี (ข้ามไปข้อ 3.7) ☐ มี stroke corner
3.2	มีจำนวนเตียงใน stroke unit/corner เท่าใด	stroke unit ☐ stroke corner ☐ (หน่วย: เตียง)
3.3	ร้อยละของผู้ป่วยโรคหลอดเลือดสมองที่รับไว้เป็นผู้ป่วยใน stroke unit/corner มีประมาณเท่าใด * เทียบกับผู้ป่วยโรคหลอดเลือดสมองทั้งหมด	ร้อยละ (โดยประมาณ) ☐
3.4	ข้อใดต่อไปนี้ที่อธิบายถึงคุณลักษณะของ stroke unit/corner ในสถานพยาบาลของท่าน * เลือกได้มากกว่า 1 ข้อ	☐ มีสถานที่ดูแลผู้ป่วยโรคหลอดเลือดสมอง แยกเป็นพื้นที่เฉพาะ ☐ มีแพทย์และ/หรือพยาบาลที่ทำหน้าที่หลักในการบริหารจัดการดูแลผู้ป่วย ☐ มีทีมสหวิชาชีพที่ได้รับการฝึกฝนและเชี่ยวชาญในการดูแลรักษาผู้ป่วยโรคหลอดเลือดสมอง ☐ มีการฝึกอบรมและให้ความรู้แก่บุคลากรการแพทย์ที่ทำหน้าที่ดูแลผู้ป่วยโรคหลอดเลือดสมอง ☐ มีการให้ความรู้และทักษะที่จำเป็นแก่ผู้ป่วย ญาติ ครอบครัว และ/หรือผู้ดูแล ☐ มีแนวทางการดูแลผู้ป่วยโรคหลอดเลือดสมองเป็นลายลักษณ์อักษร เช่น care plan ☐ อื่นๆ (โปรดระบุ) ______________________
3.5	Stroke unit/corner ในสถานพยาบาลได้รับการตรวจรับรองคุณภาพแล้วหรือไม่ (certified stroke centre)	☐ ได้รับการรับรองแล้ว ☐ ยังไม่ได้รับการรับรอง

ส่วนที่ 3 ข้อมูลการให้บริการหอผู้ป่วยโรคหลอดเลือดสมอง (Stroke unit services)

3.6 บุคลากรการแพทย์ใน stroke unit/corner ที่ให้การดูแลรักษาผู้ป่วยโรคหลอดเลือดสมองเป็นประจำ มีจำนวนเท่าใด (หน่วย: คน)

ดังนั้น

0 = ไม่มีบุคลากรการแพทย์ให้บริการใน stroke unit

*** จำนวนบุคลากรที่ให้บริการไม่เต็มเวลา** = บุคลากรการแพทย์ใน stroke unit ที่ใช้เวลาปฏิบัติงานในการดูแลรักษาผู้ป่วยโรคหลอดเลือดสมอง น้อยกว่า 40 ชั่วโมงต่อสัปดาห์

**** จำนวนบุคลากรที่ให้บริการเต็มเวลา** = บุคลากรการแพทย์ใน stroke unit ที่ใช้เวลาปฏิบัติงานในการดูแลรักษาผู้ป่วยโรคหลอดเลือดสมอง เท่ากับหรือมากกว่า 40 ชั่วโมงต่อสัปดาห์

ประเภทของบุคลากรการแพทย์	จำนวนบุคลากรใน stroke unit/corner ทั้งหมด	จำนวนบุคลากรที่ให้บริการ**ไม่**เต็มเวลา*	จำนวนบุคลากรที่ให้บริการเต็มเวลา**
แพทย์เวชปฏิบัติทั่วไป			
แพทย์อายุรกรรม			
แพทย์ประสาทวิทยา			
แพทย์อนุสาขาประสาทวิทยาโรคหลอดเลือดสมอง			
แพทย์ศัลยกรรม			
แพทย์ประสาทศัลยกรรม			
แพทย์เวชศาสตร์ฉุกเฉิน			
รังสีแพทย์/แพทย์รังสีร่วมรักษา			
แพทย์เวชศาสตร์ฟื้นฟู			
แพทย์เวชศาสตร์ครอบครัว			
พยาบาล			
เภสัชกร			
นักกายภาพบำบัด			
นักกิจกรรมบำบัด			
นักแก้ไขการพูด			
นักจิตวิทยา			
นักสังคมสงเคราะห์			
อื่นๆ (โปรดระบุ) ________________ ________________			

3.7 สถานพยาบาลของท่าน ทีมสหสาขาวิชาชีพ (เช่น แพทย์ พยาบาล เภสัชกร นักกายภาพบำบัด) มีการประชุมเพื่อวางแผนการรักษาอย่างสม่ำเสมอหรือไม่

- ☐ มีทีมสหสาขาวิชาชีพ และนัดประชุมวางแผนการรักษา 1 ครั้งต่อวัน
- ☐ มีทีมสหสาขาวิชาชีพ และนัดประชุมวางแผนการรักษา 1 ครั้งต่ออาทิตย์
- ☐ มีทีมสหสาขาวิชาชีพ และนัดประชุมวางแผนการรักษาน้อยกว่า 1 ครั้งต่ออาทิตย์ (โปรดระบุความถี่) ______________________________
- ☐ ไม่มีทีมสหสาขาวิชาชีพ

3.8 ในสถานพยาบาลของท่าน ผู้ป่วยได้รับการฟื้นฟูสมรรถภาพ (rehabilitation) หลังพ้นระยะเฉียบพลันหรือไม่ และให้บริการที่แผนกใด

* เลือกได้มากกว่า 1 ข้อ

- ☐ ได้รับบริการในหอผู้ป่วย stroke unit
- ☐ ได้รับบริการในหอผู้ป่วยอายุรกรรมทั่วไปหรือหอผู้ป่วยระบบประสาท
- ☐ ส่งต่อไปรับบริการที่สถานพยาบาลอื่นๆ ในระดับที่**สูง**กว่า
- ☐ ส่งต่อไปรับบริการที่สถานพยาบาลอื่นๆ ในระดับที่**ต่ำ**กว่า
- ☐ **ไม่มี**การให้บริการฟื้นฟูสมรรถภาพ หลังพ้นระยะเฉียบพลัน
- ☐ อื่นๆ (โปรดระบุ) ______________________________

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ส่วนที่ 3 ข้อมูลการให้บริการหอผู้ป่วยโรคหลอดเลือดสมอง (Stroke unit services)

3.9	ในกรณีที่ผู้ป่วยต้องได้รับการบริการฟื้นฟูสมรรถภาพอย่างต่อเนื่องภายหลังการจำหน่ายออกจากสถานพยาบาลของท่าน (discharge) บุคลากรใดที่เป็นผู้ให้บริการฟื้นฟูสมรรถภาพและได้รับเงินงบประมาณสนับสนุนจากแหล่งทุนใด * เลือกได้มากกว่า 1 ข้อ	ประเภทของบุคลากรการแพทย์	งบจาก ภาครัฐ	งบจาก ภาคเอกชน	อื่นๆ
		แพทย์			
		พยาบาล			
		นักกายภาพบำบัด			
		นักกิจกรรมบำบัด			
		นักแก้ไขการพูด			
		นักจิตวิทยา			
		อสม.			
		ผู้ดูแล/ครอบครัว			
		อื่นๆ (โปรดระบุ) ________			

3.10	มีการถ่ายทอดความรู้ และ/หรือ คำแนะนำสำหรับการฟื้นฟูสมรรถภาพก่อน discharge แก่ผู้ป่วย ครอบครัว และ/หรือผู้ดูแลหรือไม่	☐ มี	☐ ไม่มี (ข้ามไปข้อ 4.1)
3.11	บุคลากรใดที่เป็นผู้ถ่ายทอดความรู้ และ/หรือ คำแนะนำในการฟื้นฟูสมรรถภาพแก่ผู้ป่วย ครอบครัว และ/หรือผู้ดูแล	☐ แพทย์ ☐ นักกายภาพบำบัด ☐ นักจิตวิทยา ☐ อสม.	☐ พยาบาล ☐ นักกิจกรรมบำบัด ☐ นักแก้ไขการพูด ☐ อื่นๆ (โปรดระบุ) ________

ส่วนที่ 4 การให้บริการอื่นๆ (Other facilities and services)

4.1	สถานพยาบาลของท่านมีแนวปฏิบัติ/แนวทางการดูแลผู้ป่วยโรคหลอดเลือดสมองเป็นลายลักษณ์อักษรสำหรับบุคลากรการแพทย์หรือไม่	☐ มี	☐ ไม่มี (ข้ามไปข้อ 4.4)
4.2	มีหัวข้อใดบ้างที่ระบุไว้ในแนวปฏิบัติ/แนวทางการดูแลผู้ป่วยโรคหลอดเลือดสมอง	* โปรดระบุหัวข้อ เช่น การประเมินการกลืน (swallowing impairment) การเคลื่อนไหวร่างกาย (early mobilisation) การป้องกันภาวะแทรกซ้อน (prevention of complications) เป็นต้น	
4.3	สถานพยาบาลของท่านสามารถเผยแพร่แนวปฏิบัติ/แนวทางฯ ได้หรือไม่	☐ ได้	☐ ไม่ได้

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	ส่วนที่ 4 การให้บริการอื่นๆ (Other facilities and services)				
4.4	สถานพยาบาลของท่านมีการประเมินทางคลินิก (clinical assessment) ในขั้นตอนใดบ้าง และบันทึกไว้ที่ใด (โปรดระบุแหล่งบันทึก เช่น ฐานข้อมูลอิเล็กทรอนิคส์, เวชระเบียนผู้ป่วย, excel เป็นต้น)	ระหว่าง admit	ขณะ discharge	ระบุแหล่งบันทึก	ประเภทของการประเมินทางคลินิก
					Glasgow coma scales
					Barthel Index
					modified Rankin Score
					National Institutes of Health Stroke Scale
					Swallowing impairment
					Level of consciousness
					Malnutrition
					อื่นๆ (โปรดระบุ) ____________
4.5	สถานพยาบาลของท่านมีการตรวจประเมินทางห้องปฏิบัติการ (laboratory) ในขั้นตอนใดบ้าง และบันทึกไว้ที่ใด (โปรดระบุแหล่งบันทึก เช่น ฐานข้อมูลอิเล็กทรอนิคส์, เวชระเบียนผู้ป่วย, excel เป็นต้น)	ระหว่าง admit	ขณะ discharge	ระบุแหล่งบันทึก	ประเภทของการตรวจทางห้องปฏิบัติการ
					Blood sugar
					Haemoglobin A1c (HbA1c)
					complete blood count (CBC)
					International normalized ratio (INR)
					Creatinine
					Estimated glomerular filtration rate (EGFR)
					Total cholesterol
					Low density lipoprotein (LDL)
					High density lipoprotein (HDL)
					Triglyceride
					อื่นๆ (โปรดระบุ) ____________

		ยา	ร้อยละ (%)
4.6	สถานพยาบาลของท่านสั่งจ่ายยาดังกล่าวนี้แก่ผู้ป่วยโรคหลอดเลือดสมอง คิดเป็นร้อยละโดยประมาณเท่าใด * เทียบกับผู้ป่วยโรคหลอดเลือดสมองทั้งหมด ** ในกรณีที่สั่งจ่าย rt-PA ให้ตอบข้อ 4.7 เพิ่มเติม ในกรณีที่ไม่มีการสั่งจ่าย rt-PA ให้ข้ามไปข้อ 4.8	ยาละลายลิ่มเลือด (recombinant tissue plasminogen activator: rt-PA)**	
		ยาต้านเกล็ดเลือด (antiplatelet เช่น aspirin, ticlopidine, clopidogrel, aspirin + dipyridamole)	
		ยาต้านการแข็งตัวของเลือด (anticoagulant เช่น warfarin, dabigatran, apixaban, rivaroxaban)	
4.7	ในกรณีที่มีการให้ยา rt-PA สถานพยาบาลของท่านให้ยาในรูปแบบใด	☐ หลอดเลือดดำ (Intravenous) ☐ หลอดเลือดแดง (Intra-arterial) ☐ อื่นๆ (โปรดระบุ) ____________	

		การตรวจวินิจฉัย	ร้อยละ (%)
4.8	สถานพยาบาลของท่านมีการตรวจวินิจฉัย (investigations) ภายใน 24 ชั่วโมงแรกหลังผู้ป่วยโรคหลอดเลือดสมองรับไว้ในสถานพยาบาล รายการใดบ้าง และผู้ป่วยโรคหลอดเลือดสมองที่ได้รับบริการดังกล่าวคิดเป็นร้อยละโดยประมาณเท่าใด * เทียบกับผู้ป่วยโรคหลอดเลือดสมองทั้งหมด	Elektrokardiogram (EKG) monitor	
		Computerized Tomography (CT) brain	
		Magnetic Resonance Imaging (MRI)/Angiography (MRA)	
		Carotid Doppler ultrasound	
		อื่นๆ (โปรดระบุ) ____________ ____________	

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คณะกรรมการจริยธรรมการวิจัยในมนุษย์ฯ
สถาบันพัฒนาการคุ้มครองการวิจัยในมนุษย์ (สคม.)

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ส่วนที่ 4 การให้บริการอื่นๆ (Other facilities and services)		
4.9	สถานพยาบาลของท่านสามารถทำการรักษาผ่านสายสวนหลอดเลือด (endovascular treatment) โดยการผ่าตัดเพื่อกำจัดลิ่มเลือด (thrombectomy) ในผู้ป่วยโรคหลอดเลือดสมองระยะเฉียบพลันได้หรือไม่	☐ ทำได้ ☐ ทำไม่ได้
4.10	สถานพยาบาลของท่านมีระบบการรักษาและป้องกันภาวะแทรกซ้อนหรือไม่	☐ มี ☐ ไม่มี

ส่วนที่ 5 การบริการผู้ป่วยหลังการเกิดโรคหลอดเลือดสมอง (Post-stroke care)		
5.1	สถานพยาบาลของท่านมีการจัดหน่วยบริการดูแลผู้ป่วยโรคหลอดเลือดสมองภายหลังการรักษา (post-rehabilitation unit) หรือไม่	☐ มี ☐ ไม่มี
5.2	สถานพยาบาลของท่านให้บริการฟื้นฟูสมรรถภาพหลังพ้นระยะเฉียบพลัน (post-acute rehabilitation) ประเภทใดบ้างแก่ผู้ป่วยโรคหลอดเลือดสมอง และผู้ป่วยโรคหลอดเลือดสมองได้รับบริการนี้คิดเป็นร้อยละประมาณเท่าใด * เทียบกับผู้ป่วยโรคหลอดเลือดสมองทั้งหมด	(see table below)
5.3	สถานพยาบาลของท่านมีระบบติดตามผู้ป่วยโรคหลอดเลือดสมองหลัง discharge หรือไม่	☐ มี ☐ ไม่มี
5.4	บุคลากรประเภทใดต่อไปนี้ ที่ทำหน้าที่ให้บริการดูแลสุขภาพผู้ป่วยโรคหลอดเลือดสมองที่บ้าน (home health care services)	☐ แพทย์เวชปฏิบัติทั่วไป/แพทย์อายุรกรรม ☐ แพทย์ประสาทวิทยา/อนุสาขาฯ ☐ แพทย์เวชศาสตร์ครอบครัว ☐ แพทย์เวชศาสตร์ฉุกเฉิน ☐ แพทย์เวชศาสตร์ฟื้นฟู ☐ พยาบาล ☐ เภสัชกร ☐ นักจิตวิทยา ☐ นักกายภาพบำบัด ☐ นักกิจกรรมบำบัด ☐ นักแก้ไขการพูด ☐ นักโภชนาการ ☐ อสม. ☐ เวชกรรมสังคม ☐ แพทย์แผนไทย/ทางเลือก ☐ อื่นๆ (โปรดระบุ) ____________
5.5	สถานพยาบาลของท่านมีระบบดูแลผู้ป่วยโรคหลอดเลือดสมองระยะกลาง (intermediate care) และระยะยาว (long-term care) หรือไม่	☐ มีการดูแลระยะกลาง ☐ ไม่มี ☐ มีการดูแลระยะยาว ☐ ไม่มี

ข้อ 5.2:

บริการฟื้นฟูสมรรถภาพ	ร้อยละ (%)
การฟื้นฟูแบบผู้ป่วยใน (inpatient rehabilitation)	
การฟื้นฟูแบบผู้ป่วยในต่อด้วยแบบผู้ป่วยนอก (in and outpatient rehabilitation)	
การฟื้นฟูแบบผู้ป่วยนอก (outpatient rehabilitation)	
การฟื้นฟูที่บ้าน (home-based rehabilitation) โดยบุคลากรการแพทย์	
การฟื้นฟูโดยชุมชน (community-based rehabilitation)	
อื่นๆ (โปรดระบุ) ____________________________	

ข้อแนะนำ ข้อเสนอแนะเพิ่มเติม เพื่อให้เกิดการพัฒนาคุณภาพบริการด้านโรคหลอดเลือดสมองสำหรับประเทศไทย

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สถาบันพัฒนาการคุ้มครองการวิจัยในมนุษย์ (สคม.)

"โปรดตรวจสอบความครบถ้วนของคำถามทุกข้ออีกครั้ง"

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คำจำกัดความ

ลำดับ	คำจำกัดความ	ความหมาย
1	**การดูแลสุขภาพผู้ป่วยโรคหลอดเลือดสมองที่บ้าน** (home health care services)	การติดตามดูแลรักษาผู้ป่วยโรคหลอดเลือดสมองที่บ้าน ภายหลังการรับไว้รักษาในสถานพยาบาล ซึ่งผู้ที่ทำหน้าที่อาจเป็นทั้งเจ้าหน้าที่ของสถานพยาบาล หรืออาสาสมัครสาธารณสุขประจำหมู่บ้าน (อสม.) หรือผู้ที่ผ่านกระบวนการอบรมให้ความรู้จากเจ้าหน้าที่ของสถานพยาบาล
2	**การตรวจรับรองคุณภาพ**	ได้รับการตรวจประเมินและรับรองเกณฑ์การประเมินหอผู้ป่วยโรคหลอดเลือดสมองมาตรฐานโดยคณะกรรมการที่ได้รับการแต่งตั้ง
3	**การฟื้นฟูแบบผู้ป่วยนอก** (outpatient rehabilitation)	ผู้ป่วยได้รับการฟื้นฟูสมรรถภาพแบบผู้ป่วยนอก โดยอาจได้รับการฟื้นฟูสมรรถภาพ อย่างน้อย 45 นาทีต่อครั้ง อย่างน้อย 12 ครั้ง ภายใน 6 เดือน
4	**การฟื้นฟูโดยชุมชน** (community-based rehabilitation)	การฟื้นฟูสมรรถภาพอย่างต่อเนื่องในระดับชุมชน โดยผู้ป่วยได้รับการฟื้นฟูสมรรถภาพโดยทีมหมอครอบครัว ทีมเยี่ยมบ้าน บุคลากรทางการแพทย์ของสถานพยาบาลหรือ อสม. ที่ได้รับการอบรมเรื่องการฟื้นฟูสมรรถภาพ
5	**การฟื้นฟูแบบผู้ป่วยใน** (inpatient rehabilitation)	การฟื้นฟูสมรรถภาพขณะรับการรักษาแบบผู้ป่วยใน โดยอาจได้รับการฟื้นฟูสมรรถภาพโดยทีมสหวิชาชีพ เช่น ได้รับการฟื้นฟูสมรรถภาพอย่างน้อยวันละ 3 ชั่วโมง และอย่างน้อย 5 วันต่อสัปดาห์ (หรืออย่างน้อย 15 ชั่วโมง/สัปดาห์) เป็นต้น
6	**การฟื้นฟูที่บ้าน** (home-based rehabilitation)	ผู้ป่วยได้รับการฟื้นฟูสมรรถภาพที่บ้าน โดยผู้ป่วยและญาติหรือผู้ดูแลได้รับความรู้จากบุคลากรทางการแพทย์ของสถานพยาบาลหรือทีมเวชศาสตร์ฟื้นฟูเกี่ยวกับการปฏิบัติตัวและการฟื้นฟูสมรรถภาพที่บ้าน
7	**การฟื้นฟูระยะหลังเฉียบพลัน** (post-acute rehabilitation)	การฟื้นฟูสมรรถภาพหลังจากผู้ป่วยพ้นระยะเฉียบพลันแล้วแต่ยังอาจมีข้อจำกัดในการปฏิบัติกิจวัตรประจำวัน จำเป็นต้องได้รับการฟื้นฟูสมรรถภาพโดยทีมสหวิชาชีพ หรือส่งผู้ป่วยไปรับบริการที่หอผู้ป่วยที่รับผู้ป่วยที่ทำหน้าที่ฟื้นฟูสมรรถภาพผู้ป่วยเป็นหลัก
8	**การรักษาผ่านสายสวนหลอดเลือด** endovascular treatment)	การนำเอาลิ่มเลือดที่อุดตันหลอดเลือดในสมองออกด้วยการเปิดหลอดเลือดโดยใส่สายสวนหลอดเลือดสมอง
9	**ค่าใช้จ่ายกิจกรรมการให้ความรู้แก่บุคลากรทางการแพทย์ ผู้ป่วยโรคหลอดเลือดสมอง และ/หรือผู้ดูแล**	ค่าใช้จ่ายที่เกิดขึ้นจากการจัดหลักสูตรการสอนและให้ความรู้ในการป้องกัน ดูแลรักษาโรคหลอดเลือดสมอง ให้แก่บุคลากรทางการแพทย์ในสถานพยาบาล ผู้ป่วยโรคหลอดเลือดสมอง และ/หรือผู้ดูแลผู้ป่วย
10	**ค่าทำหัตถการ**	ค่าใช้จ่ายที่เกิดขึ้นจากกิจกรรมการรักษาพยาบาลที่ปฏิบัติโดยแพทย์ และ/หรือ พยาบาลที่กระทำต่อร่างกายผู้ป่วยเพื่อตรวจ รักษา หรือบรรเทาอาการของโรค ภายใต้ข้อกำหนดมาตรฐานการประกอบวิชาชีพ เช่น การผ่าตัด การตรวจวินิจฉัยและการรักษาทางรังสีวิทยา เป็นต้น

