



Systematic Review of Economic Evaluation Studies of Stroke Disease: Cost Effectiveness

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Abstract

Background: Updating pharmacoeconomics of stroke in the past 5 years from Europe, the Americas, and the Pacific Area. This ischemic stroke study relates to telestroke and stroke care. To evaluate the extent and economic quality of published ischemic stroke economic evaluation especially in telestroke and stroke care in the past 5 years.

Methods: A systematic review was conducted according to PRISMA guidelines. The inclusion criteria for the studies were 1) original research article, 2) cost-effectiveness, 3) comparing pharmacoeconomics with QALY's result, and 4) the limitation is from the past 5 years.

Results: A total of 12 studies were included from 2018-2022. The concern of the studies is in telestroke and stroke care which come from 5 European, 2 Americas, and 5 Pacific Area. The mean QHES scale score was 80 ± 100 . All of the studies were published in English.

Conclusion: Cost-saving the result is based on the time horizon, the base year for costing, the QALY Threshold, and the discount rate used by the authors themselves. The nationality and income country will take a few values to impact the result of studies.

Keywords: *Pharmacoeconomic, Ischemic stroke, Cost-effectiveness, Telestroke, Strokecare.*

Introduction

Stroke is the third leading cause of disability worldwide and the second leading cause of death¹. The estimated global cost of stroke in 2022 is over US\$721 billion (0.66% of the global GDP). The Global Stroke Factsheet released in 2022 reveals that the lifetime risk of developing a stroke has increased 50% over the last 17 years with an estimation of 1 in 4 people having a stroke in their lifetime. The most striking feature is that the bulk of the global stroke burden (86% of deaths due to stroke and 89% of DALYs) occurs in lower and lower-middle-income countries².

WHO data in world health statistics, that strokes, other cardiovascular diseases, and some cancers are associated with a similar and even higher risk of premature death in certain countries, moreover in Europe, the Americas, and the Pacific Area³. A stroke is a medical condition in which poor blood flow to the brain causes the death of cells. There are two main types of stroke: ischemic, due to lack of blood flow, and hemorrhagic, due to bleeding⁴. An ischemic stroke is the usual stroke that meets in the individual report in WHO. An ischemic stroke is up to 85% the majority stroke in the world than hemorrhagic stroke which is just 15% of patients

detected even though 40% of patients die because of it⁵.

An ischemic stroke happens if the blood supply to part of the brain is decreased, leading to dysfunction of the brain tissue in the area. There are four reasons this might happen: 1. Thrombosis (obstruction of a blood vessel by a blood clot forming locally); 2. Embolism (obstruction due to an embolus from elsewhere in the body); 3. Systemic hypoperfusion (general decrease in blood supply, e.g., in shock); 4. Cerebral venous sinus thrombosis⁶.

There are a lot of reports have been published on knowing the efficacy of an ischemic stroke in the world⁷. Many kinds of medicine and other alternatives are being chosen to decrease the number of sufferers of the disease⁸. With improving survival for stroke by treatment mechanical thrombectomy is the most effective reperfusion used in acute ischemic stroke⁹. Risk factors for stroke are more prevalent, and specialized stroke treatment options are less available⁵. Telemedicine for stroke has emerged as an efficacious method of delivering stroke specialist care to remote hospitalize without such expertise on-site¹⁰. Management of patients with ischemic stroke in dedicated stroke units largely contributes to improved outcomes by telemedicine¹¹.

From all these factors, we need to choose the effective way. One of the ways to choose the effective choices for stroke therapy is by knowing the cost-effectiveness from an economic evaluation study. Furthermore, the cost results in a considerable proportion of public expenditure. This article wants to review how effectiveness of the medication choices in 5-year long specified in seeing ICER/QALY by all articles around the world. So that this article aims to evaluate the extent and economic quality of published ischemic stroke for economic evaluation studies, especially in tele-stroke and stroke care; and to evaluate the quality of studies from those articles in the past 5 years.

