

COST OF ILLNESS STROKE TREATMENT: A SYSTEMATIC REVIEW

Raihana Nurul Izzah^{1*}, Dina Fatma Alia², Annora Rizky Amalia³
Yunita Dian Permata Sari⁴

Correspondensi e-mail*: raihananurulizzah@poltekindonusa.ac.id

^{1,3,4} Study Program D3 Pharmacy, Politeknik Indonusa Surakarta

² Pharmacy Study Program, Faculty of Pharmacy, Universitas Muhammadiyah A.R. Fachruddin

ABSTRACT

Background: cardiovascular disease remains the leading cause of death worldwide, with stroke playing a significant role in increasing morbidity, mortality, and the global economic burden. **Aim:** this study aimed to systematically review the cost of illness and health expenditure associated with stroke across different countries. **Methods:** a systematic review was conducted using PubMed, ScienceDirect, and Springer databases for articles published between 2021 and 2026, following PRISMA guidelines. Studies included in the criteria were original research that reported direct and/or indirect costs due to stroke, both in primary health care facilities and in hospitals. Data extraction, screening, and quality assessment were performed using the CHEERS checklist. **Results:** a total of 13 studies met the inclusion criteria. The findings indicate that the majority of studies (76%) employed the Cost of Illness (COI) approach, while the remainder used the Health Expenditure (HE) method. Direct medical costs, particularly those arising from inpatient care, constitute the largest component of stroke-related expenditures. Direct medical costs per patient varied, ranging from approximately USD 569 in middle-income countries to over USD 167,000 in high-income countries, influenced by differences in healthcare systems and service costs. Clinical severity, length of hospital stay, stroke subtype, and sociodemographic factors were identified as the primary determinants influencing total costs. Indirect cost components such as lost productivity and mortality also contribute significantly, but their reporting has not been consistent across studies. **Conclusion:** stroke imposes a substantial and heterogeneous economic burden influenced by methodological approaches, perspectives, and healthcare system differences. Comprehensive evaluation including both direct and indirect costs is essential to support effective health policy and resource allocation.

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ABSTRAK

Latar belakang: penyakit kardiovaskular tetap menjadi penyebab utama kematian di seluruh dunia, dengan stroke memainkan peran penting dalam meningkatkan morbiditas, mortalitas, dan beban ekonomi global. **Tujuan:** studi ini bertujuan untuk meninjau secara sistematis biaya penyakit dan pengeluaran kesehatan yang terkait dengan stroke di berbagai negara. **Metode:** tinjauan sistematis dilakukan menggunakan basis data PubMed, ScienceDirect, dan Springer untuk artikel yang diterbitkan antara tahun 2021 dan 2026, mengikuti pedoman PRISMA. Studi yang termasuk dalam kriteria adalah penelitian asli yang melaporkan biaya langsung dan/atau tidak langsung akibat

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stroke, baik di fasilitas perawatan kesehatan primer maupun di rumah sakit. Ekstraksi data, penyaringan, dan penilaian kualitas dilakukan menggunakan daftar periksa CHEERS. **Hasil:** Sebanyak 13 studi memenuhi kriteria inklusi. Temuan menunjukkan bahwa sebagian besar studi (76%) menerapkan pendekatan *Cost of Illness* (COI), sedangkan sisanya menggunakan metode *Health Expenditure* (HE). Biaya medis langsung, khususnya yang berasal dari perawatan rawat inap, merupakan komponen terbesar dari pengeluaran terkait stroke. Biaya medis langsung per pasien bervariasi, dari sekitar USD 569 di negara menengah hingga lebih dari USD 167.000 di negara maju, dipengaruhi oleh perbedaan sistem kesehatan dan biaya layanan. Tingkat keparahan klinis, lama rawat inap, subtipe stroke, dan faktor sosio demografis diidentifikasi sebagai penentu utama yang mempengaruhi total biaya. Komponen biaya tidak langsung seperti hilangnya produktivitas dan kematian juga berkontribusi secara signifikan, tetapi pelaporannya belum konsisten di berbagai penelitian. **Kesimpulan:** stroke menimbulkan beban ekonomi yang substansial dan heterogen yang dipengaruhi oleh pendekatan metodologis, perspektif, dan perbedaan sistem perawatan kesehatan. Evaluasi komprehensif yang mencakup biaya langsung dan tidak langsung sangat penting untuk mendukung kebijakan kesehatan dan alokasi sumber daya yang efektif.