ลำดับ	คำจำกัดความ	ความหมาย
22	**ระดับสถานพยาบาล**	ระดับของสถานพยาบาลในแบบสอบถาม อ้างอิงตามแผนพัฒนาระบบบริการสุขภาพ (service plan) พ.ศ. 2561 - 2565 แบ่งเป็น ○ ระดับ A (Advance - Level Referral Hospital) เป็นสถานพยาบาลรับผู้ป่วยส่งต่อระดับสูง (high - level referral hospital) โดยรับส่งต่อจากโรงพยาบาลตติยภูมิขนาดกลาง โดยทั่วไปมักเป็นโรงพยาบาลศูนย์ที่รับส่งต่อจากเครือข่ายบริการระดับจังหวัด สามารถรองรับผู้ป่วยที่ต้องการการรักษาที่ยุ่งยากซับซ้อนระดับเชี่ยวชาญและเทคโนโลยีขั้นสูงและมีราคาแพง (Advance & sophisticate technology) แพทย์ผู้เชี่ยวชาญทั้งสาขาหลัก สาขารองและสาขาย่อยครบทุกสาขาตามความจำเป็น และมีภารกิจด้านแพทยศาสตร์ศึกษาและงานวิจัยทางการแพทย์ ○ ระดับ S (standard - level referral hospital) เป็นสถานพยาบาลรับผู้ป่วยส่งต่อระดับสูง (high - level referral hospital) โดยรับส่งต่อจากโรงพยาบาลตติยภูมิขนาดกลาง และมักเป็นโรงพยาบาลทั่วไปที่เป็นแม่ข่ายของเครือข่ายบริการระดับจังหวัด สามารถรองรับผู้ป่วยที่ต้องการการรักษาที่ยุ่งยากซับซ้อนระดับเชี่ยวชาญเฉพาะ จึงประกอบด้วย แพทย์ผู้เชี่ยวชาญทั้งสาขาหลัก สาขารอง ครบทุกสาขาและสาขาย่อยบางสาขา นอกจากนี้ บางแห่งอาจมีศูนย์แพทย์ศาสตร์ศึกษาโดยความร่วมมือกับมหาวิทยาลัยในพื้นที่ ○ ระดับ M1 (mid - level referral hospital) เป็นสถานพยาบาลรับส่งต่อระดับกลาง โดยเป็นโรงพยาบาลทั่วไปขนาดเล็ก มีหน้าที่รับผู้ป่วยส่งต่อจากเครือข่ายบริการทุติยภูมิ มีขีดความสามารถในการรักษาที่ยุ่งยากซับซ้อนระดับเชี่ยวชาญประกอบด้วยแพทย์ผู้เชี่ยวชาญสาขาหลักทุกสาขาและสาขารองในบางสาขาที่จำเป็น
23	**ระบบการดูแลผู้ป่วยโรคหลอดเลือดสมองระยะกลาง** (intermediate care service systems)	การบริบาลฟื้นสภาพผู้ป่วยระยะกลางที่มีอาการทางคลินิกผ่านพ้นภาวะวิกฤติและมีอาการคงที่ แต่ยังคงมีความผิดปกติของร่างกายบางส่วนอยู่และมีข้อจำกัดในการปฏิบัติกิจกรรมในชีวิตประจำวัน จำเป็นต้องได้รับบริการฟื้นฟูสมรรถภาพทางการแพทย์โดยทีมสหวิชาชีพ (multidisciplinary approach) อย่างต่อเนื่องจนครบ 6 เดือนตั้งแต่ในโรงพยาบาลจนถึงชุมชน เพื่อเพิ่มสมรรถนะร่างกาย จิตใจ ในการปฏิบัติกิจวัตรประจำวัน และลดความพิการหรือภาวะทุพพลภาพ รวมทั้งกลับสู่สังคมได้อย่างเต็มศักยภาพ
24	**ระบบการดูแลผู้ป่วยโรคหลอดเลือดสมองระยะยาว** (long-term care service systems)	การจัดบริการสาธารณสุขและบริการสังคมเพื่อตอบสนองความต้องการความช่วยเหลือของผู้ที่ประสบภาวะเจ็บป่วยเรื้อรัง การประสบอุบัติเหตุ ความพิการต่างๆ ตลอดจนผู้สูงอายุที่ไม่สามารถช่วยเหลือตัวเองได้ในชีวิตประจำวัน มุ่งเน้นการฟื้นฟู บำบัด ส่งเสริมสุขภาพอย่างสม่ำเสมอ

ลำดับ	คำจำกัดความ	ความหมาย
		ต่อเนื่อง เพื่อให้คนกลุ่มนี้มีคุณภาพชีวิตที่ดีสามารถดำเนินชีวิตอย่างมีอิสระเท่าที่จะเป็นได้
25	**ระบบการลงทะเบียนผู้ป่วยโรคหลอดเลือดสมอง (stroke registry)**	การมีระบบการจัดเก็บประวัติและข้อมูลการรักษาผู้ป่วยโรคหลอดเลือดสมองเพื่อสามารถติดตามการรักษา และผลการรักษาได้ เพื่อจะได้ใช้ปรับปรุงแนวทางการดูแลรักษาผู้ป่วยให้ดียิ่งขึ้น
26	**ระบบติดตามผู้ป่วยโรคหลอดเลือดสมองหลัง discharge**	ระบบการติดตามผู้ป่วยโรคหลอดเลือดสมองภายหลังการจำหน่ายออกจากสถานพยาบาลเพื่อให้สามารถกลับมารับบริการดูแลรักษาได้อย่างต่อเนื่อง
27	**บุคลากรการแพทย์ที่ให้บริการเต็มเวลา (full-time staff**	ประเภทของการจ้างงาน แบ่งเป็น 2 ประเภท คือ 1) พนักงานประจำ/ทำงานเต็มเวลา (full-time staff) หมายถึง ผู้ที่ทำงานเท่ากับหรือมากกว่า 40 ชั่วโมงต่อสัปดาห์หรือตามที่หน่วยงานกำหนด และมักได้สวัสดิการมากกว่าพนักงานที่ทำงานบางเวลา 2) พนักงานชั่วคราว/ทำงานบางเวลา (part-time staff) หมายถึง ผู้ที่ทำงานน้อยกว่า 40 ชั่วโมงต่อสัปดาห์ ซึ่งส่วนใหญ่เป็นการจ้างให้ทำงานเฉพาะบางช่วงเวลา
28	**สถานพยาบาลภาครัฐ**	เป็นสถานพยาบาลตามพรบ.สถานพยาบาล (ฉบับที่ 4) 2559 ทั้งนี้ในการศึกษานี้ครอบคลุมเฉพาะสถานพยาบาลซึ่งดำเนินการโดยภาครัฐทั้งภายในและภายนอกสังกัดกระทรวงสาธารณสุข
29	**หน่วยบริการดูแลผู้ป่วยโรคหลอดเลือดสมองภายหลังการรักษา** (Post - rehabilitation unit)	หอผู้ป่วยที่รับผู้ป่วยหลังจากเกิดโรคหลอดเลือดสมองแล้ว 1 - 2 สัปดาห์ โดยมีวัตถุประสงค์เพื่อให้การรักษาเพื่อฟื้นฟูสมรรถภาพผู้ป่วยเป็นหลัก
30	**หอผู้ป่วยโรคหลอดเลือดสมอง** (stroke unit)	หอผู้ป่วยเฉพาะภายในสถานพยาบาลนั้นๆ ที่ใช้ในการให้ดูแลรักษาผู้ป่วยโรคหลอดเลือดสมองระยะเฉียบพลัน โดยบุคลากรการแพทย์ที่มีความเชี่ยวชาญของโรคหลอดเลือดสมองโดยตรง สามารถติดตามและเฝ้าสังเกตุอาการและภาวะแทรกซ้อนได้อย่างใกล้ชิด และเป็นไปตามมาตรฐานในการจัดบริการตามกิจกรรมบริการ ได้แก่ มีทีมสหวิชาชีพร่วมกันดูแลผู้ป่วย มีเตียงผู้ป่วยไม่น้อยกว่า 4 เตียง มีแผนการดูแลรักษาและแผนการให้ความรู้แก่ผู้ป่วยหรือญาติที่จัดเตรียมผ่านการประชุมของทีมสหวิชาชีพของสถานพยาบาลนั้นๆ

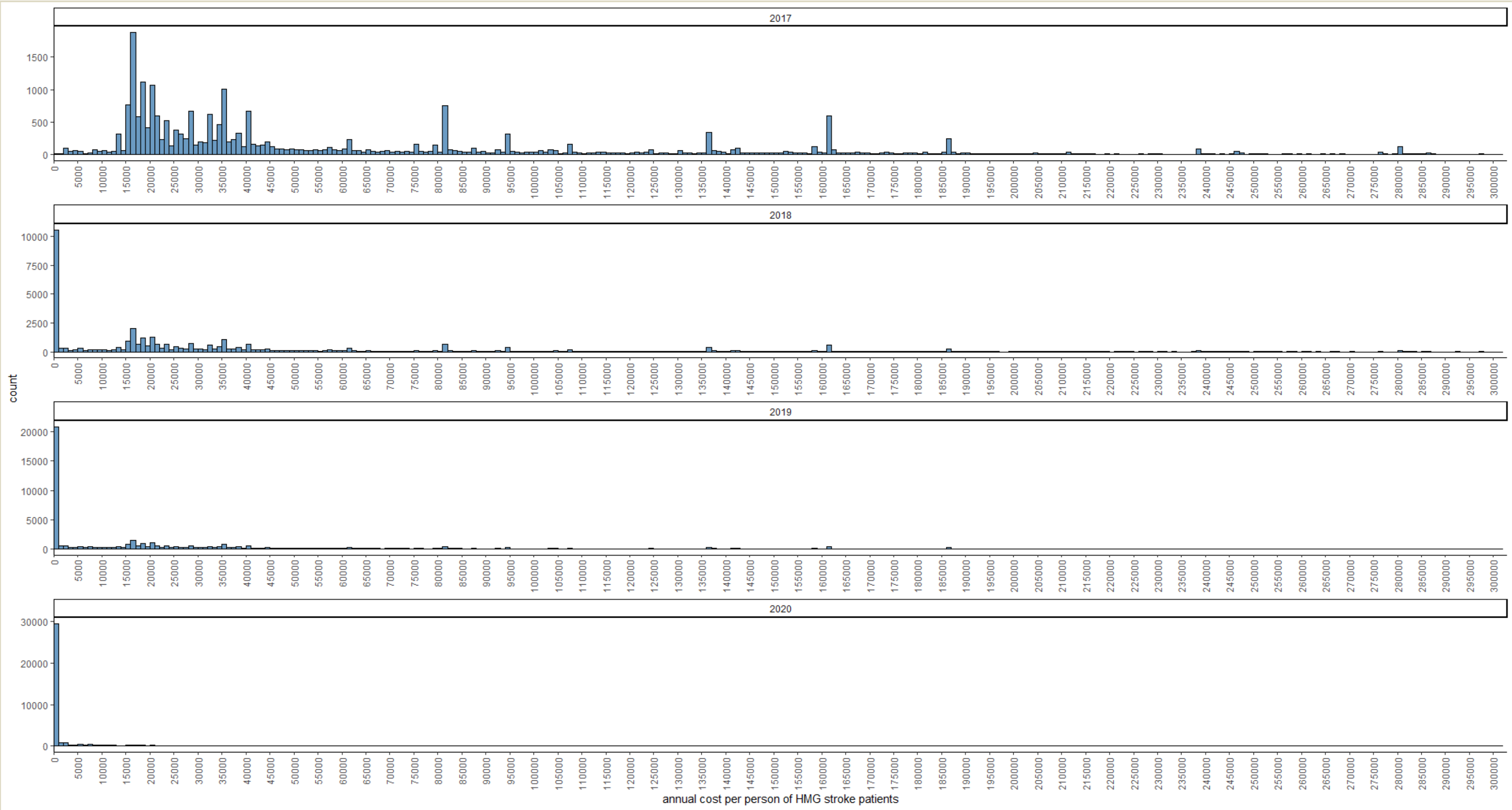
Appendix 3 Stroke patient admissions and transfers per year

Health region	Total			Ischemic stroke			Haemorrhagic stroke			Unspecified stroke		
	median	min-max	N	median	min-max	N	median	min-max	N	median	min-max	N
A. number of stroke patients admission per year												
advanced-level												
1	1,153	-	1	431	-	1	587	-	1	135	-	1
2	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-
4	1,569	-	1	1,052	-	1	490	-	1	27	-	1
5	901	-	1	621	-	1	280	-	1		-	
6	1,749	-	1	916	-	1	780	-	1	53	-	1
8	1,895	-	1	1,277	-	1	618	-	1	135	-	1
9	-	-	-	-	-	-	-	-	-	-	-	-
10	2,372	-	1	1,841	-	1	437	-	1	94	-	1
11	1,523	934 - 2,112	2	952	494 - 1,411	2	515	364 - 666	2	56	35 - 77	2
12	-	-	-	-	-	-	-	-	-	-	-	-
Median (IQR)	1,659 (1,098 - 1,949)		8	984 (589 - 1,310)		8	538 (419 - 630)		8	77 (44 - 114)		7
standard-level												
1	550	532 – 569	2	434	430 - 438	2	114	94 - 133	2	6	-	1
2	796	-	1	442	-	1	223	-	1	131	-	1
3	878	749 - 1,006	2	468	352 - 583	2	307	215 - 399	2	103	24 - 182	2
4	669	654 – 684	2	440	402 - 477	2	183	159 - 207	2	397	-	1
5	926	441 - 1,561	4	682	327 - 1,029	4	211	99 - 531	4	20	15 - 47	3
6		-			-			-			-	
8	1,784	-	1	1386	-	1	321	-	1	44	-	1
9		-			-			-		-	-	-
10		-			-			-			-	

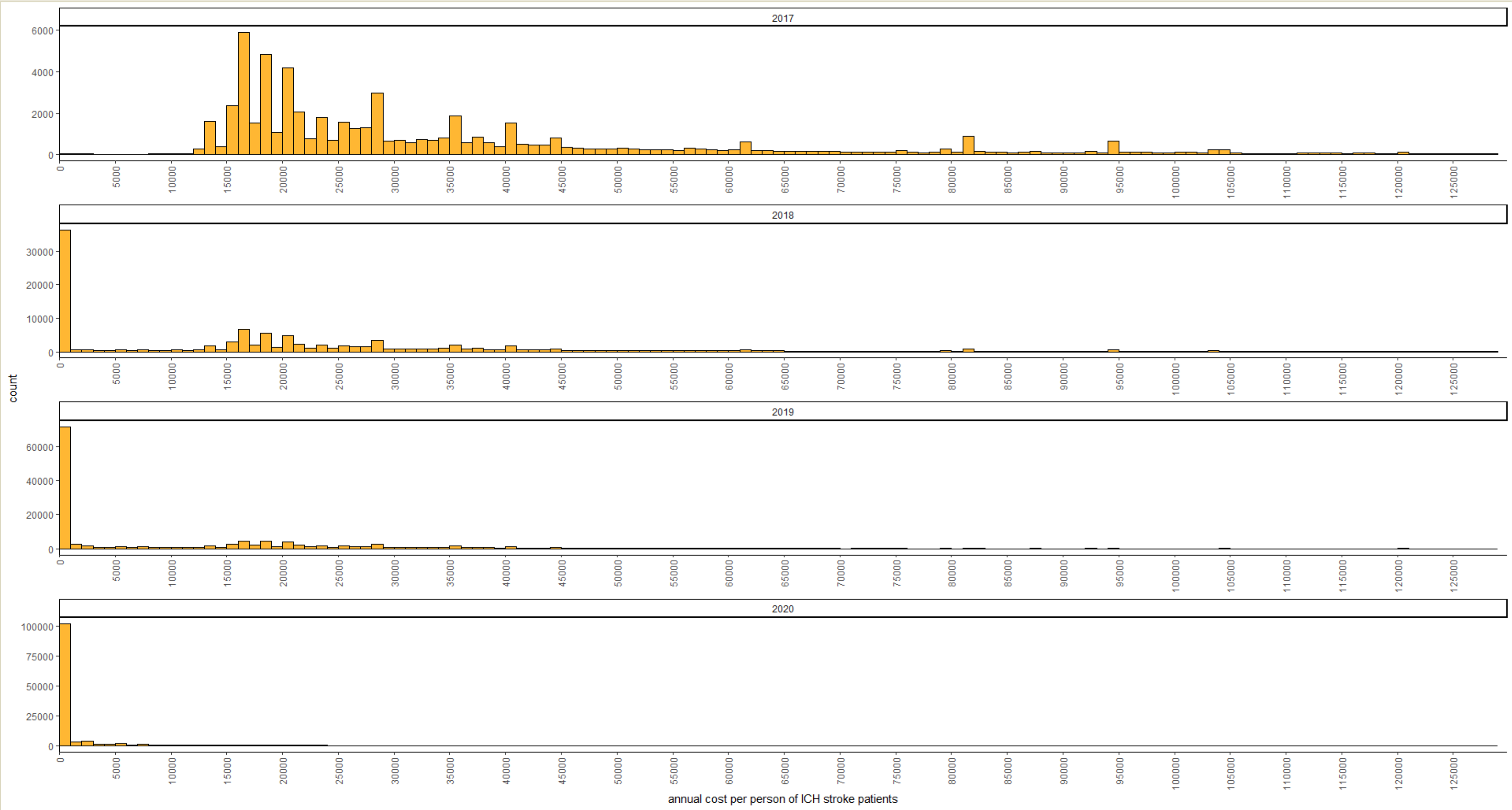
Health region	Total			Ischemic stroke			Haemorrhagic stroke			Unspecified stroke		
	median	min-max	N	median	min-max	N	median	min-max	N	median	min-max	N
11	800	461 - 1,318	4	360	177 - 584	4	176	99 - 285	4	317	30 - 497	4
12	912	525 - 1,574	3	628	268 - 1,230	3	284	114 - 344	3	133	123 - 143	2
Median (IQR)	749 (535 - 1,218)		19	438 (362 - 606)		19	215 (124 - 286)		19	123 (27 - 184)		15
mid-level												
1												
2	590	-	1	408	-	1	180	-	1	2	-	1
3												
4	427	236 – 618	2	290	169 - 411	2	130	61 - 199	2	7	06-Aug	2
5	294	211 – 376	2	217	136 - 298	2	58	37 - 78	2	38	-	1
6		-			-			-			-	
8	492	481 – 502	2	451	445 - 457	2	34	33 - 34	2	7	02-Dec	2
9	373	-	1	353	-	1	20	-	1	-	-	-
10	468	-	1	468	-	1		-			-	
11	218	-	1	143	-	1	63	-	1	12	-	1
12	521	-	1	410	-	1	111	-	1			
Median (IQR)	468 (304 - 512)		11	408 (234 - 428)		11	62 (35 - 103)		10	8 (4 - 12)		7
B. number of stroke patients who are transferred to other hospitals per year												
advanced-level												
1	57	-	1				-	-			-	
4	209	-	1	141	-	1	65	-	1	3	-	1
5	3	-	1	3	-	1	-	-			-	
6												
8												
9	186	-	1				-	-				

Health region	Total			Ischemic stroke			Haemorrhagic stroke			Unspecified stroke		
	median	min-max	N	median	min-max	N	median	min-max	N	median	min-max	N
10				63	-	1	103	-	1	20	-	1
Median (IQR)	122 (44 - 192)		4	63 (33 - 102)		3	84 (74 - 94)		2	12 (7 - 16)		2
standard-level												
1	16	Oct-23	2				15	Oct-20	2	3	-	1
2	167	-	1	84	-	1	53	-	1	35	-	1
3	394	39 - 749	2	178	5 - 352	2	124	32 - 215	2	92	2 - 182	2
4	16	16 - 17	2	5	-	1	10	May-16	2	7	-	1
5	21	Feb-22	3	5	-	1	2	Feb-22	3	14	-	1
8	45	-	1				45	-	1			
11	28	21 - 31	3	8	05-Nov	3	12	Jun-14	3	8	06-Oct	3
12	16	Oct-23	2	8	Feb-15	2	15	Aug-22	2	10	-	1
Median (IQR)	22 (17 - 40)		16	6 (5 - 14)		10	15 (8 - 24)		16	9 (6 - 13)		10
mid-level												
2	12	-	1	4	-	1	8	-	1			
4	38	38 - 39	2	26	17 - 36	2	12	Feb-22	2			
5	193	10 - 376	2	154	10 - 298	2	78	-	1			
8	36	29 - 44	2	32	-	2	3	02-Apr	2	2	-	2
9	60	-	1	40	-	1	20	-	1			
10	468	-	1	429	-	1	39	-	1		-	
11	46	-	1	10	-	1	17	-	1	19	-	1
12	6	-	1	3	-	1	3	-	1			
Median (IQR)	39 (20 - 53)		11	25 (10 - 39)		11	12 (3 - 22)		10	2 (2 - 10)		3