Methods

Search Strategy

The following database was searched from a literature article by using SUMMON (the powerful engine behind the large search box on the library website) which has been related to Gadjah Mada University Library. The following string of keywords was used: Cost Effectiveness AND Stroke OR Ischemic Stroke, Cost Utilization Analysis AND Stroke OR Ischemic Stroke, Cost Effectiveness Analysis AND Stroke OR Ischemic Stroke. The search was restricted to English-language articles. This article used the PRISMA checklist to make sure the exclude articles. The reference lists of the identified studies were manually searched for any missing clinical trials (medicine, nursing care, delivering patients) or other economic evaluation studies (Cost-Minimization Analysis, Cost Of Illness, Cost-Benefit Analysis) with no ICER or QALYs result. Cost-Effectiveness and Cost-Utility Analysis are types of full economic evaluations comparing the associated costs and consequences of alternative courses of action, whereas the latter measure outcomes in terms of quantity and quality of life¹². This article will show the risk bias of the article literature studies and gain sensitivity analysis.

Type of Study

The review included clinical trials (Telestroke and Strokecare) and other economic evaluation studies (Cost-Effectiveness Analysis, Cost-Utility Analysis) with ICER or QALYs result¹³. The patients from this study were identified and required for Acute Ischemic Stroke (AIS) from hospital records.

Assessment of Included Studies

The characteristics of articles are countries, target populations, type of studies, and results. All of them were extracted from individual studies and documented in a table. For the quality, QHES (Quality of Health Economic Studies) is used to evaluate the

methodological quality of studies to produce a numeral score rating between 0 and 100, where a higher score will indicate higher quality of articles¹². Because of the articles conducted in specific economic evaluation studies (CEA and CUA), if QALYs or ICER results do not appear, it is difficult to know the exact researchers' results when compared with other exchange rate values.

Model Structure

The model began with AIS patients, who receive either thrombolysis or usual care without thrombolysis. The model allowed for capturing all possible health states associated with stroke. We did not use age comparison to calculate all of the patients which was indicated by AIS. There are major groups of input parameters of the model: health state distribution, costs, and utility result¹⁴.

Cost-Effectiveness

A payer, provider, and societal capture all associated costs that should include cost for productivity losses and adopt to provide a comprehensive cost analysis. Utility scores were valued between 0 which represents death and 1 which represents good life¹².

Result

Literature Search

After the screening, the literature search resulted in the retrieval of 547 citations from journal articles in Summon. Excluded into 5 years limitation time, 225 records were screened. Of them, 101 duplicated articles were found, 65 citations were screened based on the title and abstract, and 28 were not available in full text. For the search strategy performed for each database PRISMA flowchart in Figure 1. and a master list of excluded and included studies are provided in the online supplementary material.

Characteristics Of Included Studies

The included studies are 5 cost-effective analyses and 4 cost-utility analyses. Furthermore, there are 13 articles included in this review. The included studies were conducted with 2 citations from Australia^{15,16}, 3 citations from United Kingdom¹⁷⁻¹⁹, 1 citation from Chicago, 1 citation from Saudi Arabia²⁰, 1 citation from French²¹, 1 citation from Spain²², 1 citation from Brazil²³, 1 citation from China⁹, 1 citation from Thailand²⁴. Of these, the base year for costing is different and adapts to the setting of places and purpose of study.