Kata kunci:

beban ekonomi; pengeluaran kesehatan; biaya langsung; biaya tidak langsung

INTRODUCTION

Cardiovascular Disease (CVD) is recognized as the leading cause of death worldwide and is responsible for a significant number of deaths and disabilities (Liu et al., 2025). CVD caused an estimated 20.5 million deaths in 2021, or nearly a third of all global deaths (Lindstrom et al., 2022). Premature deaths from Noncommunicable Diseases (NCDs) are also on the rise, partly due to stroke, which is now the leading cause of death among people under 70 worldwide (World Health Organization, 2025). This trend reflects a shift in disease patterns from infectious to noncommunicable diseases (Gulis et al., 2025).

Among the various types of stroke, ischemic stroke is the most common subtype. However, a high incidence of intracerebral hemorrhage is also observed in many countries. As populations age and the prevalence of risk factors—such as hypertension, diabetes mellitus, tobacco and alcohol consumption, physical inactivity, air pollution, and exposure to high temperatures and humidity—continues to rise, the burden of stroke is also increasing, especially in the Southeast Asian Region (SEAR) (Pandian et al., 2023).

Stroke is one of the leading causes of global morbidity and mortality, with a massive economic impact. Globally, the estimated cost of stroke exceeds US\$890 billion, or approximately 0.66% of the world's Gross Domestic Product (GDP). Between 1990 and 2021, the burden of stroke increased substantially, marked by a 70.0% rise in incidence, a 44.0% rise in mortality, an 86.0% rise in prevalence, and a 32% rise in Disability-Adjusted Life Years (DALYs) (Feigin et al., 2025). This increase was primarily driven by population growth and aging, as well as rising life expectancy (Cheng et al., 2024).

The impact of stroke is not limited to clinical aspects but also has significant macroeconomic consequences, even when analyzed by stroke subtype (Gerstl et al., 2023). In Europe, in 2017 it was estimated that the cost of informal care reached €1.3 billion, healthcare expenditures amounted to €27 billion, and losses due to post-stroke productivity decline totaled €12 billion (Luengo-fernandez et al., 2019). Meanwhile, in the United States, indirect costs accounted for approximately 66% of the total economic burden of stroke, which reached \$103.5 billion, with a relatively balanced proportion between productivity loss costs (\$38.1 billion) and costs due to premature mortality (\$30.4 billion) (Girotra et al., 2020).

Furthermore, inflation-adjusted healthcare costs are projected to increase nearly three- to fourfold by 2050, with stroke expected to be the largest contributor to the absolute increase in costs among various cardiovascular conditions (Kazi et al., 2024). The majority of this burden occurs in Low and Middle Income Countries (LMICs), which account for approximately 87.0% of deaths and 89.0% of DALYs due to stroke globally (Feigin et al., 2025). The magnitude of this clinical and economic burden indicates that stroke is not only a public health problem but also places significant strain on health systems and the economy.

Therefore, this study was conducted to provide a more comprehensive understanding of the economic burden of stroke, particularly from the perspective of the cost of illness. This study aims to conduct a systematic review of various studies reporting on stroke costs to identify the magnitude and components of costs incurred in various countries. The results of this review are expected to provide a more comprehensive picture of the variation and distribution of stroke costs, thereby serving as a basis for formulating health policies and allocating resources more efficiently.

METHODS

Methods

The methodology applied in this systematic review included a defined search strategy, eligibility criteria (inclusion and exclusion), data extraction and analysis, as well as the reporting of quality assessments.