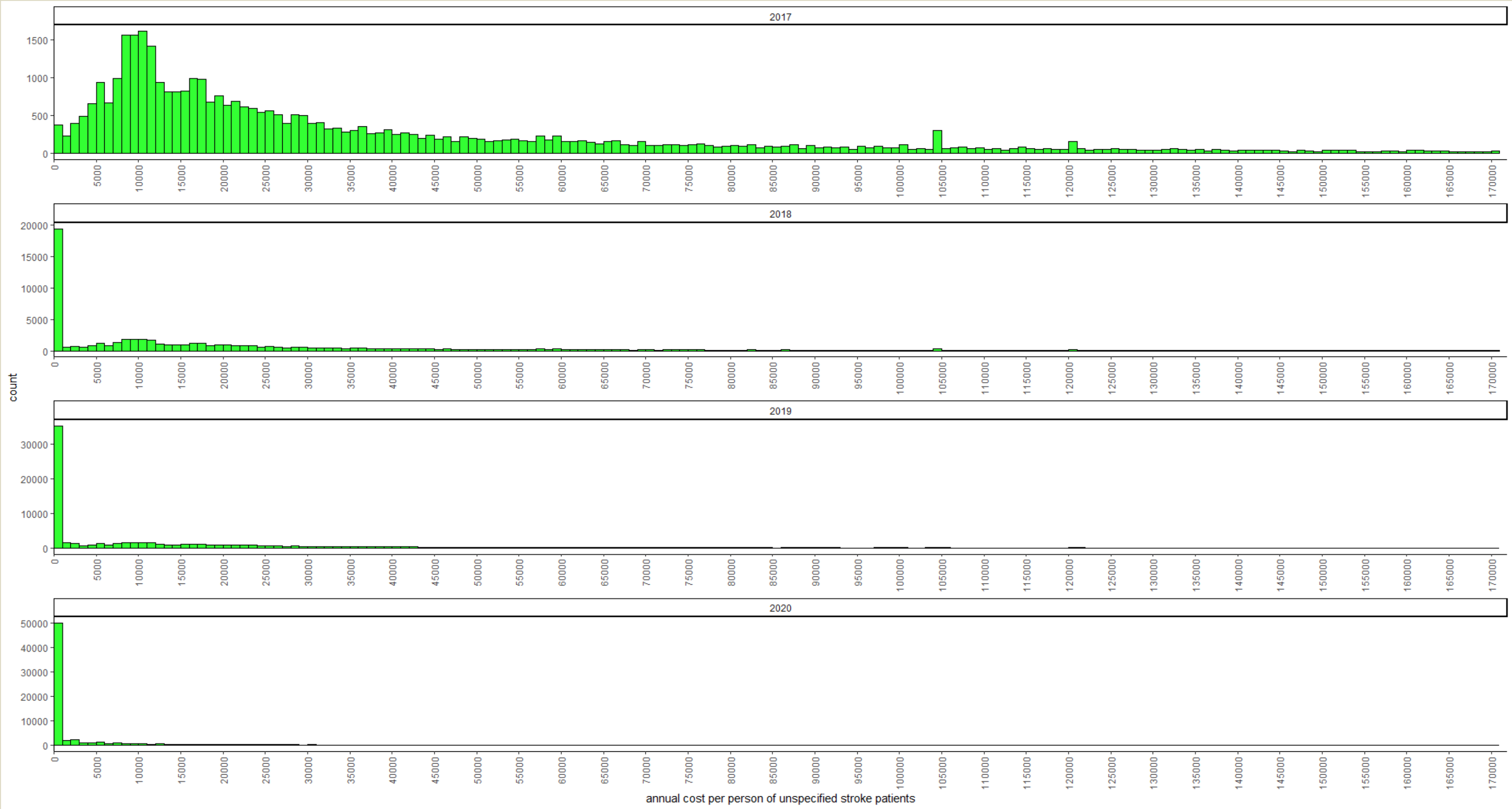
Appendix 4 Cost distribution of haemorrhagic stroke patients separated by year



Appendix 5 Cost distribution of ischaemic stroke patients separated by year



Appendix 6 Cost distribution of unspecified stroke patient separated by year

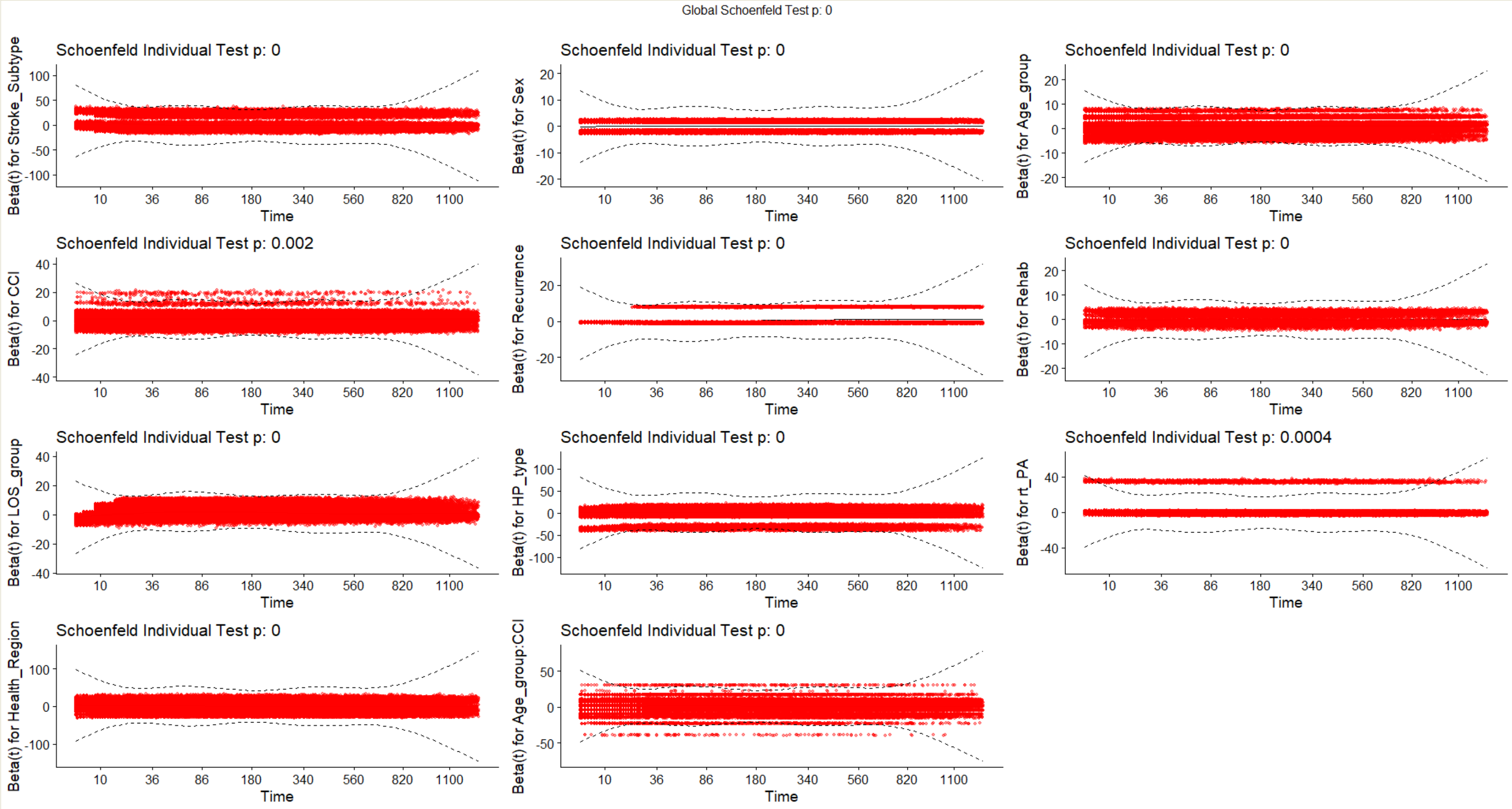


Appendix 7 The goodness-of-fit test for the proportional hazards assumption

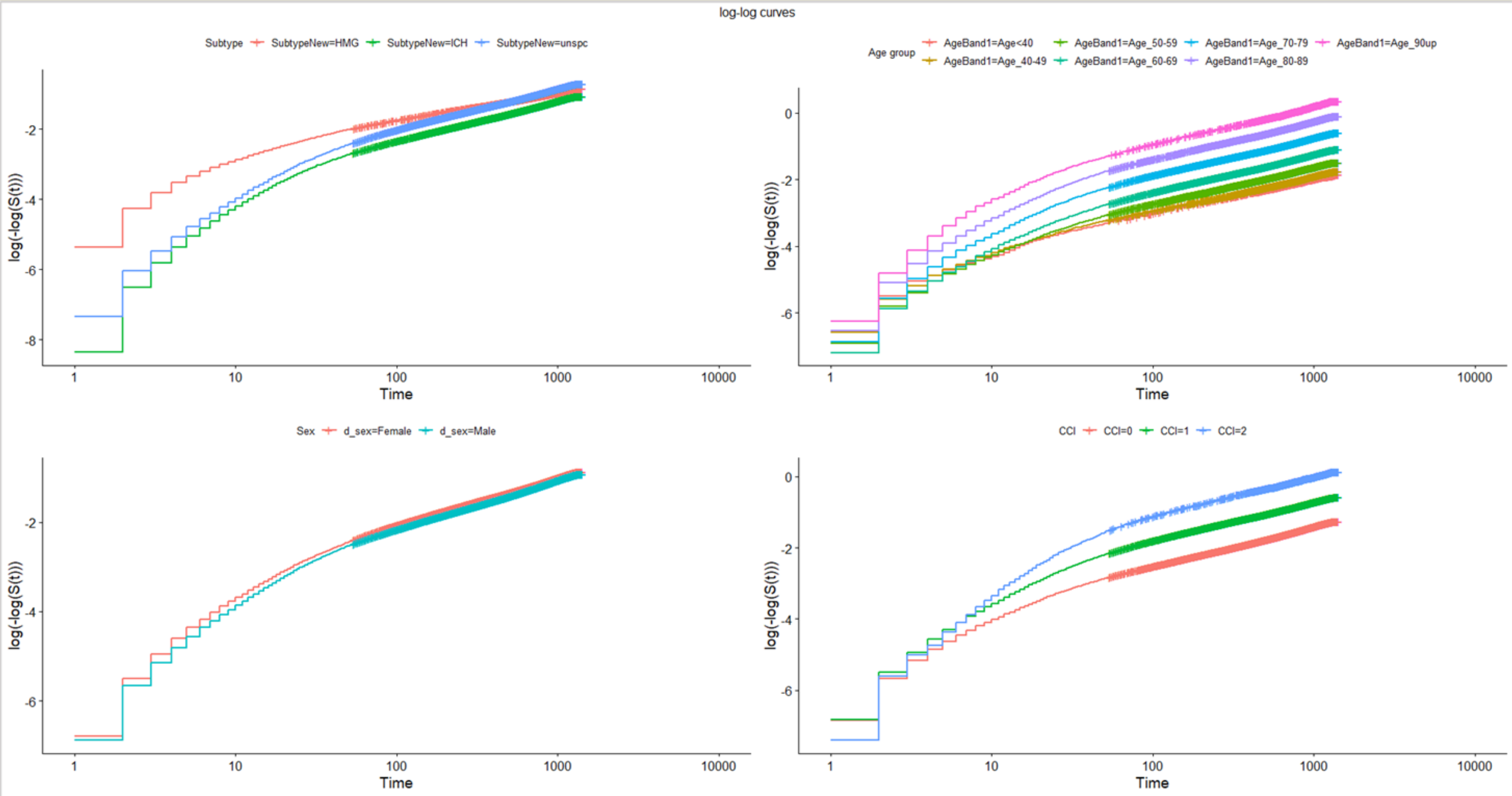
	chi-square	df	p
Stroke subtype	1,592.7	2	<0.0001
Sex	26.9	1	<0.0001
Age group	88.4	6	<0.0001
CCI	12.4	2	0.00202
Recurrence	4,354.5	1	<0.0001
Rehabilitation	256.8	1	<0.0001
rt-PA	317.6	5	0.00043
Hospital level	12.4	1	<0.0001
LOS group	175.5	3	<0.0001
Health region	491.1	12	<0.0001
Age group##CCI interaction	55.4	12	<0.0001
GLOBAL	7,553.3	46	<0.0001

From the output above, the test was statistically significant for each of the covariates as well as the global test. Therefore, the proportional hazards assumption appeared to be violated.

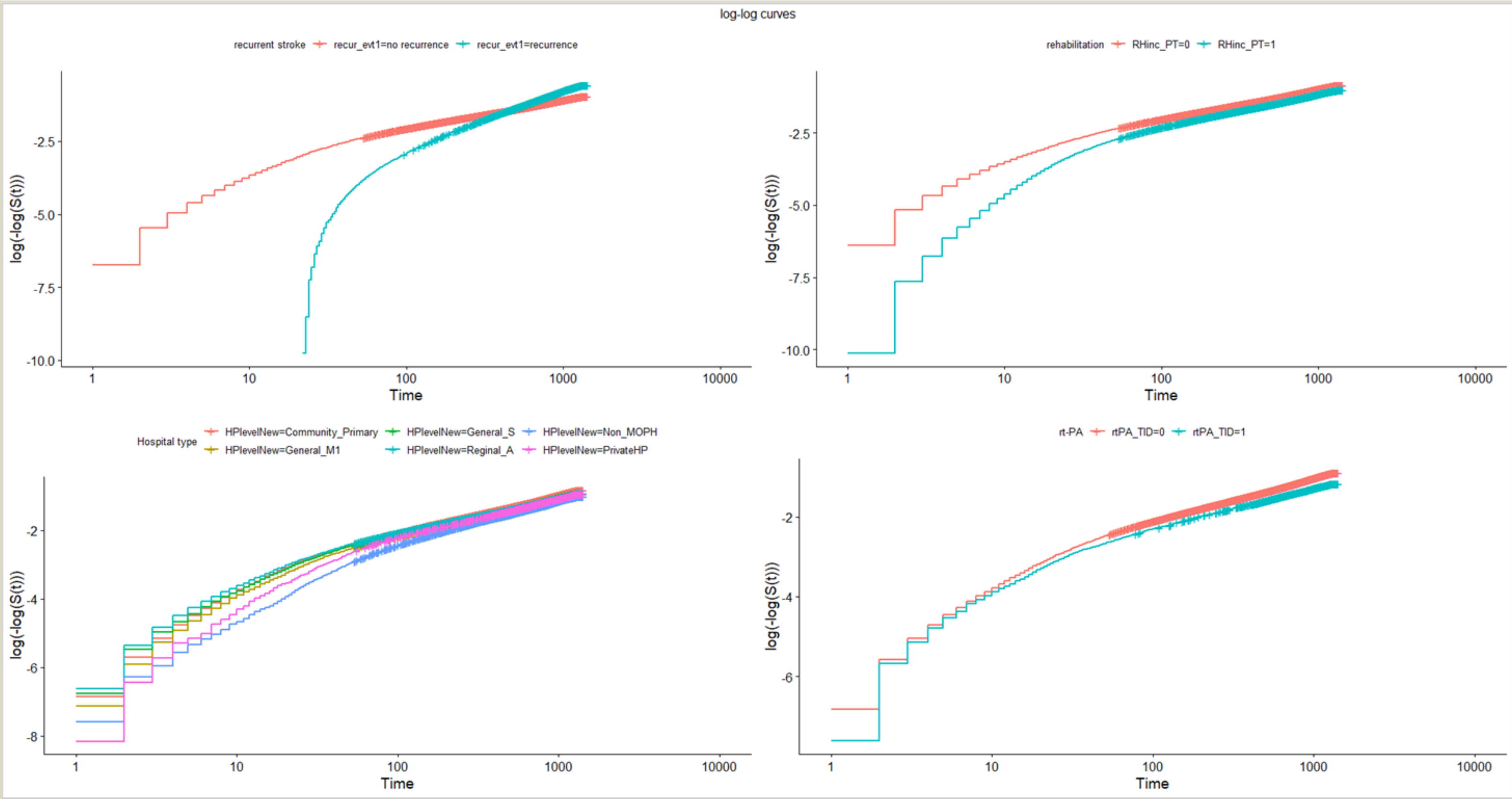
Appendix 8 Schoenfeld residuals method for testing proportional hazards model



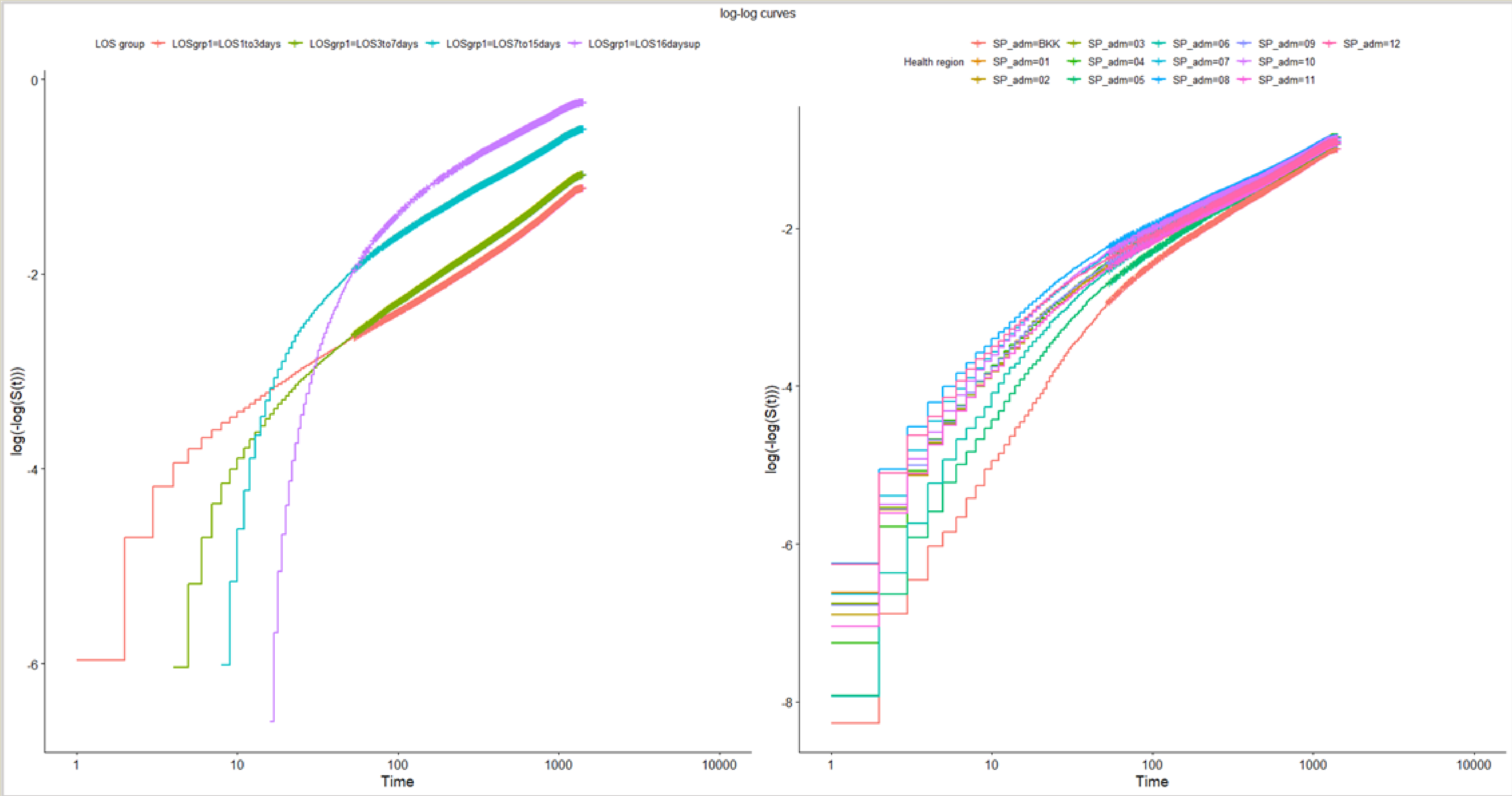
Appendix 9 The log cumulative hazards for accessing the proportional hazards assumption



Appendix 9 The log cumulative hazards for accessing the proportional hazards assumption (cont.)



Appendix 9 The log cumulative hazards for accessing the proportional hazards assumption (cont.)