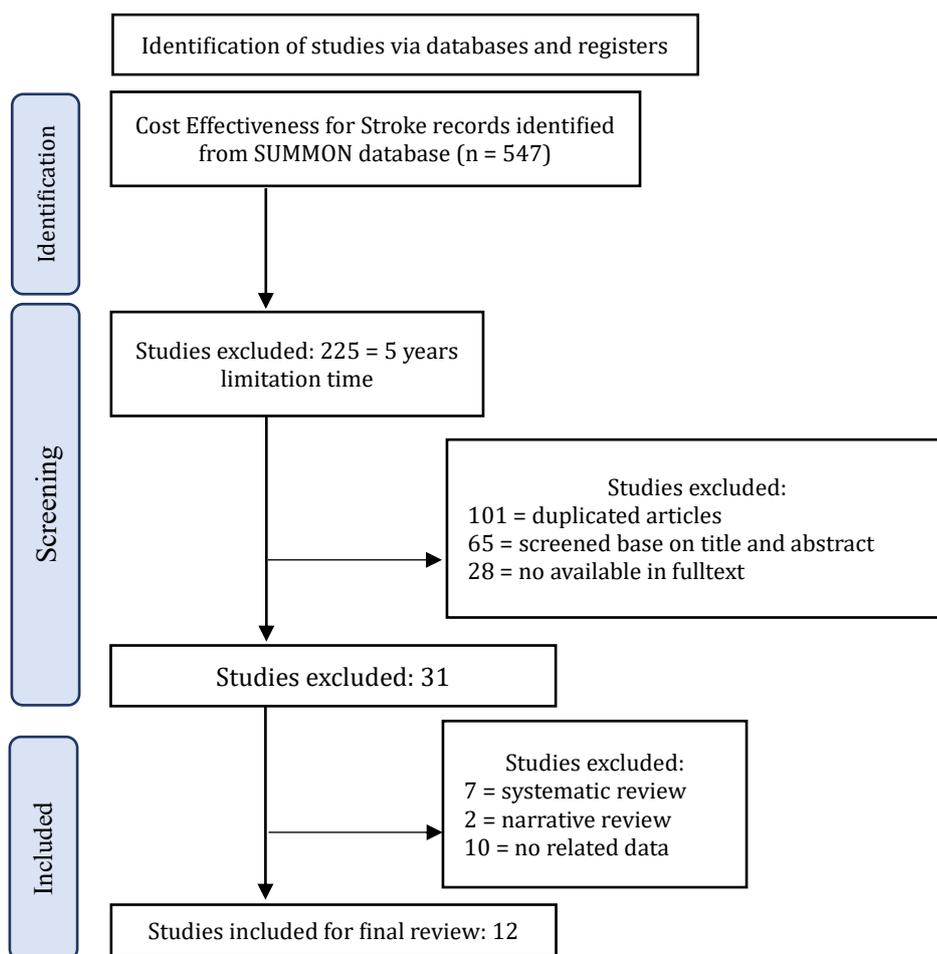


Figure 1. PRISMA Flowchart

Study Quality Assessment

This study was considered by Cohort Study, RCT Model, and Observational study. The dominant model-based uses are Randomized control trials while using a Markov model for limiting the time frame to 90 days. The trial dates ranged from 2019-2022 or last 5 years. The study perspective comes from the Societal, Provider, and Payer perspectives. The result from QALY is being main determinant aim in this review.

Cost-Effectiveness

This study wants to review the calculation of data that can be used for a model standard pharmacoeconomic in every country. Few articles do not appear the cost cost-saving in their research. This cost-saving depends on the time horizon and QALY Threshold used in the article. The evaluation type is conducted by cost effectiveness which is QALY results appear in it. The annual rate used from 3%-3,5% in most of the countries of articles.

Table 1. Economic Evaluation Information for Included Studies

Economic evaluation		No	%
Method of economic evaluation	Cost-effectiveness	3	27.27
	Cost-utility	8	72.73
Study Design	RCT	7	63.64
	Cohort study	4	36.36
Type of cost	Direct medical cost	8	72.73
	Direct nonmedical cost	1	9.09
	Indirect cost	2	18.18
Source of funding	Author's own resources	9	81.82
	Government	2	18.18
Income	Middle	3	27.27
Countries	High	8	72.73
Type of medical function	Telestroke	5	45.45
	Stroke care	6	54.55
Study Location	Australia	2	18.18
	United Kingdom	2	18.18
	Chicago	1	9.09
	Saudi Arabia	1	9.09
	French	1	9.09
	Spain	1	9.09
	Brazil	1	9.09
	China	1	9.09
	Thailand	1	9.09