Search Strategy

An electronic literature search was performed using the keywords: “cost of illness”, “burden of disease”, “cost of disease”, “health burden”, “burden of illness”, “length of stay”, “economic burden of disease”, “direct medical cost”, “stroke”, “cardiovascular disease”, “cerebrovascular stroke”. The literature search was conducted across three databases: PubMed, ScienceDirect, and Springer. These considerations include the population or participants, exposure, context—such as geographical healthcare settings and cultural factors—as well as the outcome measures framework (PECOS). This study was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The article search was conducted in February 2026, with a focus on articles published between 2021 to 2025. The articles included in this systematic review were limited to publications from the past five years (1 January 2021 to 31 December 2025) to ensure the inclusion of studies conducted during a period when multiple treatment options were available to help reduce the burden of recurrent stroke. Retrieved articles were downloaded in BIB format and subsequently imported into Mendeley for reference management

Inclusion and Exclusion Criteria

In this economic evaluation, inclusion and exclusion criteria were established to identify relevant studies for the systematic review. For the participant or population component, studies focusing on stroke patients were included, with no specific exclusion criteria applied. Regarding exposure, studies addressing the burden of stroke were eligible, and no exclusions were specified.

In terms of context, studies conducted in primary care and referral (hospital-based) healthcare settings were included, without exclusion criteria. For outcome measures, eligible studies were required to report direct and/or indirect costs. Direct costs referred to expenses related to treatment and rehabilitation, as well as non-medical costs outside the healthcare system, such as transportation, informal caregiving, or other out-of-pocket expenses borne by patients. Indirect costs encompassed productivity losses within the household affecting both patients and caregivers due to disability or premature mortality, as described in the Discussion section. No exclusion criteria were defined for this component.

Concerning study design and publication type, all forms of original research were included, such as prospective and retrospective cost studies, database analyses, mathematical modeling studies, surveys, and Cost-Of-Illness (COI) studies, while non-original articles were excluded. With respect to publication year and language, studies published between 2021 and 2025 and written in English were included, with no additional exclusion criteria specified.

Data Extraction and Analysis

After importing the articles into Mendeley and removing duplicates, titles were screened for relevance to the study objectives. Abstracts were then assessed to determine eligibility according to the inclusion and exclusion criteria, followed by a full-text review to confirm eligibility. The selection process was conducted in accordance with PRISMA guidelines.

The initial search identified 3,795 articles. After removing 1,253 duplicates, 2,542 articles remained. Of these, 9,071 were excluded during title and abstract screening, leaving 29 articles for full-text assessment. Following further evaluation, two articles were excluded, resulting in a final total of nine articles included in this review (Figure 1).