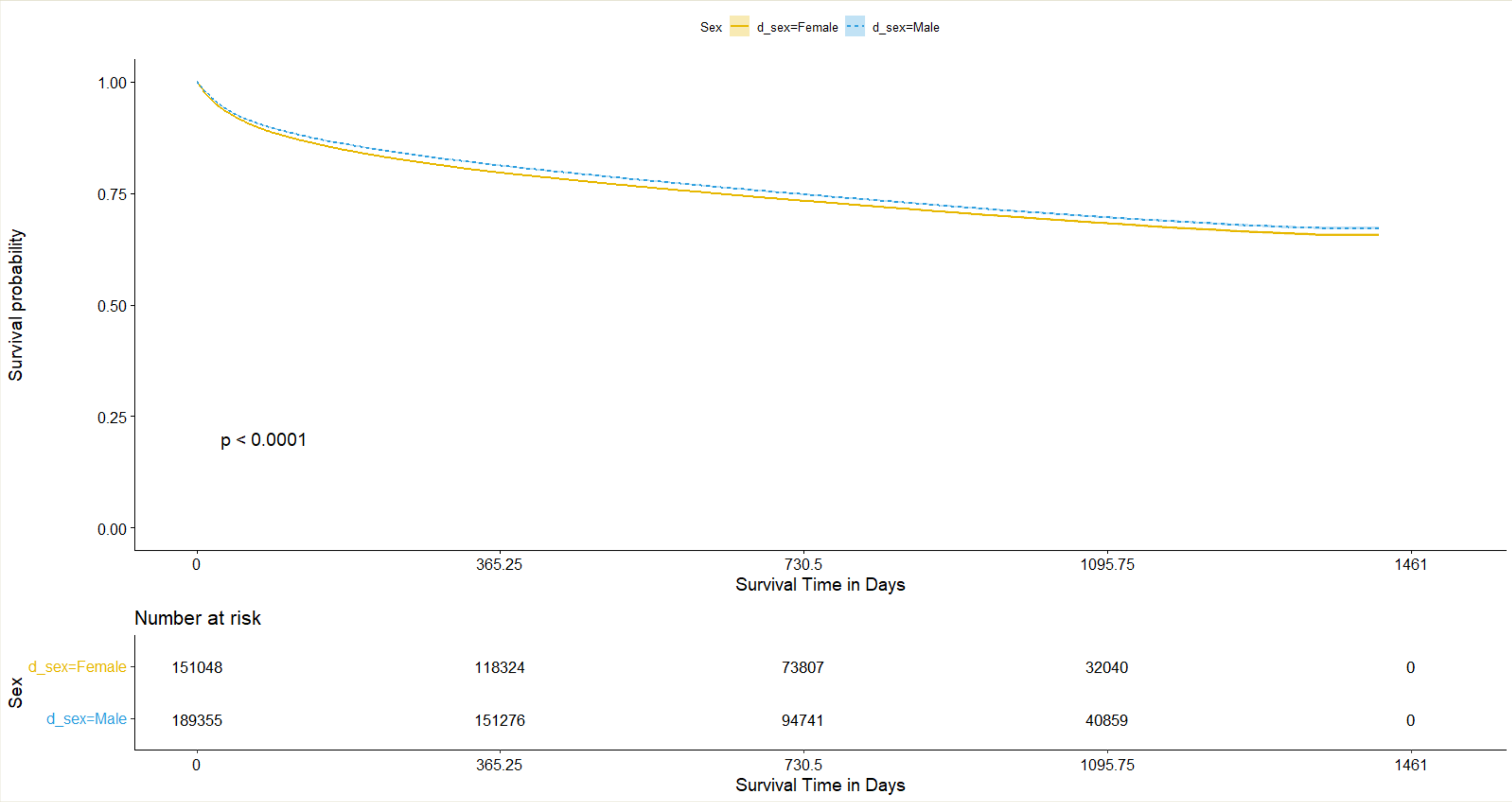


Appendix 10 Univariate analysis

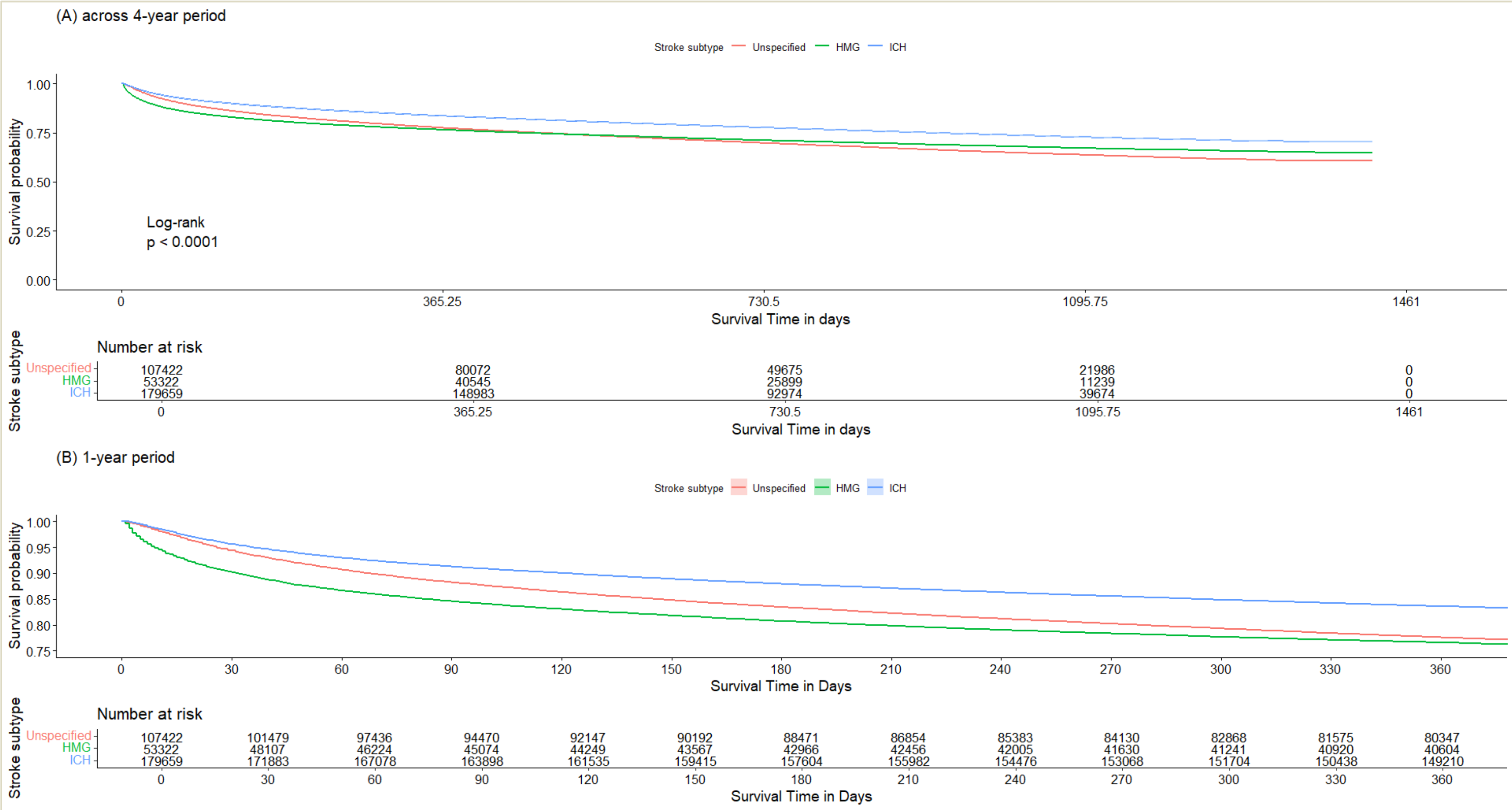
Characteristic	Odds Ratio	L95%CI	U95%CI
Age group (year)			
Age <40	Reference		
Age 40-49	0.90	0.88	0.93
Age 50-59	0.97	0.95	0.99
Age 60-69	1.11	1.08	1.14
Age 70-79	1.25	1.22	1.28
Age 80-89	1.37	1.33	1.40
Age ≥90	1.57	1.50	1.64
Sex			
Female	Reference		
Male	0.92	0.92	0.93
CCI			
No CCI	Reference		
score 1 to 2	1.36	1.35	1.38
score ≥3	2.15	2.05	2.26
Stroke subtype			
ischaemic	Reference		
haemorrhagic	0.96	0.95	0.98
Unspecified	1.03	1.01	1.04
Hospital type			
Primary and community	Reference		
Mid-level	1.00	0.98	1.02
Standard-level	1.05	1.04	1.07
Advanced-level	1.03	1.01	1.04
Non-MOPH	1.22	1.19	1.26
Private hospitals and clinics	1.07	1.04	1.11
Health regions			
Bangkok	Reference		
1	1.27	1.23	1.31
2	1.23	1.18	1.27
3	1.29	1.25	1.34
4	1.24	1.20	1.28
5	1.25	1.21	1.29
6	1.21	1.17	1.25
7	1.27	1.23	1.32
8	1.22	1.18	1.27
9	1.19	1.15	1.24
10	1.29	1.25	1.34
11	1.24	1.20	1.28
12	1.28	1.23	1.32
Rehabilitation			

Characteristic	**Odds Ratio**	**L95%CI**	**U95%CI**
Not received rehabilitation	Reference		
Received rehabilitation	0.87	0.86	0.88
Thrombolytic therapy			
Not received thrombolytic therapy	Reference		
Received thrombolytic therapy	1.13	1.10	1.16
LOS group			
LOS <3 days	Reference		
LOS 3 to 7 days	0.97	0.96	0.98
LOS 8 to 15 days	1.09	1.07	1.10
LOS >15 days	1.32	1.29	1.35
Year of admission			
2017	Reference		
2018	5.57	5.50	5.64
2019	3.00	2.97	3.04
2020	1.00	-	-

Appendix 11 Kaplan-Meier curves of all-cause mortality classified by sex

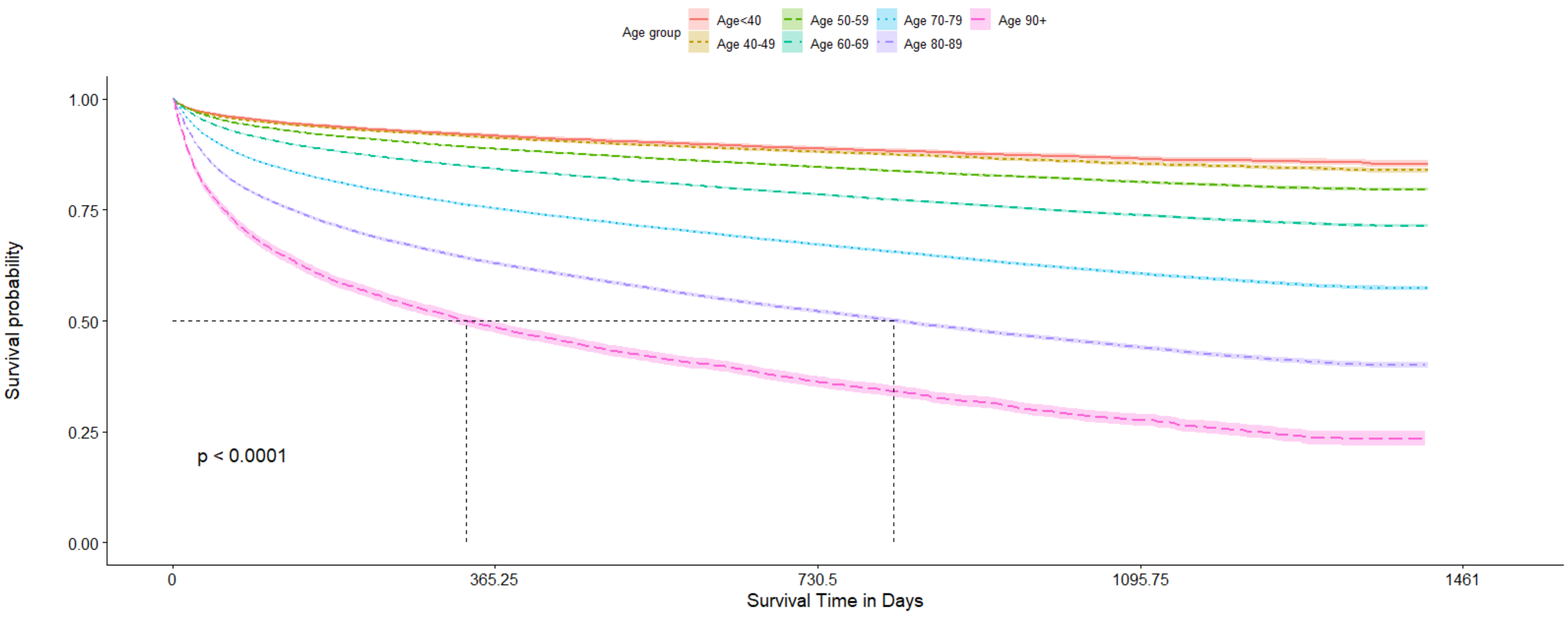


Appendix 12 Kaplan-Meier curves of all-cause mortality classified by stroke subtypes



ICH: ischaemic stroke, HMG: haemorrhagic stroke

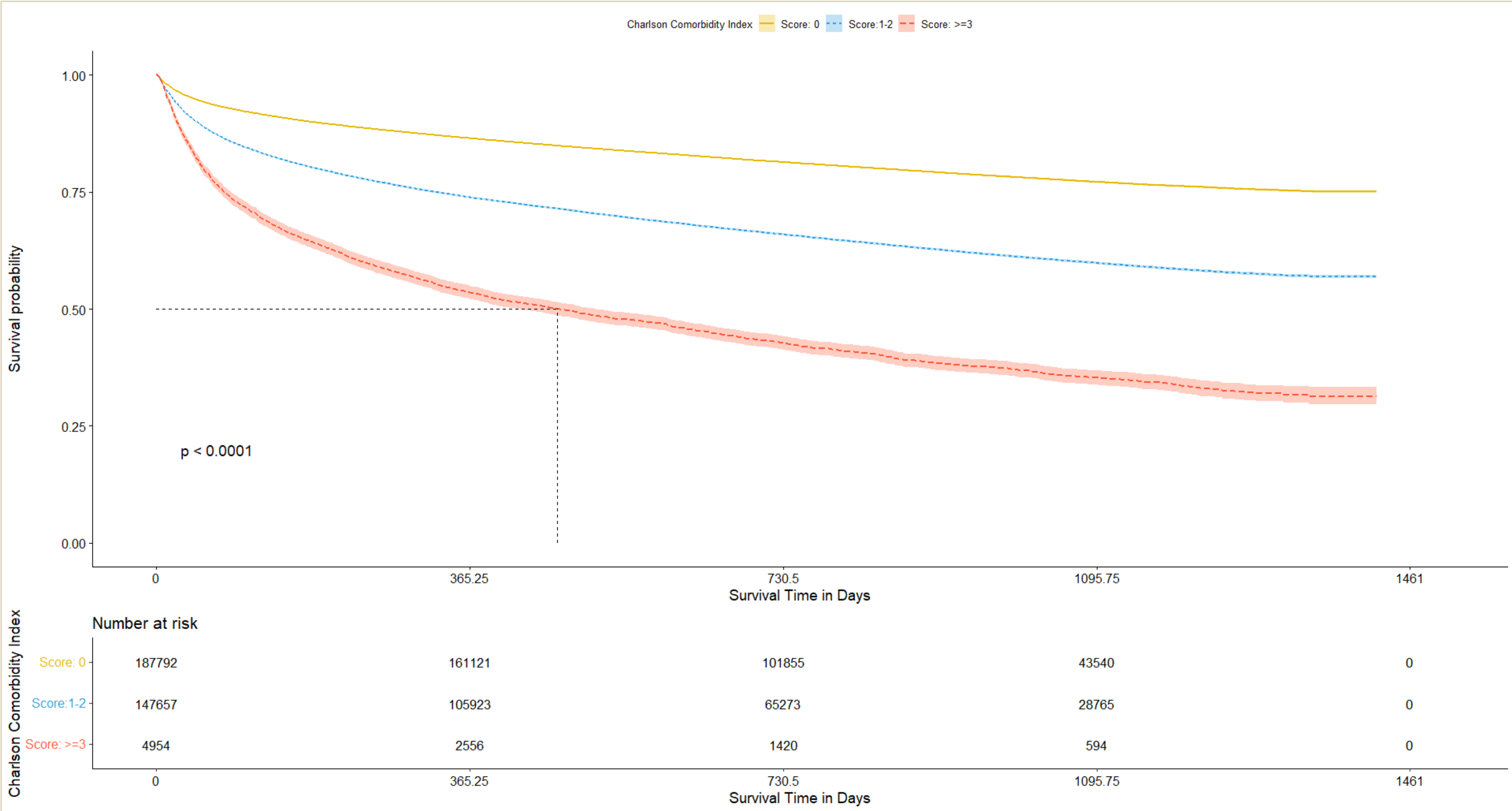
Appendix 13 Kaplan-Meier curves of all-cause mortality classified by age group



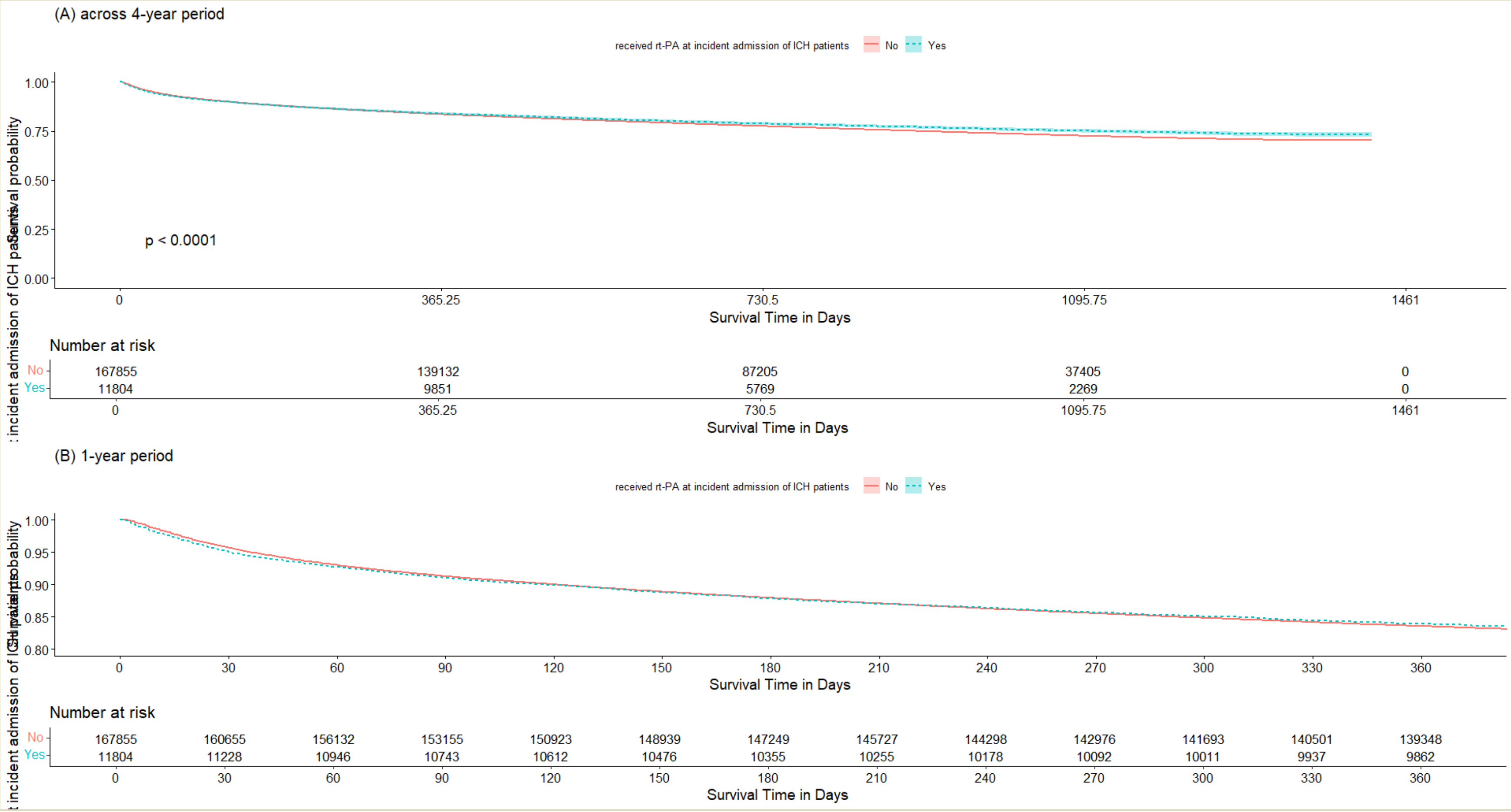
Age group	0	365.25	730.5	1095.75	1461
Age<40	13838	12608	8332	3814	0
Age 40-49	32411	29325	19250	8694	0
Age 50-59	68365	59873	38648	17192	0
Age 60-69	93272	77205	48829	21235	0
Age 70-79	80981	59773	36399	15390	0
Age 80-89	45314	27892	15662	6077	0
Age 90+	6222	2924	1428	497	0

Survival Time in Days

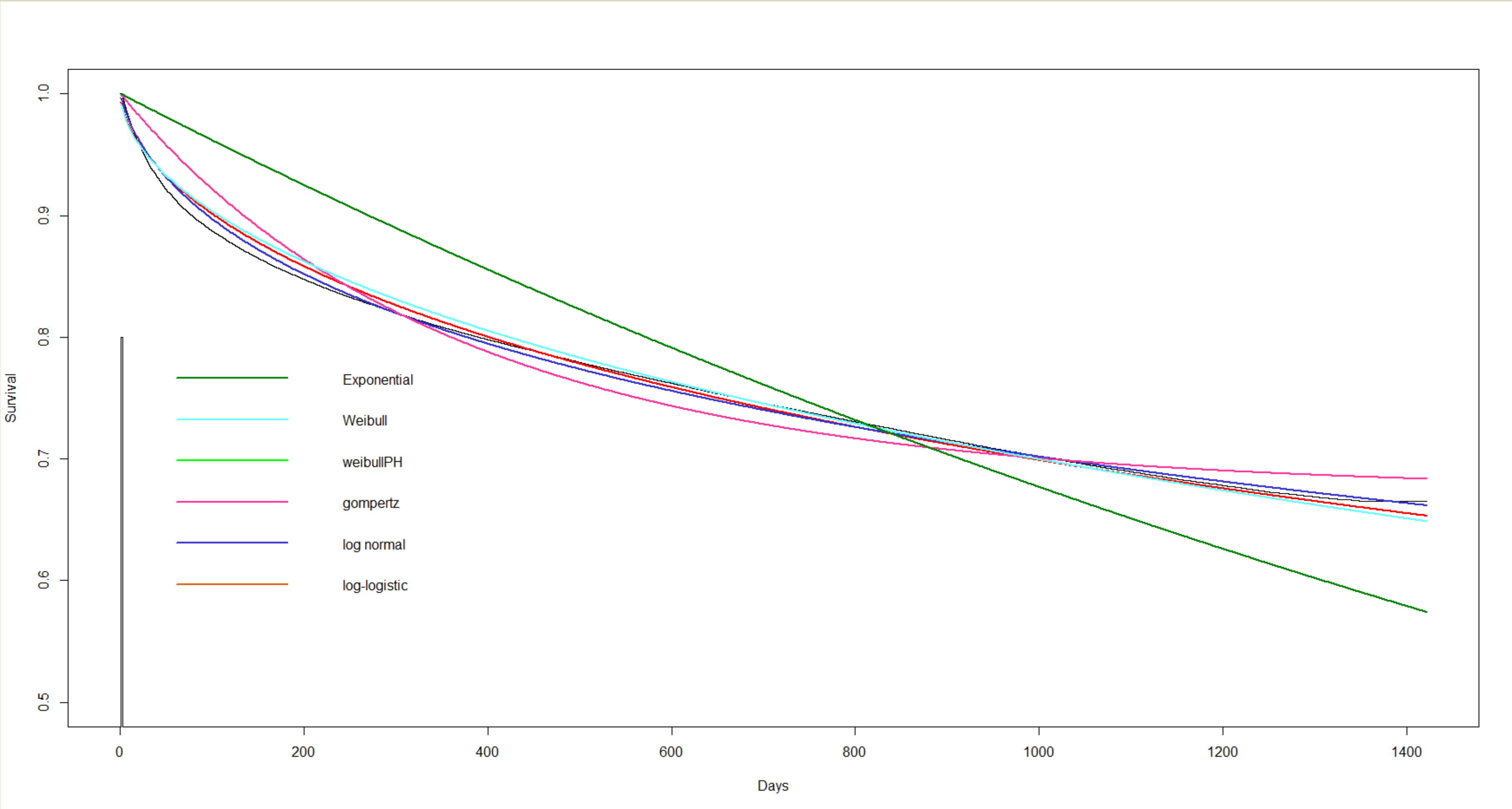
Appendix 14 Kaplan-Meier curves of all-cause mortality classified by CCI score