Table 2 The general characteristics of included studies

Author and Year	Country	Setting	Perspective	Type of Evaluation	Model-Based	Time Frame	Time Horizon	Base year for costing	DR (%)	QALY Threshold
Al-Senani, et al (2019) ²⁰	Saudi Arabia	The Hospitals in Saudi	Societal	CEA	RCT	3 months	15 years	2019 US dollars	3%	NM
Wallut L, et al (2020) ²¹	France	French tele-stroke network	Payer	CEA	RCT	3 months	Long-term	2012 US dollars	N	\$50,000
Heggie R, et al (2020) ¹⁷	United Kingdom	NICE (National Institute for Clinic ²³ al Excellence)	Payer	CUA	RCT	90-days	A lifetime	UK pounds Sterling 2015	3.5%	£20,000 in the UK
Bhattarai N, et al (2021) ¹⁸	United Kingdom	Three UK ambulance services	Provider Payer	CUA	RCT	3 months		2017/2018 UK Sterling Pounds	N	£50 k
Rattanavipapong W, et al (2022) ²⁴	Thailand	Siriraj Stroke Centre	Societal	CUA	RCT	3 months	A lifetime	THB 33=US\$1 in 2021	3%	160,000 THB
Gao L, et al (2022) ¹⁵	Victoria, Australia	Non-urban or suburban hospitals in Australia	Societal Provider	CUA	Cohort Study	3 & 12 months	A lifetime (25 years simulated)	2018 Australian dollars	3%	AU\$50,000
Kim J et al (2022) ¹⁶	Victoria, Australia	The regional hospitals participating in the VST program	Societal	CUA	Cohort Study	12 months after stroke	A lifetime	2018 \$ Australian dollars	N	AU\$50 000
Candio P, et al (2022) ¹⁹	United Kingdom	Conventional hospital in 32 European countries	Provider	CUA	Cohort Study	3 months	5 years	2017 Euros	3.5%	€22,727 (£20,000)
Hornby T. G, et al (2022) ²⁵	Chicago	Outpatient laboratory	Provider	CEA	RCT	1-6 months	A lifetime	2016 US dollars	N	\$30,000 - 50,000
Diaz E, et al (2022) ²²	Spain	The Spanish National Health System	Payer	CEA	Cohort Study	3 months	A lifetime	2020 Euros	3%	€ 30,000
de Souza AC, et al (2022) ²³	Brazil	the Brazilian public healthcare system	Payer	CUA	RCT	Trial follow-up	A lifetime	International Dollars (\$) using Purchasing Power Parity (PPP) 2018	5%	NM
Ni, et al (2022) ⁹	China	Chinese	Provider	CUA	Observational Study	3 months	A lifetime	2019 Chinese Yuan	3%	¥71,000 (\$10,281)

Table 3 The results from included studies

Author and Year	Cost Saving per year	Effectiveness (LYs/QALYs)	Incremental	Research Result	ICER	Intervention	Description of cost data	QHES (%)
Al-Senani, et al (2019) ²⁰	\$602 million (\$40.13 million per year)	0.29	-\$3,131	ICER Dominant		Current stroke care program vs stroke care development program	Direct and Indirect cost	81.25
Wallut L, et al (2020) ²¹	EUR 25,474	0.2	HD = EUR 138; D3M = EUR 154; Dis3M = EUR 97	EUR 2,990	HD = EUR 74,755; D3M = EUR 25,474; Dis3M = EUR 2,990	hospital death (HD), death at 3 months (D3M), and disability 3 months (Dis3M)	Direct cost	75
Heggie R, et al (2020) ¹⁷	£33,190	0.025	£5,207	BMC £39,035 / BMC + MT £46,684	£3466 per QALY	MT plus best medical care, compared with best medical care alone	Direct cost	93.75
Bhattarai N, et al (2021) ¹⁸	-£440 -£470	PASTA=0.108 SC=0.100	£-3700 - £900	PASTA=11,630 SC=13,103	PASTA Dominant (difference=cost - 1,473; QALY 0.007	PASTA vs Standard Care (SC) in compliant and non-compliant hospital	Direct cost	81.25
Rattananavipapong W, et al (2022) ²⁴	88,100 THB	3.045 (LYs)	211,100 THB	115,000 THB	148,800 THB	Alteplase vs no-alteplase	Direct medical and non-medical cost	93.75
Gao L, et al (2022) ¹⁵	\$1,568 \$779	0.45	\$2,959	\$127,224 \$76,2905	\$1,736 per QALY	VST program with 3 scenarios	Direct cost	100
Kim J et al (2022) ¹⁶	A\$25,300	0.43	A\$25,852	\$82,259		Patients with VST program vs without VST between 3 & 12 months hospitalize	Totally cost	75
Candio P, et al (2022) ¹⁹	€237 million (€47.4 million per year) €352 million (€70.4 million per year)	0.95	NM NM	61,888		Home-based and Centre-based	Indirect cost	87.5
Hornby T. G, et al (2022) ²⁵	\$1,267	0.05	-\$9,364 up to \$123,211	\$6,180 per QALY		HIT (high intensity training) vs conventional therapy	Direct cost	93.75
Diaz E, et al (2022) ²²	€16 583	1.2	-30 072	€30 072		FPE vs non-FPE group	Direct cost	93.75
de Souza AC, et al (2022) ²³	NM	1.04	I\$ 7,440	I\$ 7,153		MT plus SMC vs SMC alone (Short-term, Mid-term, Lifetime)	Direct cost	87.5
Ni, et al (2022) ⁹	¥15,105 (\$2,187)	0.45	-\$1436	¥16,409 (\$2376)	¥15,000-¥18,000	EVT vs non-EVT	Direct cost	93.75