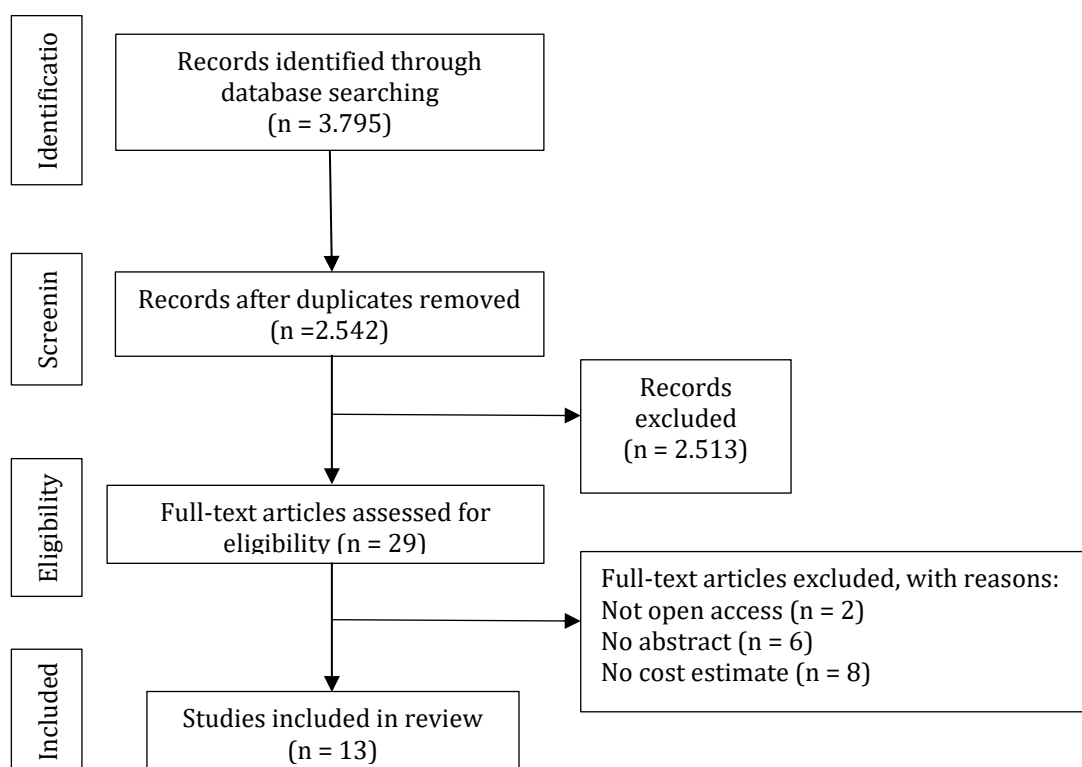


Figure 1. PRISMA flowchart

Quality Assessment Reporting

The quality of the included studies was evaluated using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist. Each domain within the checklist was scored as 0 if not reported and 1 if reported. The results of the quality appraisal for all included articles are presented in Table 1. All thirteen studies demonstrated high methodological quality based on the CHEERS criteria, with each achieving a score of 22 out of a possible 24 points. However, none of the studies reported the discount rate or specified the model choice applied in their analyses.

RESULTS

The quality of the articles discussed in this review was assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS). Thirteen studies in this review were rated as high quality according to the CHEERS checklist. The characteristics of the included studies ($n = 13$) are shown in Table 1. Furthermore, of the included studies, 13 articles (100%) were studies on types of stroke (Azahar et al., 2022; Canciu et al., 2025; Dobe et al., 2025; Lv et al., 2023; Ma et al., 2024b; Marques et al., 2021; Mohammed et al., 2025; Omari, Mohammed et al., 2023; Santoso et al., 2024; Su et al., 2022; Tan et al., 2022; Vyas et al., 2023; Zhu et al., 2022). Most studies (76%) used the Cost of Illness (COI) approach to estimate the economic burden of stroke (Azahar et al., 2022; Canciu et al., 2025; Dobe et al., 2025; Mohammed et al., 2025; Omari, Mohammed et al., 2023; Santoso et al., 2024; Su et al., 2022; Tan et al., 2022; Vyas et al., 2023; Zhu et al., 2022), while three articles (24%) used the Health Expenditure (HE) approach (Lv et al., 2023; Ma et al., 2024b; Marques et al., 2021). These studies originated from various groups of countries based on income classification, namely high-income countries (Romania, Portugal, Australia, Canada) (Canciu et al., 2025; Marques et al., 2021; Tan et al., 2022; Vyas et al., 2023), upper-middle-income countries (Malaysia, China, and Indonesia) (Azahar et al., 2022; Lv et al., 2023; Ma et al., 2024b; Mohammed et al., 2025; Santoso et al., 2024; Su et al., 2022; Zhu et al., 2022), and lower-middle-income countries (Mozambique and Morocco) (Dobe, 2025; Omari, Mohammed et al., 2023). Geographically, the studies are spread across Asia, Europe, Africa, Australia, and North America, indicating a fairly broad distribution of research, although it is still dominated by upper-middle-income countries.

Based on study design, the majority of studies (92%) used a retrospective design (Azahar et al., 2022; Canciu et al., 2025; Lv et al., 2023; Ma et al., 2024b; Marques et al., 2021; Mohammed et al., 2025; Omari, Mohammed et al., 2023; Santoso et al., 2024; Su et al., 2022; Tan et al., 2022; Vyas et al., 2023; Zhu et al., 2022) while only one study (8%) used a prospective design (Dobe et al., 2025). The most commonly applied analytical approach was the cross-sectional method (Azahar et al., 2022; Canciu et al., 2025; Marques et al., 2021; Omari, Mohammed et al., 2023; Santoso et al., 2024), accompanied by other methods such as cohort (Mohammed et al., 2025), Monocentric (13, and the use of a markov model (Tan et al., 2022) in one study. Several articles did not report in detail the analytical methods used. The predominance of retrospective designs indicates that stroke cost estimates are largely based on secondary data, such as medical records or administrative databases.