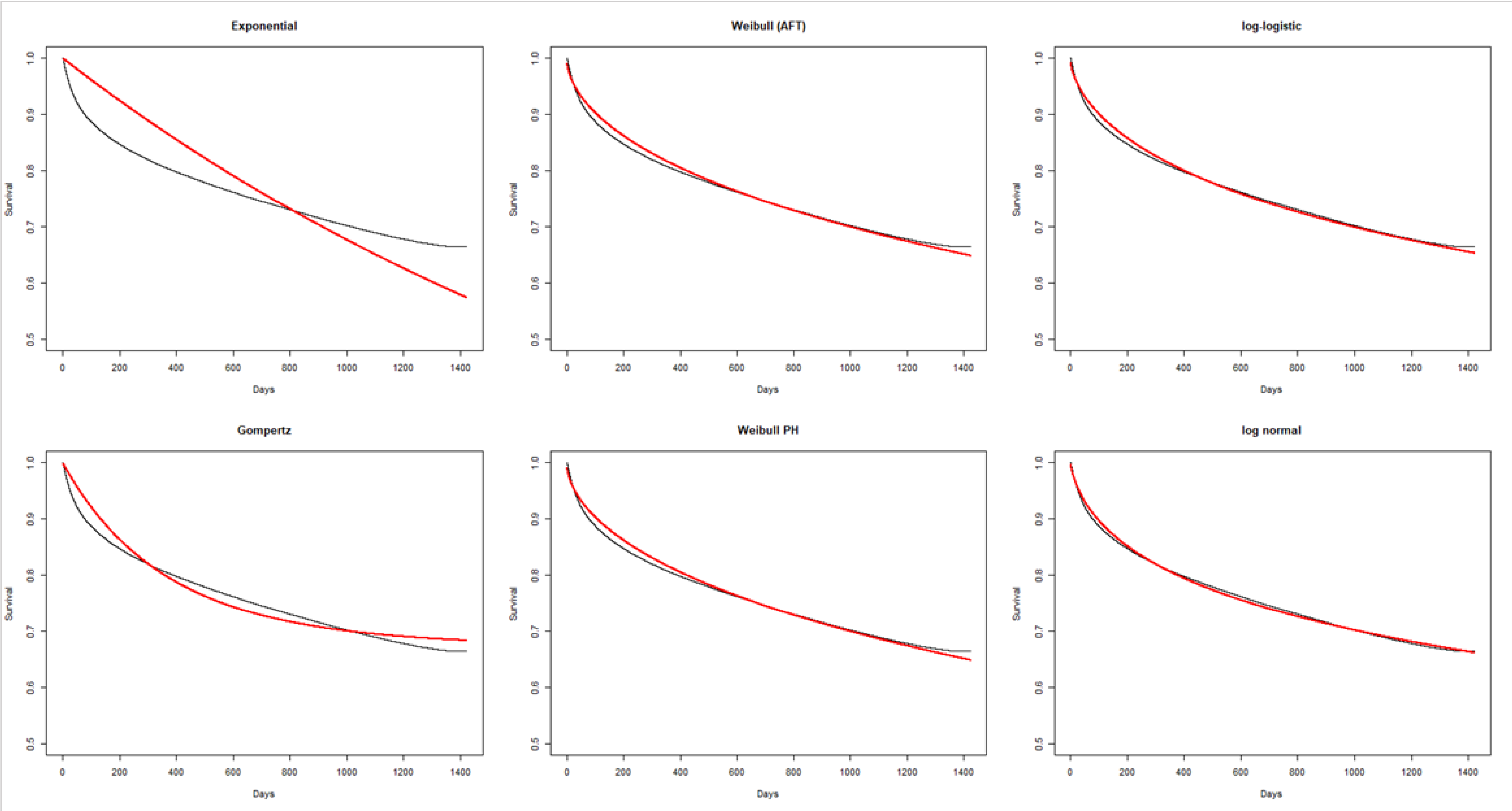
Appendix 15 Kaplan-Meier curves of all-cause mortality classified by thrombolytic treatment



Appendix 16 Plots the survivor functions compared between the different distributions of parametric models

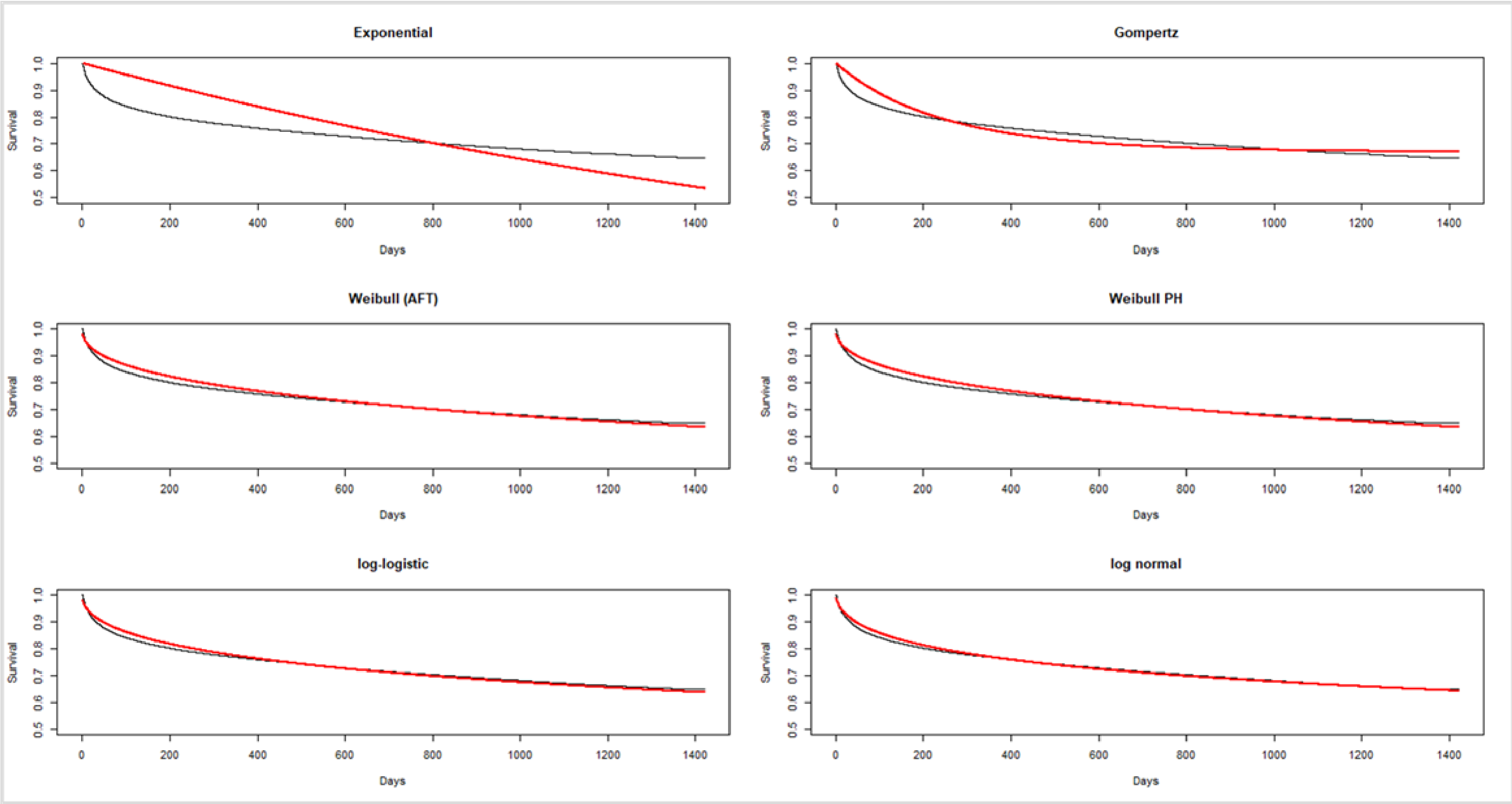


Appendix 17 Plots the survivor functions for overall survival from different parametric models



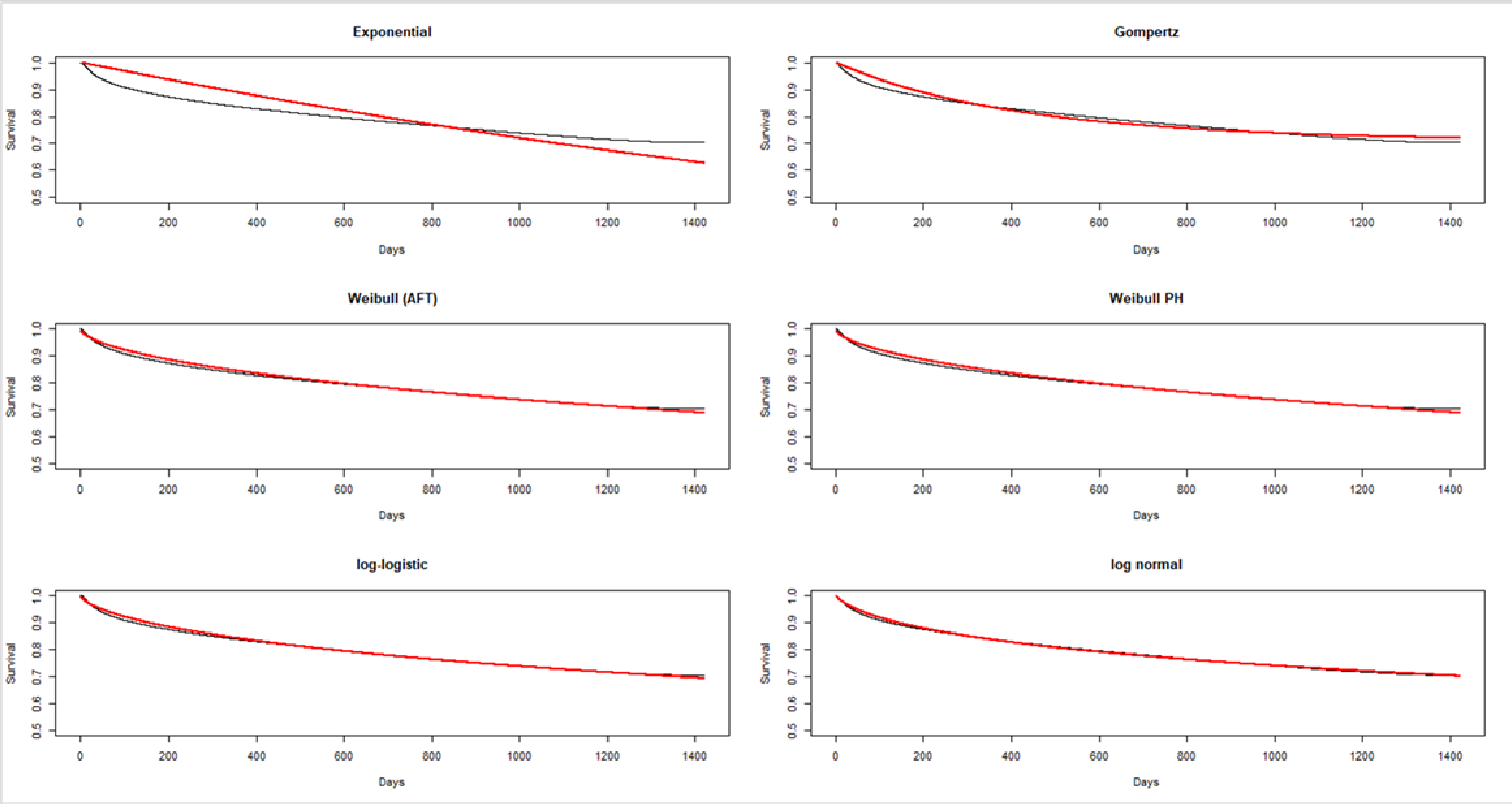
A: all stroke subtypes

Appendix 17 Plots the survivor functions for overall survival from different parametric models (cont.)



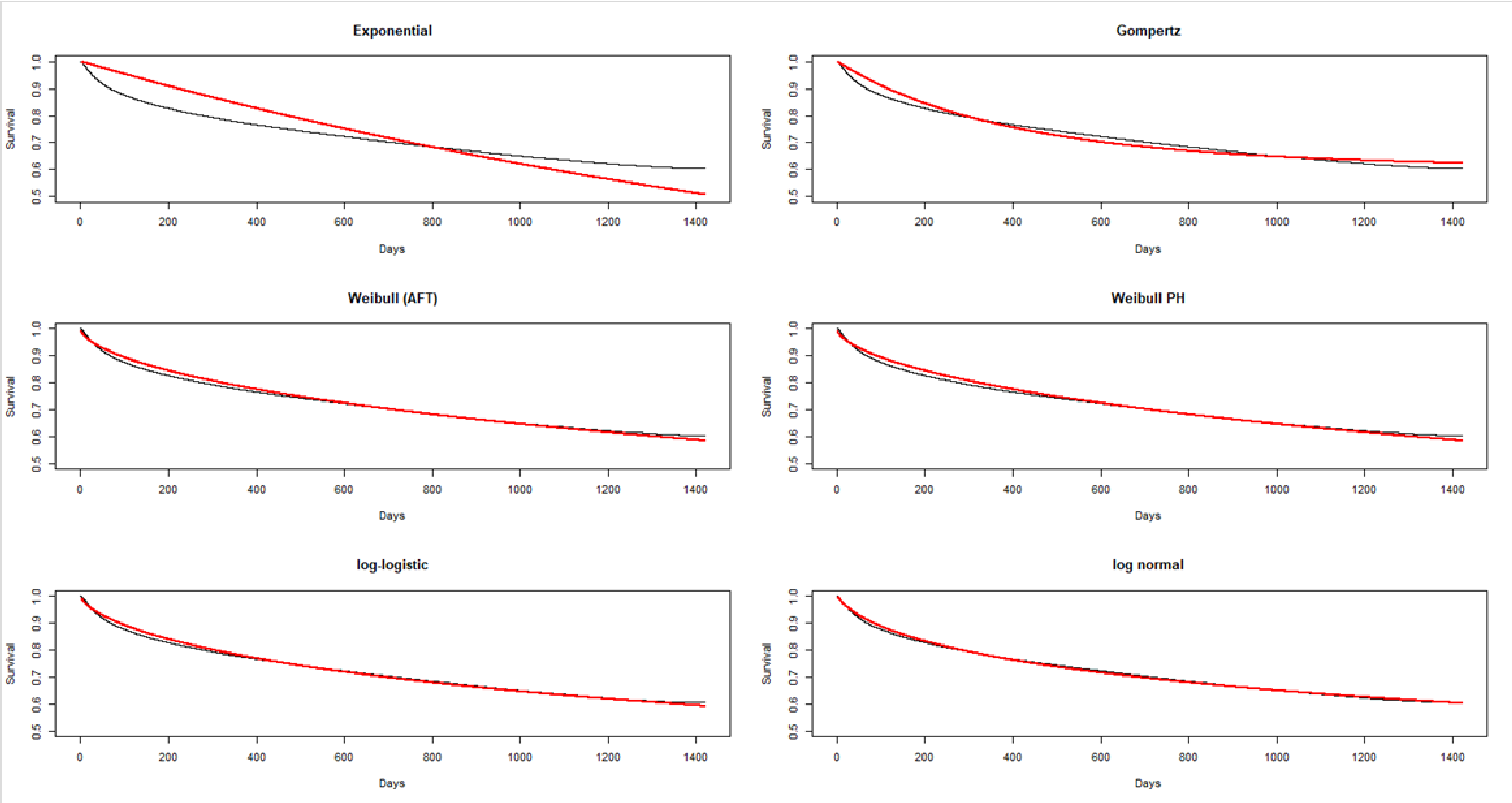
B: stroke subtype: haemorrhagic stroke

Appendix 17 Plots the survivor functions for overall survival from different parametric models (cont.)



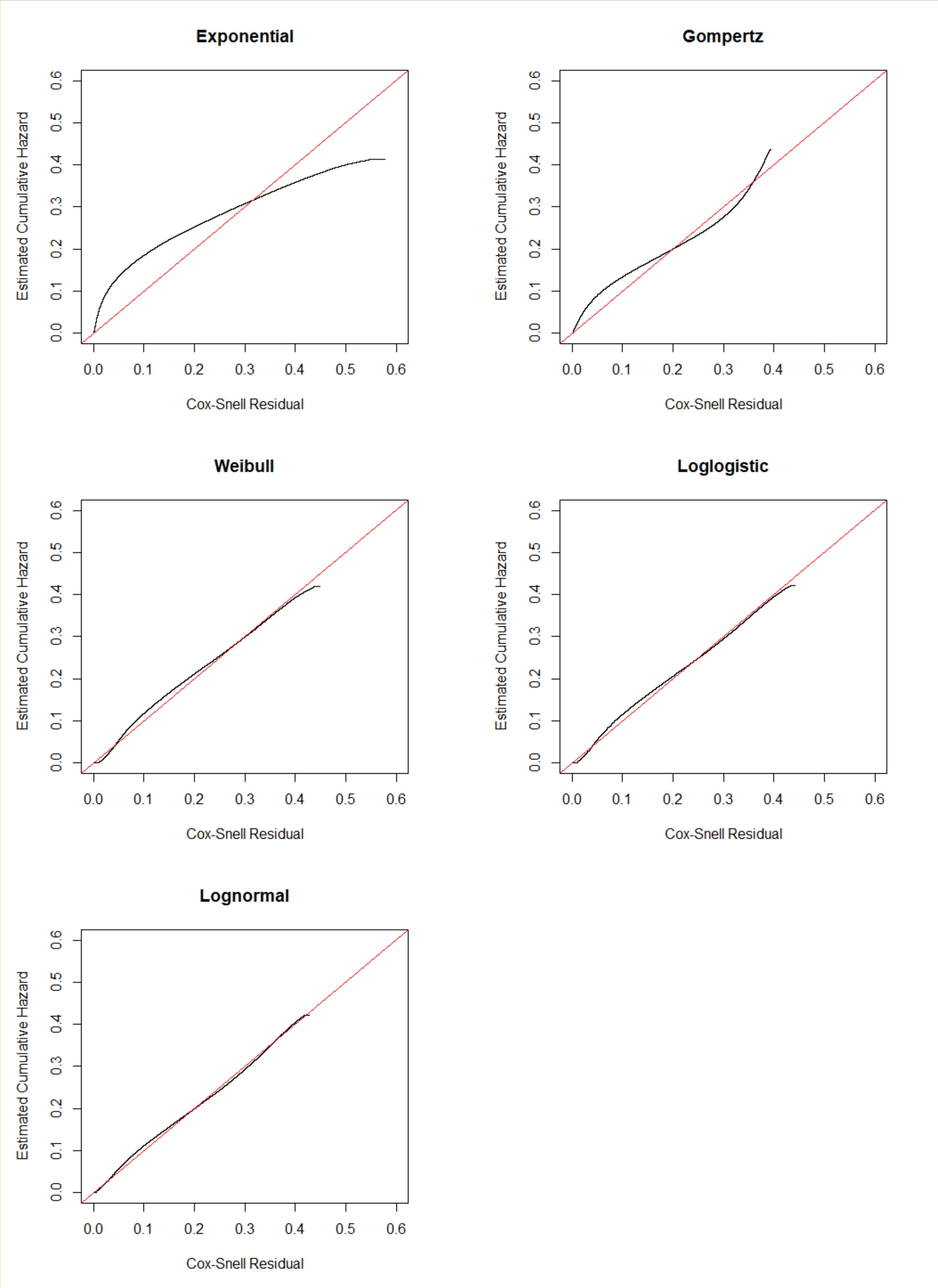
C: stroke subtype: ischaemic stroke

Appendix 17 Plots the survivor functions for overall survival from different parametric models (cont.)



D: stroke subtype: unspecified stroke

Appendix 18 Cox-Snell Residuals



Appendix 19 The Akaike information criterion and Bayesian information criterion values for parametric models

	-2log likelihood	Parameters	AIC	BIC
AIC for overall survival models (no covariate)				
Exponential	1684036	1	1684039	1684049
Weibull	1634435	2	1634439	1634461
Gompertz	1646231	2	1646235	1646256
Lognormal	1628796	2	1628800	1628822
Log-logistic	1632907	2	1632911	1632932
AIC for overall survival models (full model)				
Exponential	1625294	47	1625388	1625893
Weibull	1582655	48	1582751	1583266
Gompertz	1593529	48	1593625	1594141
Lognormal	1581376	48	1581472	1581987
Log-logistic	1581147	48	1581243	1581758
AIC for overall survival models (haemorrhagic, full model)				
Exponential	274520	45	274610	275010
Weibull	258514	46	258606	259014
Gompertz	263521	46	263613	264021
Lognormal	257423	46	257516	257924
Log-logistic	257957	46	258049	258458
AIC for overall survival models (ischaemic, full model)				
Exponential	758946	45	759036	759491
Weibull	743380	46	743472	743937
Gompertz	746859	46	746951	747415
Lognormal	742587	46	742679	743144
Log-logistic	742380	46	742472	742937
AIC for overall survival models (unspecified, full model)				
Exponential	588421	45	588511	588942
Weibull	576304	46	576396	576837
Gompertz	578560	46	578652	579093
Lognormal	575607	46	575699	576139
Log-logistic	575707	46	575799	576240

AIC: Akaike information criterion; BIC: Bayesian information criterion

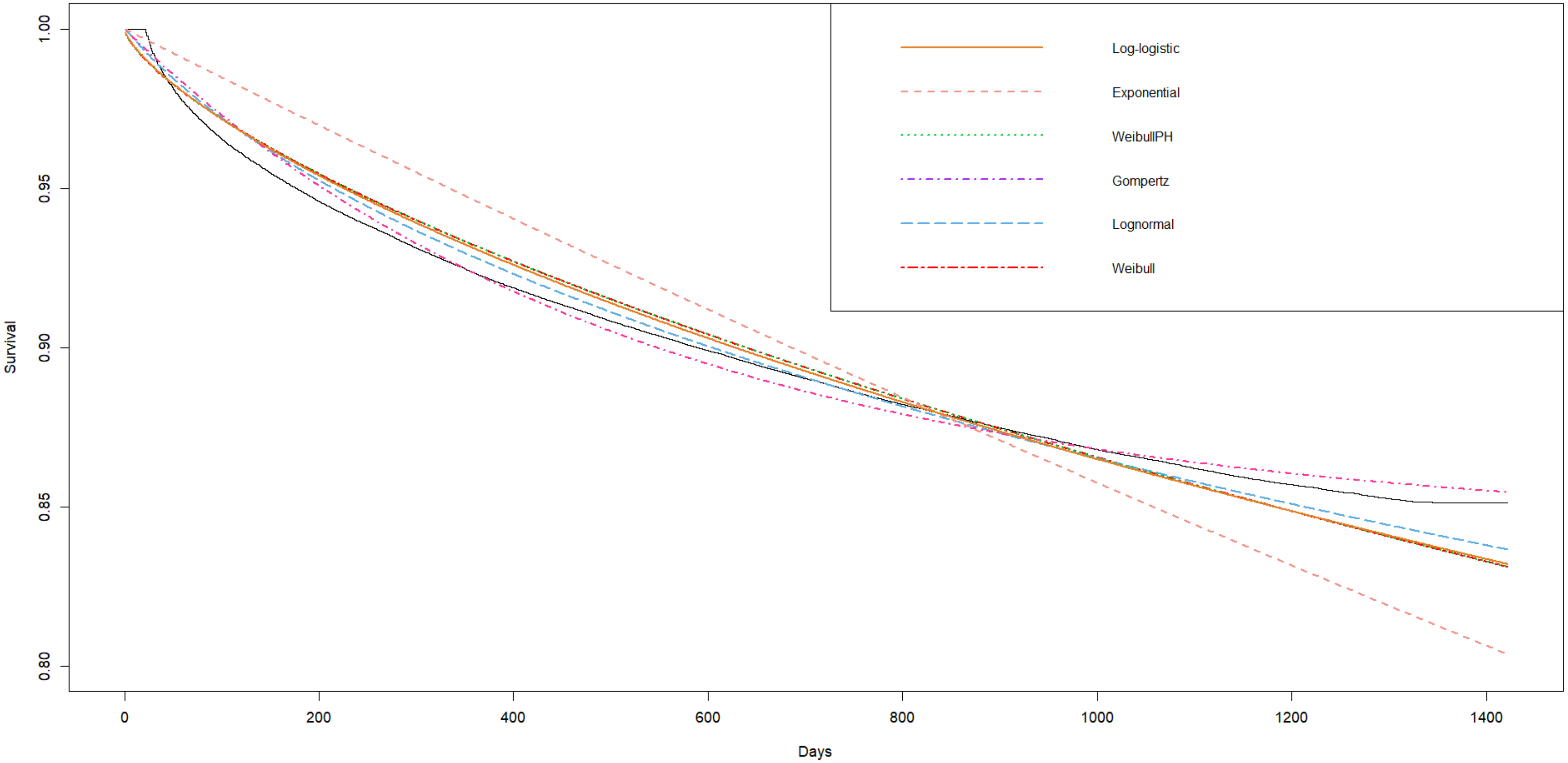
Appendix 20 All-cause mortality risk during four years for patients with the first-ever stroke by stroke subtype (Gompertz model)