Discussion

This study assesses the pharmacoeconomics from the ischemic stroke article in Telestroke and Stroke Care 2019-2022 which included. We make 3 parts of continents which come from Americas, European and Pacific Area. In Table 2. Societal perspective is used for hospital respondents setting studies^{15,16,19,20,24}. The payer perspective was taken from national institutes; ambulance services; national health system; and public healthcare setting studies^{17,18,21-23}. As one of the high-income countries, Brazil used the highest differentiation rate (5%)²³. While using the cohort study method, Kim and Gao had the longest time frame^{15,16}.

In Table 3. can be seen that 4 studies had LYs/QALYs results over 1,00^{19,22-24}. This high score has a similar result with Li (QALYs=9,51)²⁶ and Martinez (QALYs=4,81)²⁷. The highest cost-effectiveness of direct cost is 1.2²² and the lowest is 0,025¹⁷, which means the high-income country does not guarantee high QALY results. Between middle-income countries, de Souza had the high cost-effectiveness (QALYs=1,04)²³ and Wallut was the lowest (QALYs=0,2)²¹.

Even though the countries are included in high and middle-income countries, we still have to make it clear how the cost-saving of AIS can be useful for increasing population income. The highest cost saving from high-income countries is Hornby²⁵ from America with \$1.267 per year. From Europe is Candio¹⁹ with €237-352 million in lifetime. Western and Southeast Pacific have Al-Senani²⁰ with \$602 million per 15 years.

Conclusions

This study evaluates the extent and economic quality by some evaluations of the study including the method of economic evaluation, the study design of the study, type of cost used, source of funding, income country, type of medical function, and study location. Comparing the general characteristics of the included study being the result of quantity from those articles. The nationality and income country will take a few of values to impact the result of studies even those are the most differences seen. With this study, hopefully can improve another country to raise the cost-saving. Not only pharmacoeconomic study but also other research areas of medical science can enhance the economic crisis. This study is a recent systematic review that is taken from the past 5 years of articles related to tele-stroke and stroke care. Many more articles haven't been included in this study because the other studies have low QHES scores, which it

makes difficult to determine the cost-effectiveness of Lys or QALYs as the result identified.

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Author Contribution

NFA designed study; NFA, DE analyzed the data; NFA wrote the manuscript; All the authors read and approved the final version of the manuscript.

Competing Interests

This study talks deeply about cost-effectiveness in an economic evaluation of a systematic review. All which included in this study have been extracted from SUMMON big data which included all other data from Gadjah Mada University affiliation.

Abbreviation

AIS	: Acute Ischemic Stroke
CEA	: Cost-Effectiveness Analysis
CUA	: Cost-Utility Analysis
EVT	: Endovascular Therapy
FPE	: First Pass Effect
HIT	: High Intensity Training
ICER	: Incremental Cost-Effectiveness Ratio
MT	: Mechanical Thrombectomy
QALY	: Quality-Adjusted Life Years
QHES	: Quality Of Health Economic Studies
RCT	: Randomized Clinical Trial
SMC	: Standard Medical Care
VST	: Victorian Stroke Telemedicine

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