The cost perspectives used in the studies vary, including the provider perspective (Azahar et al., 2022; Canciu et al., 2025; Su et al., 2022), the payer perspective 16,18,20,23,24), and the societal perspective (Dobe et al., 2025; Lv et al., 2023; Marques et al., 2021; Omari, Mohammed et al., 2023; Tan et al., 2022). The payer and societal perspectives are used more frequently than the provider perspective. Studies using the societal perspective generally calculate more comprehensive cost components, including direct medical costs, direct non-medical costs, and indirect costs resulting from lost productivity.

The data sources for these studies primarily consist of hospital data and medical records of stroke patients, with sample sizes varying widely, ranging from 31 patients to more than 300,000 patients. Some studies use national health survey data and health statistics reports to generate population-based estimates. Regarding cost burden indicators, all studies reported direct medical costs as the primary component. However, only some studies included direct non-medical costs and indirect costs in their total cost calculations.

Stroke is a noncommunicable disease that imposes a significant economic burden on both the healthcare system and society. In this systematic review, we sought to synthesize the evidence regarding estimates of the Cost Of Illness (COI) and Health Expenditure (HE) associated with stroke treatment across various countries with different healthcare system characteristics. In general, the results indicate considerable variation in the methods,

perspectives, and cost components used, which ultimately leads to heterogeneity in the cost estimates.

This review is dominated by the use of the COI method over the HE method. This aligns with the characteristics of health economics studies, which often employ the COI approach to describe the magnitude of a disease's economic burden in a more practical manner (Onukwughu et al., 2015). However, as seen in the results, the COI approach tends to focus more on direct costs and some indirect costs, without considering the loss of utility or patients' quality of life. In contrast, the HE approach provides a broader picture of health expenditures, including costs borne by households and the health financing system, although it requires more complex and detailed data. This difference in approach is one of the main reasons why it is difficult to directly compare results across studies.

In addition to methodology, variations in analytical perspectives also contribute to differences in cost estimates. Studies using a societal perspective tend to yield higher cost estimates because they include all cost components, including indirect costs such as lost productivity and informal care. In contrast, provider and payer perspectives generally cover only direct medical costs. These findings underscore that the choice of perspective in economic evaluations significantly determines the magnitude of the resulting costs; therefore, the interpretation of results must take into account the context of the perspective used.

Table 1. A summary of the indicators of disease burden studied in selected articles (n = 13)

No	Researcher and Year	Research Setting	Country Group	Approach				Source of Data		Indicator of Calculated Disease Burden	
				Research Design	Calculation Method	Method	Cost Perspective				
1	Azahar, et al. (Azahar et al., 2022)	Malaysia	Upper-middle income	Retrospective	Cost of Illness (COI)	Cross-sectional	Provider	3,689 patients	stroke	Direct medical cost	
2	Canciu, et al. (Canciu et al., 2025)	Romania	High income	Retrospective	Cost of Illness (COI)	Monocentric	Provider	584 patients	stroke	Direct medical cost	
3	Dobe, et al. (Dobe et al., 2025)	Mozambique	Lower-Middle Income	Prospective	Cost of Illness (COI)	Cross-sectional	Societal	50 patients	stroke	Direct medical cost and direct non-medical cost	
4	Lv, et al. (Lv et al., 2023)	China	Upper-middle income	Retrospective	Health Expenditure (HE)	N/A	Societal	520 patients	stroke	Direct medical cost, direct non-medical cost, and indirect costs	
5	Ma, et al. (Ma et al., 2024b)	China	Upper-middle income	Retrospective	Health Expenditure (HE)	N/A	Payer	Estimated direct costs from sample data, the National Health Service Survey and the National Health Account and Health Statistical Yearbook. A human capital method was		Direct medical cost and direct non-medical cost	