Covariates	Haemorrhagic					Ischemic					Unspecified				
	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI
Shape	-0.003	0.0001	-	-0.004	-0.003	-0.002	0.0001		-0.002	-0.002	-0.002	0.0001		-0.002	-0.0018
Scale/Rate	0.0004	0.00004	-	0.0004	0.001	0.0001	0.00001		0.00007	0.0001	0.0002	0.00002		0.00015	0.00022
Female	1 [Reference]														
Male	0.005	0.016	1.005	0.974	1.037	0.06	0.01	1.062	1.042	1.083	0.114	0.011	1.121	1.097	1.145
Age<40	1 [Reference]														
Age 40-49	0.177	0.07	1.194	1.041	1.368	0.22	0.075	1.247	1.076	1.444	0.139	0.103	1.149	0.94	1.405
Age 50-59	0.428	0.064	1.534	1.352	1.741	0.569	0.069	1.767	1.543	2.023	0.374	0.093	1.453	1.21	1.744
Age 60-69	0.902	0.063	2.464	2.177	2.788	1.015	0.068	2.760	2.417	3.151	0.828	0.09	2.289	1.918	2.731
Age 70-79	1.492	0.063	4.446	3.93	5.029	1.63	0.067	5.105	4.474	5.825	1.449	0.089	4.260	3.578	5.074
Age 80-89	2.081	0.064	8.014	7.072	9.082	2.264	0.068	9.624	8.431	10.985	1.987	0.09	7.296	6.115	8.705
Age 90up	2.583	0.082	13.231	11.259	15.548	2.89	0.073	17.996	15.604	20.754	2.605	0.104	13.533	11.041	16.586
CCI: score 0	1 [Reference]														
CCI: score 1 to 2	0.535	0.082	1.707	1.454	2.004	0.999	0.086	2.717	2.293	3.218	0.614	0.101	1.847	1.514	2.254
CCI: score 3 or over	1.757	0.413	5.797	2.582	13.016	1.590	0.276	4.903	2.854	8.423	1.734	0.245	5.663	3.502	9.158
Not received rehabilitation	1 [Reference]														
Received rehabilitation	-0.287	0.018	0.75	0.725	0.777	-0.145	0.01	0.865	0.848	0.882	-0.084	0.016	0.919	0.892	0.948
Not received rt-PA	1 [Reference]														
Received rt-PA	0.018	0.163	1.018	0.74	1.401	-0.156	0.02	0.855	0.822	0.89	-0.106	0.105	0.899	0.732	1.104
No recurrent stroke	1 [Reference]														
Having recurrent stroke	0.135	0.023	1.144	1.094	1.196	0.309	0.013	1.362	1.327	1.398	0.208	0.018	1.231	1.188	1.275
LOS < 3 days	1 [Reference]														

Covariates	Haemorrhagic					Ischemic					Unspecified				
	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI
LOS 3 to 7 days	-0.46	0.022	0.631	0.605	0.659	0.279	0.012	1.321	1.291	1.352	0.193	0.013	1.213	1.183	1.244
LOS 7 to 15 days	-0.28	0.023	0.756	0.722	0.792	0.939	0.015	2.558	2.485	2.633	0.591	0.016	1.807	1.751	1.864
LOS ≥ 16 days	0.122	0.024	1.130	1.078	1.184	1.263	0.018	3.536	3.414	3.663	0.875	0.021	2.399	2.304	2.498
hospital type: primary and community	1 [Reference]														
Mid-level	0.048	0.043	1.049	0.964	1.141	-0.001	0.02	0.999	0.96	1.04	-0.144	0.022	0.865	0.829	0.903
Standard-level	0.091	0.034	1.095	1.025	1.169	0.081	0.017	1.084	1.049	1.121	-0.063	0.017	0.939	0.908	0.971
Advanced-level	-0.007	0.031	0.993	0.935	1.055	0.01	0.016	1.010	0.978	1.043	-0.155	0.015	0.857	0.832	0.883
Non-MOPH	-0.189	0.048	0.828	0.754	0.909	-0.276	0.031	0.759	0.714	0.807	-0.413	0.032	0.661	0.621	0.704
Private hospitals/clinics	0.023	0.062	1.023	0.906	1.156	0.047	0.038	1.048	0.974	1.129	-0.051	0.039	0.951	0.88	1.027
Bangkok	1 [Reference]														
Health Region 1	0.176	0.051	1.193	1.078	1.319	0.186	0.035	1.205	1.124	1.291	0.006	0.038	1.006	0.934	1.084
Health Region 2	0.162	0.054	1.176	1.058	1.307	0.166	0.036	1.180	1.099	1.267	-0.007	0.040	0.993	0.918	1.074
Health Region 3	0.379	0.062	1.460	1.293	1.65	0.274	0.040	1.315	1.217	1.422	0.01	0.042	1.010	0.93	1.097
Health Region 4	0.433	0.056	1.542	1.382	1.721	0.353	0.037	1.423	1.324	1.53	0.017	0.037	1.018	0.946	1.094
Health Region 5	0.018	0.059	1.019	0.908	1.143	0.128	0.038	1.137	1.056	1.224	-0.107	0.04	0.898	0.831	0.971
Health Region 6	0.219	0.055	1.245	1.118	1.385	0.196	0.036	1.217	1.133	1.306	-0.01	0.038	0.990	0.918	1.068
Health Region 7	0.267	0.056	1.306	1.171	1.457	0.331	0.037	1.392	1.294	1.498	0.127	0.040	1.136	1.051	1.227
Health Region 8	0.334	0.053	1.397	1.259	1.551	0.295	0.036	1.343	1.252	1.441	0.052	0.039	1.053	0.975	1.137
Health Region 9	0.065	0.056	1.068	0.957	1.191	0.19	0.037	1.210	1.124	1.301	-0.057	0.039	0.944	0.875	1.019
Health Region 10	0.297	0.057	1.345	1.204	1.503	0.291	0.039	1.338	1.240	1.443	0.041	0.041	1.041	0.96	1.129
Health Region 11	0.217	0.06	1.242	1.104	1.397	0.186	0.039	1.204	1.116	1.299	-0.115	0.041	0.891	0.822	0.965
Health Region 12	0.326	0.06	1.385	1.231	1.559	0.268	0.039	1.308	1.212	1.412	-0.01	0.041	0.990	0.914	1.072

Covariates	Haemorrhagic					Ischemic					Unspecified				
	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI
Age <40 # CCI score 0	1 [Reference]														
Age 40-49 # score 1 to 2	0.182	0.098	1.2	0.99	1.454	-0.113	0.1	0.893	0.734	1.086	0.183	0.12	1.201	0.948	1.52
Age 50-59 # score 1 to 2	0.218	0.09	1.243	1.042	1.483	-0.143	0.091	0.866	0.725	1.036	0.142	0.109	1.152	0.93	1.427
Age 60-69 # score 1 to 2	0.123	0.088	1.131	0.952	1.343	-0.347	0.089	0.707	0.594	0.841	-0.036	0.105	0.965	0.784	1.186
Age 70-79 # score 1 to 2	-0.058	0.088	0.943	0.794	1.121	-0.537	0.088	0.584	0.492	0.694	-0.301	0.104	0.74	0.603	0.908
Age 80-89 # score 1 to 2	-0.227	0.09	0.797	0.669	0.95	-0.73	0.088	0.482	0.405	0.573	-0.48	0.105	0.619	0.503	0.761
Age 90up # score 1 to 2	-0.48	0.122	0.619	0.488	0.786	-0.978	0.098	0.376	0.31	0.455	-0.722	0.12	0.486	0.384	0.615
Age 40-49 # score 3 or over	0.028	0.521	1.028	0.37	2.856	-0.138	0.343	0.871	0.445	1.705	-0.214	0.29	0.807	0.457	1.425
Age 50-59 # score 3 or over	0.02	0.453	1.02	0.42	2.48	0.236	0.295	1.266	0.71	2.257	-0.02	0.258	0.98	0.591	1.625
Age 60-69 # score 3 or over	-0.189	0.435	0.828	0.353	1.943	-0.178	0.284	0.837	0.48	1.461	-0.535	0.251	0.586	0.358	0.958
Age 70-79 # score 3 or over	-0.856	0.437	0.425	0.18	1.001	-0.732	0.283	0.481	0.276	0.838	-0.985	0.249	0.374	0.229	0.609
Age 80-89 # score 3 or over	-0.982	0.443	0.375	0.157	0.892	-0.994	0.285	0.37	0.212	0.647	-1.322	0.251	0.267	0.163	0.436
Age 90up # score 3 or over	-1.629	0.584	0.196	0.062	0.616	-1.574	0.338	0.207	0.107	0.402	-1.675	0.273	0.187	0.11	0.32

Appendix 21 Plots the survivor functions compared between the different distributions of parametric models for recurrent stroke events



Appendix 22 Recurrence free survival during four years for patients with the first-ever stroke by stroke subtype (Gompertz model)

Covariates	Haemorrhagic					Ischemic					Unspecified				
	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI
Shape	-0.003	0.096	0.997	0.826	1.204	-0.002	0.0002	0.998	0.998	0.999	-0.001	0.000	0.999	0.998	0.999
Scale/Rate	0.0002	0.00002	-	0.0002	0.0003	0.00019	0.00001	-	0.00016	0.00022	0.0003	0.00002	-	0.0002	0.0003
Female	1 [Reference]														
Male	-0.069	0.096	0.933	0.773	1.127	-0.022	0.014	0.978	0.951	1.006	-0.038	0.021	0.963	0.924	1.004
Age<40	1 [Reference]														
Age 40-49	0.037	0.096	1.037	0.859	1.253	0.109	0.057	1.115	0.997	1.248	-0.140	0.082	0.869	0.740	1.021
Age 50-59	0.079	0.096	1.082	0.896	1.307	0.161	0.054	1.175	1.058	1.306	-0.184	0.075	0.832	0.718	0.963
Age 60-69	0.174	0.096	1.190	0.985	1.437	0.200	0.053	1.221	1.101	1.354	-0.020	0.073	0.980	0.849	1.130
Age 70-79	0.180	0.096	1.197	0.991	1.445	0.270	0.053	1.310	1.180	1.455	-0.042	0.076	0.959	0.827	1.112
Age 80-89	0.317	0.096	1.373	1.137	1.659	0.273	0.057	1.314	1.175	1.469	-0.010	0.086	0.990	0.838	1.171
Age 90up	-0.226	0.096	0.798	0.661	0.963	0.157	0.101	1.170	0.959	1.427	-0.316	0.197	0.729	0.495	1.074
CCI: score 0	1 [Reference]														
CCI: score 1 to 2	-0.284	0.096	0.753	0.623	0.909	0.056	0.090	1.057	0.887	1.260	-0.686	0.105	0.504	0.410	0.619
CCI: score 3 or over	-0.061	0.974	0.940	0.139	6.341	-0.536	0.717	0.585	0.144	2.384	-0.760	0.710	0.468	0.116	1.881
Not received rehabilitation	1 [Reference]														
Received rehabilitation	-0.029	0.096	0.972	0.805	1.174	0.017	0.015	1.017	0.988	1.047	-0.126	0.030	0.882	0.832	0.935
Not received rt-PA	1 [Reference]														
Received rt-PA	0.247	0.096	1.280	1.060	1.546	0.121	0.028	1.129	1.070	1.192	0.204	0.150	1.227	0.914	1.647
LOS < 3 days	1 [Reference]														
LOS 3 to 7 days	-0.225	0.096	0.799	0.661	0.964	0.063	0.016	1.065	1.033	1.099	-0.092	0.024	0.912	0.869	0.956
LOS 7 to 15 days	-0.188	0.096	0.829	0.686	1.001	0.085	0.026	1.089	1.034	1.147	-0.180	0.039	0.835	0.773	0.902

Covariates	Haemorrhagic					Ischemic					Unspecified				
	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI
LOS ≥16 days	0.650	0.096	1.916	1.586	2.314	0.522	0.034	1.685	1.578	1.799	-0.017	0.055	0.983	0.882	1.095
hospital type: primary and community	1 [Reference]														
Mid-level	0.237	0.096	1.268	1.050	1.531	0.171	0.030	1.186	1.118	1.259	-0.032	0.043	0.968	0.889	1.054
Standard-level	0.141	0.096	1.151	0.953	1.390	0.044	0.026	1.045	0.994	1.099	-0.051	0.034	0.950	0.888	1.016
Advanced-level	0.253	0.096	1.288	1.066	1.555	0.122	0.025	1.130	1.077	1.186	-0.028	0.031	0.972	0.915	1.033
Non-MOPH	0.301	0.096	1.351	1.118	1.631	0.066	0.046	1.068	0.976	1.169	0.363	0.052	1.438	1.298	1.593
Private hospitals and clinics	0.167	0.096	1.181	0.978	1.427	0.116	0.057	1.123	1.005	1.256	0.187	0.075	1.205	1.041	1.395
Bangkok	1 [Reference]														
Health Region 1	0.177	0.096	1.193	0.988	1.441	0.094	0.051	1.099	0.994	1.215	0.129	0.067	1.138	0.999	1.297
Health Region 2	0.240	0.096	1.271	1.053	1.535	0.073	0.053	1.076	0.970	1.194	0.227	0.071	1.255	1.092	1.444
Health Region 3	0.176	0.096	1.193	0.988	1.441	0.031	0.059	1.032	0.918	1.159	0.204	0.076	1.226	1.057	1.421
Health Region 4	0.285	0.096	1.329	1.101	1.605	0.024	0.056	1.024	0.918	1.143	-0.013	0.067	0.988	0.867	1.125
Health Region 5	0.167	0.096	1.182	0.979	1.427	0.063	0.056	1.065	0.955	1.187	0.090	0.072	1.094	0.951	1.259
Health Region 6	0.210	0.096	1.234	1.022	1.490	-0.008	0.054	0.992	0.893	1.102	0.131	0.068	1.140	0.998	1.302
Health Region 7	0.171	0.096	1.187	0.983	1.433	0.030	0.055	1.030	0.924	1.148	0.276	0.069	1.317	1.150	1.509
Health Region 8	0.331	0.096	1.393	1.153	1.682	0.193	0.053	1.213	1.094	1.345	0.274	0.069	1.316	1.148	1.507
Health Region 9	0.342	0.096	1.407	1.165	1.700	0.265	0.054	1.304	1.173	1.450	0.319	0.067	1.376	1.206	1.570
Health Region 10	0.242	0.096	1.273	1.054	1.538	0.095	0.057	1.100	0.984	1.230	0.341	0.074	1.406	1.216	1.625
Health Region 11	0.282	0.096	1.326	1.098	1.601	0.235	0.056	1.266	1.134	1.413	0.282	0.071	1.326	1.155	1.522
Health Region 12	0.334	0.096	1.397	1.157	1.687	0.192	0.058	1.212	1.083	1.357	0.260	0.071	1.297	1.129	1.489
Age < 40 # CCI score 0	1 [Reference]														
Age 40-49 # score 1 to 2	0.387	0.096	1.472	1.219	1.777	0.030	0.104	1.030	0.840	1.263	0.383	0.127	1.467	1.143	1.883

Covariates	Haemorrhagic					Ischemic					Unspecified				
	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI	Coef.	SE	HR	L95%CI	U95%CI
Age 50-59 # score 1 to 2	0.455	0.096	1.576	1.305	1.903	0.116	0.096	1.123	0.931	1.355	0.414	0.116	1.512	1.205	1.898
Age 60-69 # score 1 to 2	0.448	0.096	1.565	1.296	1.890	0.062	0.094	1.064	0.885	1.279	0.297	0.112	1.345	1.080	1.677
Age 70-79 # score 1 to 2	0.557	0.096	1.746	1.446	2.109	-0.012	0.094	0.988	0.821	1.190	0.307	0.114	1.359	1.086	1.700
Age 80-89 # score 1 to 2	0.445	0.096	1.561	1.293	1.885	0.048	0.099	1.049	0.863	1.274	0.199	0.124	1.220	0.958	1.555
Age 90up # score 1 to 2	0.211	0.096	1.235	1.023	1.491	-0.046	0.167	0.955	0.688	1.325	0.333	0.241	1.396	0.870	2.240
Age 40-49 # score 3 or over	0.143	1.057	1.154	0.145	9.162	-0.658	1.007	0.518	0.072	3.723	0.533	0.786	1.704	0.365	7.951
Age 50-59 # score 3 or over	0.947	0.991	2.578	0.369	17.988	0.723	0.762	2.061	0.463	9.173	0.863	0.735	2.370	0.561	10.005
Age 60-69 # score 3 or over	0.494	0.990	1.640	0.236	11.402	0.779	0.734	2.179	0.516	9.190	0.648	0.721	1.912	0.466	7.853
Age 70-79 # score 3 or over	0.249	0.996	1.283	0.182	9.043	0.647	0.734	1.910	0.453	8.058	0.453	0.721	1.573	0.383	6.463
Age 80-89 # score 3 or over	-1.339	1.157	0.262	0.027	2.530	0.623	0.747	1.865	0.432	8.060	-0.101	0.739	0.904	0.212	3.843
Age 90up # score 3 or over	-12.799	962.651	0.000	0.000	Inf	1.122	0.878	3.070	0.550	17.148	0.869	0.826	2.385	0.473	12.031

Appendix 23 Data comparation between the final data set and the NHSO annual report.

Fiscal year	2016	2017	2018	2019
Population (persons)				
Registered UCS aged ≥15 years	37,368,474	37,276,475	37,112,839	37,035,674
Admission: PDX I630-I639 and Age 15-124 years				
NHSO annual report	72,333	78,384	86,160	93,180
Final data extract	77,582	84,569	92,946	100,409
Total admission (persons)				
NHSO annual report	63,843	68,631	74,970	80,323
Final data extract	65,130	70,137	76,637	81,652
Admission rate (per 100,000)				
NHSO annual report	170.85	184.11	202.01	216.88
Final data extract	174.29	188.15	206.5	220.47
Thrombolytic therapy (persons)				
NHSO annual report	3,181	4,093	5,097	6,399
Final data extract	3,184	4,102	5,108	6,375
Anti-thrombolytic rate				
NHSO annual report	4.98	5.96	6.8	7.97
Final data extract	4.89	5.85	6.67	7.81
Death (persons)				
NHSO annual report	7,242	6,846	7,095	7,142
Final data extract	8,033	7,690	8,113	8,217
Death rate				
NHSO annual report	11.34	9.98	9.46	8.89
Final data extract	12.58	11.2	10.82	10.23

Appendix 24 Search strategy

No	Search term	Results
A. Medline via PubMed (31 July 2022)		
1.	"Vascular Diseases"[Mesh] OR "Basal Ganglia Cerebrovascular Disease"[Mesh] OR "Cerebrovascular Disorders"[Mesh]	1,729,647
2.	"Stroke"[Mesh] OR "Stroke, Lacunar"[Mesh] OR "Infarction, Anterior Cerebral Artery"[Mesh] OR "Infarction, Posterior Cerebral Artery"[Mesh] OR "Infarction, Middle Cerebral Artery"[Mesh] OR "Brain Stem Infarctions"[Mesh] OR "Cerebral Arteries"[Mesh] OR "Basilar Artery"[Mesh]	170,305
3.	("Hemorrhagic Stroke"[Mesh] OR "Cerebral Hemorrhage"[Mesh]) OR "Subarachnoid Hemorrhage"[Mesh]	54,837
4.	"Ischemic Stroke"[Mesh] OR "Embolic Stroke"[Mesh] OR "Thrombotic Stroke"[Mesh] OR "Brain Ischemia"[Mesh] OR "Brain Infarction"[Mesh] OR "Intracranial Thrombosis"[Mesh] OR "Cerebral Infarction"[Mesh]	118,266
5.	"Ischemic Attack, Transient"[Mesh]	20,667
6.	"Carotid Artery Diseases"[Mesh] OR "Carotid Arteries"[Mesh]	88,031
7.	"Intracranial Embolism and Thrombosis"[Mesh]	21,525
8.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	1,880,294
9.	"stroke"[Title/Abstract] OR "vascular disease*"[Title/Abstract] OR "cerebrovascular*"[Title/Abstract] OR "cerebral infarc*"[Title/Abstract] OR "cerebral ischemi*"[Title/Abstract] OR "cerebral ischaemi*"[Title/Abstract] OR "cerebral hemorrhag*"[Title/Abstract] OR "cerebral haemorrhag*"[Title/Abstract]	379,391
10.	"cerebellar*"[Title/Abstract] OR "brainstem*"[Title/Abstract] OR "vertebrobasilar*"[Title/Abstract]	116,986
11.	"cerebral vascular accident*"[Title/Abstract] OR "cerebrovascular accident*"[Title/Abstract]	8,375
12.	"hemorrhag*"[Title/Abstract] OR "haemorrhag*"[Title/Abstract]	274,517
13.	"ischaemi*"[Title/Abstract] OR "ischemi*"[Title/Abstract]	396,590
14.	"thrombo*"[Title/Abstract] OR "thrombu*"[Title/Abstract] OR "emboli*"[Title/Abstract]	498,214
15.	"Transient ischemic attack"[Title/Abstract] OR "TIA"[Title/Abstract]	14,699
16.	#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15	1,483,542
17.	#8 OR #16	2,663,241
18.	"Neurologic Manifestations"[Mesh]	1,255,469
19.	"Rehabilitation Centers"[Mesh] OR "Hospitals, Rehabilitation"[Mesh] OR "Stroke Rehabilitation"[Mesh] OR "Telerehabilitation"[Mesh] OR "Rehabilitation"[Mesh]	352,720
20.	"Physical Therapy Modalities"[Mesh] OR "Physical Therapy Specialty"[Mesh] OR "Exercise Therapy"[Mesh] OR "Occupational Therapy"[Mesh] OR "Occupational Therapy Department, Hospital"[Mesh] OR "Occupational Therapists"[Mesh] OR "Subacute Care"[Mesh]	188,479
21.	#18 OR #19 OR #20	1,552,041
22.	"rehabilitat*"[Title/Abstract] OR "rehabilitation center*"[Title/Abstract] OR "rehabilitation centre*"[Title/Abstract] OR "rehabilitation care*"[Title/Abstract]	184,592
23.	"physiotherap*"[Title/Abstract] OR "physical therap*"[Title/Abstract] OR "Physical rehabilitat*"[Title/Abstract] OR "Physical management"[Title/Abstract] OR "neurological therap*"[Title/Abstract] OR "neurological physiotherap*"[Title/Abstract] OR "occupational therap*"[Title/Abstract]	66,942
24.	"Activities of Daily Living"[Title/Abstract] OR "functional recovery"[Title/Abstract] OR "Recovery of Function"[Title/Abstract] OR "function recover*"[Title/Abstract]	57,087
25.	#22 OR #23 OR #24	317,008
26.	#21 OR #25	1,730,730
27.	"Cost-Benefit Analysis"[Mesh]	90,272
28.	Cost?effective*[Title/Abstract] OR "Cost?utility*"[Title/Abstract] OR "economic analysis"[Title/Abstract] OR "economic evaluation"[Title/Abstract]	172,851
29.	#27 OR #28	212,932
30.	#17 AND #26 AND #29	2,015

No	Search term	Results
31.	#31 Filters: in the last 10 years (01/01/2011-31/07/2022), Humans	870
B. Embase via Ovid (31/07/2022)		
1.	exp cerebrovascular disease/ or exp basal ganglion hemorrhage/ or exp basal ganglia cerebrovascular disease/	779,463
2.	exp cerebrovascular accident/ or exp lacunar stroke/ or exp cerebral artery disease/ or exp brain stem infarction/ or exp basilar artery/	293,798
3.	exp brain hemorrhage/ or exp subarachnoid hemorrhage/	171,045
4.	exp brain infarction/ or exp brain ischemia/ or exp brain embolism/ or exp stroke/ or exp ischemia/ or exp occlusive cerebrovascular disease/	1,123,803
5.	exp transient ischemic attack/ or exp carotid artery disease/ or exp thromboembolism/	745,674
6.	1 or 2 or 3 or 4 or 5	1,861,065
7.	(stroke or post?stroke or cerebrovascular$ or "basal ganglion h?emorrhage" or basal ganglia$ or "lacunar stroke").ab,ti.	562,093
8.	(cerebral infarc$ or cerebral ischaemi$ or cerebral h?emorrhag$ or cerebellar$ or brainstem$ or vertebrobasilar$ or "transient ischemic attack" or TIA).ab,ti.	235,032
9.	((cerebral$ or cerebellar or brainstem or vertebrobasilar or stroke) adj5 (infarct$ or isch?emi$ or thrombo$ or thrombu$ or emboli$)).ab,ti.	260,848
10.	((cerebral or brain or subarachnoid) adj5 h?emorrhage$).ab,ti.	59,898
11.	("cerebrovascular accident$" or "cerebral vascular accident$").ab,ti.	14,571
12.	7 or 8 or 9 or 10 or 11	818,757
13.	6 or 12	2,193,556
14.	exp rehabilitation nursing/ or exp rehabilitation patient/ or exp rehabilitation/ or exp rehabilitation center/ or exp "speech and language rehabilitation"/ or exp stroke rehabilitation/ or exp community based rehabilitation/ or exp rehabilitation care/ or exp home rehabilitation/ or exp rehabilitation equipment/ or exp rehabilitation medicine/ or exp speech rehabilitation/ or exp virtual rehabilitation system/	557,962
15.	exp physiotherapy/ or exp home physiotherapy/ or exp physiotherapy practice/	110,328
16.	exp occupational therapy/ or exp daily life activity/	130,705
17.	14 or 15 or 16	722,303
18.	((physical or neurological or occupational) adj3 (rehabilitat$ or management or therap$ or activit$)).ab,ti.	254,332
19.	(rehabilitat$ or exercise$ or physiotherap$ or rehabilitation center$ or rehabilitation centre$ or rehabilitation care$).ab,ti.	692,117
20.	(functio$ adj3 recover$).ab,ti.	69,553
21.	(improv$ adj3 (function or mobil$ or recover$)).ab,ti.	155,815
22.	18 or 19 or 20 or 21	1147,,082
23.	17 or 22	1,580,262
24.	exp economic evaluation/ or exp "cost effectiveness analysis"/ or exp "cost utility analysis"/ or exp "cost benefit analysis"/ or exp "cost minimization analysis"/	337,443
25.	(Cost?utility$ or Cost?effective$ or Cost?benefit$ or economic analysis$ or economic evaluation$ or economic model$).ab,ti.	36,985
26.	24 or 25	348,371
27.	13 and 23 and 26	2,270
28.	limit 27 to last 10 years	1,301
29.	limit 28 to human	1,284
C. NHS Economic Evaluation Database (NHS EED) via CRD (31/07/2022)		
1.	MeSH DESCRIPTOR Cerebrovascular Disorders EXPLODE ALL TREES	2,019
2.	MeSH DESCRIPTOR stroke EXPLODE ALL TREES	1,356
3.	MeSH DESCRIPTOR Ischemic Attack, Transient EXPLODE ALL TREES	89
4.	MeSH DESCRIPTOR basal ganglia EXPLODE ALL TREES	22
5.	MeSH DESCRIPTOR Thromboembolism EXPLODE ALL TREES	534
6.	MeSH DESCRIPTOR brain ischemia EXPLODE ALL TREES	328
7.	MeSH DESCRIPTOR brain infarction EXPLODE ALL TREES	45
8.	MeSH DESCRIPTOR Intracranial Embolism and Thrombosis EXPLODE ALL TREES	30

No	Search term	Results
9.	MeSH DESCRIPTOR Hemorrhagic Stroke EXPLODE ALL TREES	0
10.	((cerebral* or cerebellar or brainstem or vertebrobasilar or stroke) adj5 (infarct* or isch?emi* or thrombo* or thrombu* or emboli*))	735
11.	((cerebral or brain or subarachnoid) adj5 h?emorrhage*)	285
12.	MeSH DESCRIPTOR rehabilitation EXPLODE ALL TREES	3,348
13.	MeSH DESCRIPTOR Exercise Therapy EXPLODE ALL TREES	1,055
14.	MeSH DESCRIPTOR Neurological Rehabilitation EXPLODE ALL TREES	2
15.	MeSH DESCRIPTOR Rehabilitation Centers EXPLODE ALL TREES	101
16.	MeSH DESCRIPTOR Rehabilitation Nursing EXPLODE ALL TREES	8
17.	((physical or neurological or occupational) NEAR3 (rehabilitat* or management or therap* or activit*))	2,460
18.	rehabilitat* or exercise* or physiotherap* or rehabilitation center or rehabilitation centre or rehabilitation care	8,524
19.	(functio* NEAR3 recover*)	85
20.	(improv* NEAR3 (function or mobil* or recover*))	854
21.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11)	2,866
22.	(#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20)	10,969
23.	#21 AND #22	566
24.	(#23) FROM 2011 TO 2022	205

Appendix 25 Descriptions of quality assessment tools

Tools	Descriptions	Type of EE	Advantages	Disadvantages
Drummond and Jefferson (BMJ) checklist 1996 [195]	• 35 items: defining the research question, establishment of appropriate alternatives, effectiveness and costs, analytical approach, accounting for uncertainty, and presentation of results • It is relevant for assessments of methodological quality but not sufficient for modelling studies[202]	• trial-based and model-based[198]	• most widely used tools [198] • It has a wide range of global influence and essential guideline for EE in the healthcare field[297] • it is recommended by the Cochrane handbook for systematic reviews of interventions version 5.1[201, 202]	• no score[198], might subjective
The Quality of Health Economic Studies (QHES) 2003 [196]	• a validated 16-item instrument[201]	• trial-based[201] and model-based[198, 201]	• quantitative scoring[198, 201]	• double-barrelled question in a single criterion[298]
The Philips checklist 2006 [199]	• Three dimension of 60 items which were answered 'Yes', 'Unclear', 'Not Applicable' or 'No'[198] • if the expected number of included studies is low (e.g., <10 studies), this checklist is the preferred list[299]	• model-based [198, 201, 202, 299]	• it is recommended Specifically for critical appraisals of decision-analytic models by the Cochrane handbook for systematic reviews of interventions version 5.1 [201, 202]	• no score, qualitative evaluation[198]
Drummond checklist 2005 [217]	• preferred option if want to use the same checklist for the appraisal of both trial-based and model-based EEs [299]	• trial-based and model-based [198, 201, 299]	• most widely used tools [198, 300]	• no score[198]

Tools	Descriptions	Type of EE	Advantages	Disadvantages
The Consensus on Health Economic Criteria (CHEC) checklist 2005 [200]	• has 19 items relating to cost-effectiveness and is scored as "yes" or "no" [201] • preferred option if want to use the same checklist for the appraisal of both trial-based and model-based EEs[299]	• trial-based [198, 201, 299]	• it is recommended by the Cochrane Handbook for Systematic Reviews of Interventions for critical appraisal of the methodological quality of EE studies version 5.1[201, 202]	• no question on the characteristics of model[301]
The Consolidated Health Economic Evaluation Reporting Standards statement (CHEERS) guideline 2013 [302]	• It is divided into 3 sections; (a) research question, (b) estimation of resource use, costs and outcomes and (c) are the results useful and generalizable. • A 24-item including 6 categories. Scoring was marked using 'yes'(reported in full),'partially re-ported', 'no'(not reported), or 'not applicable. • if the expected number of included studies is high (e.g., >10 studies), this checklist is the preferred list[299]	• trial-based and model-based [198]	• most widely used tools and specific checklists to report acceptable methods of EE [198]	• no score[198], qualitative evaluation
The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach 2011 [213, 303, 304]	• to incorporate economic evidence in developing CPGs[299] • the 'GRADE evidence profile' (a specific form of balance sheet) and in 'Summary of Findings tables' are the preferred way for summarizing the data [299] • for model-based EEs, the GRADE approach is not applicable[299] • The GRADE approach specifies four levels of the certainty for a body of	• trial-based [299]	• the most widely used approach worldwide • to ensure that researchers are accessing the same information to inform their judgements • to ensure transparency in formulating an	• not suitable for model-based EEs[191]

Tools	Descriptions	Type of EE	Advantages	Disadvantages
	evidence for a given outcome: high, moderate, low and very low • GRADE assessments of certainty are determined through consideration of five domains: risk of bias, inconsistency, indirectness, imprecision and publication bias. For evidence from non-randomized studies and rarely randomized studies, assessments can then be upgraded through consideration of three further domains		interpretation of the evidence	

Appendix 26 Comparison of topic in the assessment tools

No	Section*	Descriptions	BMJ, 1996 [195]	QHE, 2003 [196]	Philips, 2006 [199]	CHEC, 2005 [200]	CHEERS, 2013 [302]
Title and abstract							
1	Title	does the title contain economic evaluation or specific terms and describe the interventions compared					/
2	Abstract	Is it provided a structured summary of the purpose, perspective, setting, (including study design and inputs), results (including base case and uncertainty analyses), and conclusions?					/
Introduction							
3	Background and objectives	is it clearly described of the research background, research question and related health policies	/ 1,2	/ 1	/ S1	/ 3	/
Methods							
4	Target population and subgroups	describe of characteristics of the base case population and subgroups and reasons for selection		/ 4		/ 1	/
5	Setting and location	describe of systems that need to make a decision					/
6	perspective	describe the perspective and relate this to the costs being evaluated	/ 3	/ 2	/ S2	/ 6	/
7	Comparators	describe the intervention as a control group and the reasons for selection	/ 4,5,30	/	/ S5	/	/ 2
8	Time horizon	describe the time horizon and reasons for determining	/ 22	/ 8	/ S7	/ 5	/
9	Discount rate	describe the discount rate(s) used for calculating the cost and outcomes and reasons	/ 23,24,25	/ 8		/ 14	/
10	health outcomes selection	describes the type of type of outcomes for the type of analysis performed	/ 11,12	/ 10,11	/ D2c	/ 11,12	/
11	effectiveness measurement	describe fully the design and method used (based on single study-based or synthesis-based) and the reasons	/ 8,9,10,14,15	/ 3	/ D2b	/ 10	/
12	Measurement and valuation of preference-based outcomes	describe the population and methods used to elicit preferences for outcomes	/ 13	/ 7	/ D2a		/
13	Estimating resources and costs	describe the methods of cost and resource estimation (based on single study-based or model-based EE)	/ 16,17	/ 9		/ 7,8,9	/
14	Currency, price date, and conversion	describe dates of the estimated resource quantities and unit costs and method for adjusting price to the year of study, exchange rate and methods of cost conversion	/ 18,19				/

No	Section*	Descriptions	BMJ, 1996 [195]	QHE, 2003 [196]	Philips, 2006 [199]	CHEC, 2005 [200]	CHEERS, 2013 [302]
15	Model selection	describes the type and reason of the decision analysis model used	/ 6,7,20	/ 12	/ S3,S6	/ 4	/
16	Assumptions	describes all assumptions used in the model		/ 13	/ S4		/
17	Analytical methods	Describe all analytical methods supporting the evaluation including handling bias/missing data, extrapolation, pooling data, population heterogeneity and uncertainty, approaches to validate or make adjustments	/ 26	/ 14	D2/D2b		/
Results							
18	parameters	describe the values, ranges, references, probability distributions and reasons	/ 21	/ 11	/ D1, D3,D4d		/
19	Incremental costs and outcomes	report mean values for the main categories of estimated costs and outcomes of interest, mean differences and incremental cost-effectiveness ratios	/ 31,32	/ 6		/ 13	/
20	Uncertainty analysis	the uncertainty of the research and the possible impact are reported based on type of study (Single study-based or Model-based EE)	/ 27, 28, 29	/ 5	/ D4, D4a, D4b	/ 15	/
21	Heterogeneity analysis	describe the heterogeneity among subgroups or other observed variability in effects			/ D4c		/
Discussion							
22	Study findings, limitations, generalisability, and current knowledge	Summarise key study findings, limitations, generalisability and how the findings fit with current knowledge	/ 33,34,35	/ 15	/ C2	/ 16,17	/
Other							
23	Source of funding	describe the source of research funding and role of the funder		/ 16		/ 18	/
24	Conflicts of interest	Describe any potential for conflict of interest of study				/ 18	/
Questions from other tools							
		Are ethical and distributional issues discussed appropriately?				/ 19	
Structure (S)							
	Disease states/pathways	Disease states/pathways reflect the underlying biological/clinical process of the disease			S8		

No	Section*	Descriptions	BMJ, 1996 [195]	QHE, 2003 [196]	Philips, 2006 [199]	CHEC, 2005 [200]	CHEERS, 2013 [302]
	Cycle length	Is the cycle length defined and justified			S9		
Data (D)							
	Data identification				D1		
	Pre-model data analysis				D2		
Consistency (C)							
	Internal consistency	mathematical logic of the model has been tested thoroughly before use			C1		
	External consistency	explained and justified any differences if the model has been calibrated against independent data			C2		
	External consistency	compare the results of the model with those of previous models and any differences in results explained?			C2		

*Base reference: The CHEERS checklist (24 questions)

Appendix 27 Summary of studies

Author (Year)	Intervention	Control	Setting	Perspective	Model	Costing	Outcomes	Incremental Costs Effectiveness Ratios (ICER)	Results
Improvement of rehabilitation services									
Khiaocharoen, 2012[54]	usual rehabilitation services >1 time	rehabilitation services 1 time or no rehabilitation	Thailand	societal	CUA No model	- direct medical cost (hospitalisation) - direct non-medical cost - loss of income of patient and relatives	modified BI, EQ-5D-3L	THB24,571/QALY	rehabilitation services were cost-effective
Sampson, 2014[203]	pre-discharge home assessment visit (home visit)	pre-discharge home assessment structured interview (at hospital)	UK	healthcare system/payer	CUA No model	cost of home visit (staff attending time, travel time, travel cost, administration time, & equipment)	EQ-5D-3L	£21,986.92 (95%CI: £6,292 - £8,953,709)/QALY	Home visits are shown to be more expensive and more effective than a hospital-based interview. (47% chance that home visits are cost-effective at a WTP of £20,000/QALY
Forster, 2015[204]	longer-term stroke care system of care + usual care	usual care	UK	- healthcare system/payer - societal	CUA No model	- direct medical cost including cost of stroke multi-disciplinary meeting and cost per hour of co-ordinator - average wage and cost per leisure time of carer	General Health Questionnaire-12, EQ-5D	dominated	no benefit in cost-effectiveness outcomes associated with the new system of care

Author (Year)	Intervention	Control	Setting	Perspective	Model	Costing	Outcomes	Incremental Costs Effectiveness Ratios (ICER)	Results
Lloren, 2015[214]	Home-based Virtual Reality-based telerehabilitation system	in-clinic program using the same VR	Spain	not stated	CBA No model	- cost per physical therapist hours - instrumentation e.g. computer, TV, internet, program	- Berg Balance Scale - overall expenses.	- in-clinic: $1490, - home-based: $835	VR-based telerehabilitation benefits in the same way as do in-clinic.
Sackley, 2016[205]	Personalised 3-month course of occupational therapy (OT)	usual care for care home residents	UK	healthcare system/payer	CUA No model	- cost of intervention - direct medical cost - equipment (e.g. arm supports, palm protectors) and travel costs	BI, EQ-5D-3L	£49,825/QALY	OT is not cost effective
Nagayama, 2017[216]	occupation therapy for care home residents living with stroke-related disabilities	usual care (did not include an OT component)	Japan	societal	CUA No model	- direct medical cost (prescription, inspection, radiographic examinations, nursing care, rehabilitation)	Short Form questionnaire-36 (SF-36)	not stated	the potential for the occupation-based approach to be cost effective was 65%

Author (Year)	Intervention	Control	Setting	Perspective	Model	Costing	Outcomes	Incremental Costs Effectiveness Ratios (ICER)	Results
Allen, 2019[207]	Community Care Access Centres (CCACs) rehab services in home care	usual care (limited or no further rehab service)	Canada	societal	CUA Decision tree and Markov	- physician visits - hospitalizations and surgeries, diagnostic tests, laboratory expenses, devices, special treatments, household help, travel costs. - long term care - patient out of pocket expenses (no detail)	EQ-5D-5L	cost saving	CCACs dominated usual care
Gao, 2019[211]	A very early rehab intervention within 24 hours of stroke onset	UC vs usual stroke-unit care alone	Australia, New Zealand, UK, Singapore, Malaysia	- healthcare system/payer - societal	CUA No model	- Intervention delivery costs - direct medical cost - direct non-medical cost included community service, home modification, informal care, special equipment etc.	mRS scores, quality of life-4 dimension (AQoL-4D)	dominated	VEM is unlikely to be cost-effective (negative QALY gain, but more expensive)
Rodgers, 2019[206]	extended stroke rehabilitation + usual care	Usual care post early supported discharge	UK	healthcare system/payer	CUA No model	- direct medical cost - Social care costs - Benefit/allowance	Nottingham Extended Activities of Daily Living Scale (NEADL), EQ-5D-5L	£1,711/QALY	On average extended stroke rehabilitation intervention dominates usual care

Author (Year)	Intervention	Control	Setting	Perspective	Model	Costing	Outcomes	Incremental Costs Effectiveness Ratios (ICER)	Results
Tam, 2019[208]	outpatient high intensity fast-track stroke rehab within 1 week of discharge	inpatient rehab with no fast-track program (usual care)	Canada	healthcare system/payer	CEA No model	- inpatient rehabilitation - hospitalisation - medication - physician billing	number of inpatient rehabilitation bed days saved	direct from acute care admissions: $37 ($20-55)/day saved	fast-track is a cost-effective method of providing appropriate rehabilitation intensity
Aziz, 2020[215]	integrated care pathway for post stroke (iCaPPS©)	Conventional care	Malaysia	societal	CUA No model	- provider cost: capital and re-current cost incurred to operate the health centre - patient cost: out of-pocket, Loss of productivity	BI, EQ-5D-5L	RM1144/QALY	the iCaPPS© is a very cost-effective method for monitoring post stroke patients who are residing at home
Chen, 2020[209]	transferred to the rehab ward (TR)	without being transferred to the rehab ward or no rehab (NR)	Taiwan	societal	CEA No model	- hospitalisation (reimbursement cost) - patient cost: out of-pocket	Survival period after first stroke	ICLYG/year = -USD388.5 (95% CI -396.2, -380.8)	TR was more cost-effective than NR
Louw, 2020[213]	individualized 8-week workplace rehab intervention programme + usual care	usual care (not described)	South Africa	healthcare system/payer	CBA No model	- rehabilitation programme cost (Rates of pay for rehabilitation providers)	net saving from intervention	cost-benefit analysis (CBA)	Potential Impact of the workplace programme over 5 years Net savings = R536,638,676

Author (Year)	Intervention	Control	Setting	Perspective	Model	Costing	Outcomes	Incremental Costs Effectiveness Ratios (ICER)	Results
van Mastrigt, 2020[212]	self-management intervention (SMI)	stroke-specific education-based intervention	the Netherlands	societal	CUA No model	- Intervention costs and education training (hourly wages of medical professionals) - direct medical cost (health care utilization) - direct non-medical cost - Productivity costs	Utrecht Proactive Coping Scale, EQ-5D-3L	€44,687.9/QALY	SMI is not cost-effective
Tung, 2021[210]	Home-Based Post-Acute Care (PAC)	inpatient (IP) intensive PAC	Taiwan	healthcare system/payer	CEA No model	- cost of rehabilitation (reimbursement cost)	improvement in BI and Taiwanese EQ-5D-3L scores (ED5Q)	Total cost (USD): mead (SD) IP PAC: 2,699.2 ± 1,107.1 Home-Based PAC: 1,053.9 ± 418.6 Mean improvement ED5Q scores: IP PAC =1.72 home-based=1.64 Cost per improvement in ED5Q score IP PAC: 849.2±1,758.1 home-based: 520.8±618.8	The home-based PAC program was non-inferior to the IP PAC in terms of the functional recovery and life quality. - home-based PAC make it a promising rehabilitative model in terms of cost-effectiveness versus functional and ED5Q improvements

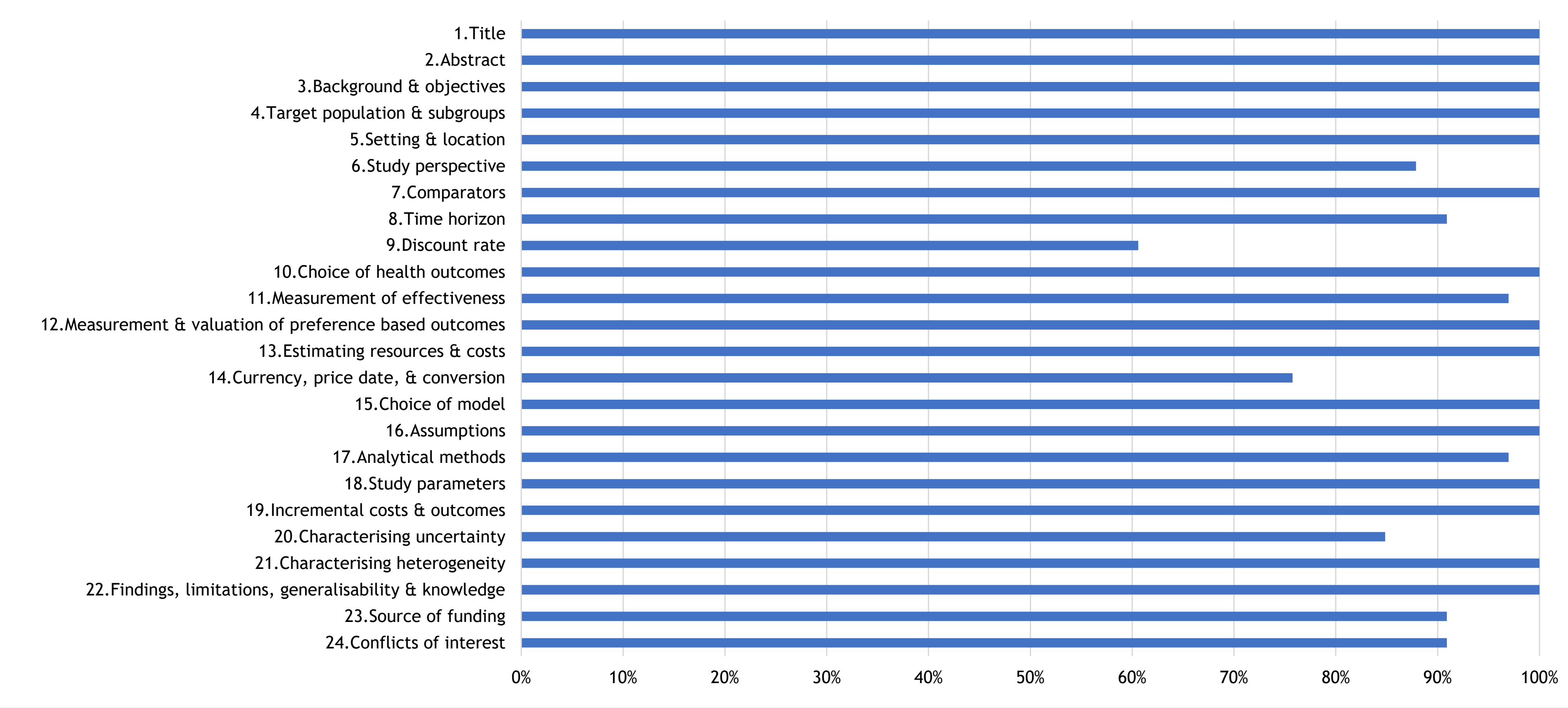
Author (Year)	Intervention	Control	Setting	Perspective	Model	Costing	Outcomes	Incremental Costs Effectiveness Ratios (ICER)	Results
Candio, 2022[42]	Home-based rehabilitation	centre-based rehabilitation: conventional hospital-based care (IP and outpatient)	32 European countries	healthcare system/payer and societal	CUA Decision tree and Markov	- intervention cost - health and social care resource use - informal care cost - productivity losses (Mortality and absence from work in age <65 years)	3-month mRS score and EQ-5D-3L	Cost-saving of €237 million (95% CI: -237 to 1,764) and of €352 million (95% CI: -340 to 2,237) in health- and social-care and societal costs, respectively	home-based rehabilitation was likely to be cost-effective (>90%) in most European countries compared to conventional hospital-based care.
Improvement of function, mobility or strength									
Wagner, 2011[223]	robot-assisted therapy + usual care	usual care alone	USA	healthcare system/payer	CUA No model	- therapist time - travel cost - cost per robot session - caregiving costs	Health Utilities Index, Stroke Impact Scale	cost-saving ICER = $-25,770 with a wide bootstrapped confidence region (-$450255, +$393356)	robotic was more cost-effective than usual care
Taylor, 2013[218]	walking with using Functional Electrical Stimulation (FES) device	walking without using FES device	UK	not stated	CUA No model	standard hospital tariff covers all device, consumables and clinical cost	QALY gained (from review literature)	£15,268	FES used to correct dropped foot is an effective long-term intervention
Logan, 2014[219]	outdoor mobility therapy + initial mobility and transport information	initial mobility and transport information	UK	healthcare system/payer	CUA No model	- training cost - travel costs - intervention and control visit - Other health-care professional visits by patient - patient-borne costs - lost productivity	EQ-5D-3L	dominated	intervention was not cost-effective

Author (Year)	Intervention	Control	Setting	Perspective	Model	Costing	Outcomes	Incremental Costs Effectiveness Ratios (ICER)	Results
Chan, 2015[225]	increased physiotherapy intensity	standard levels of physiotherapy	Canada	healthcare system/payer	CUA Markov model	- additional physiotherapist time required - hospitalisation	EQ-5D	cost-saving	may result in cost savings and improvement
Adie, 2017[220]	using the Nintendo Wii Sports™ at home	usual care + exercise (seated position) at home	UK	not stated	CUA No model	- Unit costs of health and social care services - Wii™ equipment	EQ-5D-3L	not stated	Wii™ was not superior to arm exercises
Collins, 2018[221]	group physical fitness sessions	relaxation	UK	not stated	CUA Decision tree	- Costs of running classes - ambulance transportation - training costs	SF-36 (SF-6D)	£2,343	group-based physical fitness was cost-effective
Geng, 2018[227]	Bobath rehabilitation	traditional massage	China	Societal	CUA Markov model	Direct medical costs (no detail)	Health utility value from specialists	￥109,421.96	cost-effectiveness of Bobath rehabilitation
Fernandez-Garcia, 2021[222]	1) robot-assisted training plus usual care 2) enhanced upper limb therapy (EULT; repetitive functional task practice) plus usual care	usual care (not stated)	UK	healthcare system/payer	CUA No model	- intervention costs - capital costs for robot-assisted training - direct medical cost (hospital attendance)	EQ-5D-5L map to EQ-5D-3L	EULT plus usual care vs usual care: £74,100 Robot-assisted therapy was dominated by EULT (more costly and less effective)	neither robot-assisted training nor EULT were likely to be cost-effective at any cost per QALY thresholds.
Christie, 2022[226]	Constraint-induced movement therapy (CIMT) for arm recover	standard inpatient rehabilitation upper limb therapy	New South Wales, Australia	healthcare system/payer	CEA No model	- Costs of the implementation package and follow up. - resource use and equipment for CIMT (no overhead cost)	proportion of patients who achieved a clinically meaningful improvement in arm function on the Action Research Arm Test	$7048.39 AUD for per additional person gaining a meaningful change in arm function	poor value for money when planning to deliver the CIMT implementation package and introducing CIMT into routine practice

Author (Year)	Intervention	Control	Setting	Perspective	Model	Costing	Outcomes	Incremental Costs Effectiveness Ratios (ICER)	Results
Hornb, 2022[224]	high-intensity training (walking task in variable context, to 80% max heart rate reserve)	conventional physical therapy: active & passive range of motion (targeted intensity range up to 40% heart rate reserve)	USA	healthcare system/payer	CUA No model	costs of personnel who provided the training and total number of staff required for each participant	SF-36 (SF-6D)	$6180 (95%CI, -$96,364, $123,211/QALY	At a WPT of $30,000 - 50,000 /QALY, high-intensity training had a 48%-52% probability of being cost-effective
Improvement of specific skills									
Bowen, 2012[228]	early well-resourced flexible speech and language therapy by NHS speech and language therapists	Attention control: same intensity by employed visitors who did not provide therapy	UK	- healthcare system/payer - societal	CUA No model	- healthcare and social care resources used - costs associated care of the patient - cost year 2008/9	EQ-5D	not stated	intervention is likely to be cost-effective only if decision-makers are prepared to pay ≥£25,000 to gain one unit of utility
Latimer, 2013[229]	speech and language therapy intervention + usual care	usual care	UK	healthcare system/payer	CUA No model	- intervention cost - Patient and carer diaries for healthcare resource use costs	EQ-5D	£3,058	computer therapy for people with long-standing aphasia is likely to represent a cost-effective use of resources
Humphreys, 2014[231]	behavioural therapy	usual care	UK	healthcare system/payer	CUA No model	- standard unit cost for healthcare cost - cost year 2011	Stroke Aphasic Depression Questionnaire Hospital (SADQH21) scores	£263 (cost/point reduction of SADQH21)	behavioural therapy was resulted in some convincing savings in resource utilisation
van Eeden, 2015[232]	cognitive behavioural therapy (CBT) augmented with occupational and movement therapy	computerized cognitive training program	the Netherlands	societal	CUA No model	- self-report questionnaire - cost year 2012	EQ-5D-3L	€-160,389.9 (greater effects and fewer costs)	potential cost-effectiveness of CBT group

Author (Year)	Intervention	Control	Setting	Perspective	Model	Costing	Outcomes	Incremental Costs Effectiveness Ratios (ICER)	Results
Latimer, 2020[230]	computerised word finding for SL therapy + usual care	usual care	UK	healthcare system/payer	CUA Markov model	- computer, software - therapist time - travel cost - cost year 2016/17	EQ-5D-5L	£42,686	Computerised therapy is unlikely to be cost-effective
Others									
Forster, 2013[233]	structured training programme for caregivers	usual care	UK	- healthcare system/payer - societal	CUA No model	- Healthcare costs and questionnaire (interview and self-complete) - cost year 2009/2010	EQ-5D	Control dominates (both perspective)	intervention group is less likely to be cost-effective than the control group
Angerova, 2020[234]	early inpatient rehabilitation after stroke in different disability category	NA	the Czech Republic	healthcare system/payer	CEA	- micro-costing (therapeutic cost) - cost year 2017	BI, functional independence measure	1. self-sufficient = CZK8,603 2. partly self-sufficient CZK5,116 3. requires an enhanced level of supervision = CZK 8,179 4. immobile = CZK8,088	inpatient rehab proved to be most effective for partly self-sufficient patients

Appendix 28 Distribution of CHEERS score for each items (Excluded NA answer)



Appendix 29 Consumer price index inflation rates

Year	Medical care[272]
2009	91.81
2010	91.91
2011	92.47
2012	93.35
2013	94.26
2014	95.57
2015	96.95
2016	97.83
2017	98.40
2018	99.29
2019* (Base year)	100.00
2020	100.42
2021	101.04

Appendix 30 Estimated cost of carer time loss

Year	GNI per capita	GNI per day
2015	191,723.00	614.50
2016	203,521.00	652.31
2017	215,041.00	689.23
2018	225,451.00	722.60
2019	234,652.00	752.09
2020	219,796.00	704.47
2021	221,153.04	708.82

GNI: gross national income (GNI)[273]

Appendix 31 Utilities of each health state

health state	BI score	rehabilitation		usual care		adjusted value	
		Utility (SD)	N	Utility (SD)	N	Utility (SD)	N
non to mild	20	0.71 (0.23)	8	0.90 (0.06)	7	**0.81 (0.17)**	**15**
moderate to severe	11-19	0.60 (0.24)	30	0.55 (0.24)	18	**0.58 (0.24)**	**48**
long-term care	1-10	0.56 (0.23)	12	0.26 (0.37)	5	**0.41 (0.27)**	**17**

Appendix 32 Results of one-way sensitivity analysis

Parameter		Value (Base case)	Min	Max	Lower bound		Upper bound	
					Value	%Change	Value	%Change
Provider perspective (ICER: -132,460.32)								
Transition Probabilities	'non to mild' to 'moderate to severe'	0.286	0.000	0.599	-219,665	-119,201	65.83%	-10.01%
	'non to mild' to 'LTC'	0.017	0.001	0.032	-135,335	-129,862	2.17%	-1.96%
	'non to mild' to death	0.049	0.017	0.081	-110,749	-157,301	-16.39%	18.75%
	'moderate to severe' to LTC	0.072	0.031	0.113	-173,171	-111,141	30.73%	-16.09%
	'moderate to severe' to death	0.099	0.049	0.149	-121,349	-142,048	-8.39%	7.24%
	'LTC' to death	0.220	0.217	0.224	-133,522	-131,428	0.80%	-0.78%
Cost	direct medical cost (rehabilitation): ±20%	18,300	14,640	21,960	-161,747	-103,173	22.11%	-22.11%
	yearly direct medical cost (non-mild): ±20%	29,067	23,254	34,880	-140,214	-124,706	65.83%	-10.01%
	yearly direct medical cost (non-mild): ±50%	29,067	14,533	43,600	-151,845	-113,076	2.17%	-1.96%
Utility	'non to mild'	0.81	0.64	0.97	-171,920	-107,733	-16.39%	18.75%
	'moderate to severe'	0.58	0.43	0.72	-144,666	-122,154	30.73%	-16.09%
	LTC	0.41	0.06	0.76	-95,004	-218,675	-8.39%	7.24%
Others	Discount rate							
Societal perspective (ICER: 246,207.48)								
Transition Probabilities	'non to mild' to 'moderate to severe'	0.286	0.000	0.599	377,055	226,889	53.15%	-7.85%
	'non to mild' to 'LTC'	0.017	0.001	0.032	250,380	242,443	1.69%	-1.53%
	'non to mild' to death	0.049	0.017	0.081	224,211	271,358	-8.93%	10.21%
	'moderate to severe' to LTC	0.072	0.031	0.113	307,091	214,620	24.73%	-12.83%
	'moderate to severe' to death	0.099	0.049	0.149	236,533	254,548	-3.93%	3.39%
	'LTC' to death	0.220	0.217	0.224	246,740	245,690	0.22%	-0.21%
Cost	direct medical cost (rehabilitation): ±20%	18,300	14,640	21,960	216,921	275,494	-11.90%	11.90%
	direct non-medical cost & informal care cost (rehabilitation): ±20%	59,127	47,302	70,953	151,583	340,832	-38.43%	38.43%
	yearly direct medical cost (non-mild): ±20%	29,067	23,254	34,880	238,454	253,961	-3.15%	3.15%
	yearly direct medical cost (non-mild): ±50%	29,067	14,533	43,600	226,823	265,592	-7.87%	7.87%
Utility	'non to mild'	0.81	0.64	0.97	319,552	200,246	29.79%	-18.67%
	'moderate to severe'	0.58	0.43	0.72	268,894	227,051	-7.44%	8.74%
	LTC	0.41	0.06	0.76	176,587	406,456	-7.44%	8.74%
Others	Discount rate	0.03	0.00	0.06	223,608	269,587	-9.18%	9.50%

Appendix 33 Costs of implementation of new rehabilitation policy

Costs of implementation of new rehabilitation policy (I) were calculated based on recommendations from the new IMC guidelines[51]. This guidelines suggests that the levels of improvement in activities of daily living should differ by type of hospital. Also, the national KPIs for IMC focus on mid-level and first-level hospitals and the improvement of IMC beds or IMC wards in these hospitals. Advanced-level and standard-level hospitals should provide academic support and consultation. Additionally, results from the survey reported in Chapter 2 and the wider literatures[43, 256, 259] showed that most of the advanced-level and standard-level hospitals have been able to provide intensive rehabilitation before launching the new rehabilitation programme. Consequently, this thesis assumed that advanced-level and standard-level hospitals could relocate their resources to improve rehabilitation provisions without extra budget. Hence, the extra budget for investment in implementation of new rehabilitation programme were estimated based on these mid-level and first-level hospitals.

Costs of implementing new rehabilitation policy were calculated based on health workforce only, assuming that these hospitals have not bought any new equipment, but would just re-allocate their equipment to facilitate implementation. Thus, only additional training requirements for nurses, physiotherapist and occupational therapists were included as per recommendation in the new rehabilitation guidelines and MOPH inspection report[43, 51].

Training course registration fees were used to measure implementation costs. As the guidelines did not state the optimal number of health workforce that should be trained per year, it was assumed that the number nurses undergoing 4-months training was one person per hospital. Eligible nurses will already have at least two years' experience in stroke service provision and most of them have experience working as case managers. However, this thesis assumed the number nurses undergoing a 5-day training was two person per hospital as it seems that the training time does not consume much time.

Furthermore, this thesis assumed that physiotherapists are the leading role; as a result, this thesis assumed the training costs for two physiotherapists per hospitals. Accordingly, due to a national shortage of occupational therapists, it was assumed that there was only one occupational therapist who could register for a 4-month training.

In terms of the number of health facilities to be considered in the analysis, the MOPH inspection report fiscal year 2021[43] indicated that the number of middle- and first-level hospitals that were able to provide either IMC beds or IMC wards was 767 out of 816 hospitals across Thailand and the number of provinces, being able to provide IMC beds at least at one middle- or first-level hospitals, were 45 out of 76 provinces.

The number of eligible patients over five years was calculated from the total number of stroke patients (ICD10: I60-I69) from Thai national stroke data (Chapter 3) which were 386,484 stroke patients. Of these, there were 340,403 stroke survivors. However, the new rehabilitation policy includes only stroke patients with ICD10 codes I60 to I64. Therefore, the number of eligible stroke survivors for value of implementation analysis was adjusted accordingly (277,071 patients over a five-year period, or 67,635 per year). As the programme is evaluated over five years, the total number of eligible patients was 338,176. It is expected that the utilisation rate following the implementation activity should be set at perfect implementation ($\sigma = 1$). Based on results from Chapter 3, rehabilitation services were provided at a rate of 32%; therefore, the current utilisation (ρ) is 0.32.

Appendix 33 Costs of implementation of new rehabilitation policy (Cont.)

Set-up costs for implementation of rehabilitation programme	Assumptions	Quantity	Unit	Sum	Reference
Nurses					
1) Registration cost of 4-month training nurse					
1.1) Costs of registration	same registration price for 5 years	40,000	THB per person		305
1.2) Number of nurses		1	person		
1.3) Number of provinces need to improve					
1.3.1) First year: remaining hospital to improve their capacities	IMC ward criteria	76-45 = 31	hospitals		43
Total cost first year for 4-month training nurse		40,000 THB x 1 nurse x 31 hospitals		**1,240,000**	
1.3.2) Next 4 years: number of provinces need to be improved	training new nurse every year up to 5 years	76	hospitals		
Total cost of the next 4 year for 4-month training nurse		40,000 THB x 1 nurse x 76 hospitals x 4 years		**12,160,000**	
2) Registration cost of 5-day training nurse					
2.1) Costs of registration	assume 1 week of 4-month cost (40,000THB/16 weeks)	2,500	THB per person		
2.2) Number of nurse		2	person		
2.3) Number of hospitals need to improve					
2.3.1) First year: remaining hospitals to improve their capacities	IMC bed criteria	816-767 = 49	hospitals		
Total cost first year for 5-day training nurse		2,500 THB x 2 nurse x 49 hospitals		**245,000**	
2.3.2) Next 4 years: number of hospitals need to be improved	training new nurse every year up to 5 years	816	hospitals		
Total cost of the next 4 year for 5-day training nurse		2,500 THB x 2 nurse x 816 hospitals x 4 years		**16,320,000**	
Doctors					
1) Registration cost of training					

Set-up costs for implementation of rehabilitation programme	Assumptions	Quantity	Unit	Sum	Reference
1.1) Costs of registration	same as registration price for 5-day training nurse				
1.2) Number of doctors		1	person		
1.3) Number of hospitals need to improve					
1.3.1) First year: remaining hospitals to improve their capacities	IMC bed criteria	816-767 = 49	hospitals		
Total cost first year for 5-day doctor training		2,500 THB x 1 doctor x 49 hospitals		**122,500**	
1.3.2) Next 4 years: number of hospitals need to be improved	training every year up to 5 years	816	hospitals		
Total cost of the next 4 year for 5-day doctor training		2,500 THB x 1 doctor x 816 hospitals		**8,160,000**	
Physiotherapist					
1) Registration cost of 4-month training					
1.1) Costs of registration	same registration price for 5 years	47,000	THB per person		306
1.2) Number of physiotherapists		2	person		
1.3) Number of hospitals need to improve					43
1.3.1) First year: remaining hospitals to improve their capacities	IMC bed criteria	816-767 = 49	hospitals		
Total cost first year for 4-month training physiotherapist		47,000 THB x 2 physiotherapist x 49 hospitals		**4,606,000**	
1.3.2) Next 4 years: number of hospitals need to be improved	training every year up to 5 years	816	hospitals		
Total cost of the next 4 year for 4-month training physiotherapist		47,000 THB x 2 physiotherapist x 816 hospitals x 4 years		**306,816,000**	
Occupational therapist					
1) Registration cost of 4-month training					
1.1) Costs of registration	same as physiotherapist registration price	47,000	THB per person		
1.2) Number of occupational therapists		1	person		

Set-up costs for implementation of rehabilitation programme	Assumptions	Quantity	Unit	Sum	Reference
1.3) Number of hospitals need to improve					
1.3.1) First year: remaining hospitals to improve their capacities	IMC bed criteria	816-767 = 49	hospitals		
Total cost first year for 4-month training occupational therapist		47,000 THB x 1 occupational therapist x 49 hospitals		**2,303,000**	
1.3.2) Next 4 years: number of hospitals need to be improved					
Total cost of the next 4 year for 4-month training occupational physiotherapist		47,000 THB x 1 occupational therapist x 816 hospitals x 4 years		**153,408,000**	
Implementation cost					
year 1				**8,516,500**	
year 2-4				**496,864,000**	
Total implementation cost (I)				**505,380,500**	