No	Researcher and Year	Research Setting	Country Group	Approach				Source of Data		Indicator of Calculated Disease Burden	
				Research Design	Calculation Method	Method	Cost Perspective				
								used to conservatively estimate indirect costs			
6	Marques, <i>et al.</i> (Marques <i>et al.</i> , 2021)	Portugal	High income	Retrospective	Health Expenditure (HE)	Cross-sectional	Societal	31 patients	stroke	Indirect cost	
7	Mohammed, <i>et al.</i> (Mohammed <i>et al.</i> , 2025)	Malaysia	Upper-middle income	Retrospective	Cost of Illness (COI)	Cohort	Payer	122 patients	stroke	Direct medical cost	
8	Omari, <i>et al.</i> (Omari, Mohammed <i>et al.</i> , 2023)	Morocco	Lower-Middle Income	Retrospective	Cost of Illness (COI)	Cross-sectional	Societal	267 patients	stroke	Direct medical cost	
9	Santoso, <i>et al.</i> (Santoso <i>et al.</i> , 2024)	Indonesia	Upper-middle income	Retrospective	Cost of Illness (COI)	Cross-sectional	Payer	3,528 patients	stroke	Direct medical cost	
10	Su, <i>et al.</i> (Su <i>et al.</i> , 2022)	China	Upper-middle income	Retrospective	Cost of Illness (COI)	N/A	Provider	235 patients	stroke	Direct and indirect cost	
11	Tan, <i>et al.</i> (Tan <i>et al.</i> , 2022)	Australia	High income	Retrospective	Cost of Illness (COI)	Markov Model	Societal	Data from the Australian Institute of Health and Welfare (AIHW)		Direct medical cost, direct non-medical cost, and indirect costs	
No	Researcher and Year	Research Setting	Country Group	Approach				Source of Data		Indicator of Calculated Disease Burden	
				Research Design	Calculation Method	Method	Cost Perspective				
12	Vyas, <i>et al.</i> (Vyas <i>et al.</i> , 2023)	Canada	High income	Retrospective	Cost of Illness (COI)	Cohort	Payer	185,271 patients	stroke	Direct medical cost	
13	Zhu, <i>et al.</i> (Zhu <i>et al.</i> , 2022)	China	Upper-middle income	Retrospective	Cost of Illness (COI)	N/A	Payer	371,891		Direct medical cost	

Table 2. Descriptions of length of hospitalization for stroke patients

No	Research Cited	Factors that influence costs
1	Azahar, <i>et al.</i> (Azahar <i>et al.</i> , 2022)	Stroke type (AF versus non-AF stroke) ($p = 0.013$), stroke severity ($p = 0.010$) and discharge status ($p < 0.001$) significantly influenced stroke costs.
2	Canciu, <i>et al.</i> (Canciu <i>et al.</i> , 2025)	Higher mRS disability scores ($p < 0.001$).
3	Dobe, <i>et al.</i> (Dobe <i>et al.</i> , 2025)	N/A
4	Lv, <i>et al.</i> (Lv <i>et al.</i> , 2023)	Higher admission NIHSS scores were independently associated with higher direct medical costs, indirect costs and total cost
5	Ma, <i>et al.</i> (Ma <i>et al.</i> , 2024b)	N/A
6	Marques, <i>et al.</i> (Marques <i>et al.</i> , 2021)	N/A
7	Mohammed, <i>et al.</i> (Mohammed <i>et al.</i> , 2025)	Stroke subtypes, length of stay, risk factors, and functional status
8	Omari, <i>et al.</i> (Omari, Mohammed <i>et al.</i> , 2023)	Age, National Institutes of Health Stroke Scale (NIHSS) score, and length of hospitalization
9	Santoso, <i>et al.</i> (Santoso <i>et al.</i> , 2024)	Length of Hospital Stay (LOHS)
10	Su, <i>et al.</i> (Su <i>et al.</i> , 2022)	N/A
11	Tan, <i>et al.</i> (Tan <i>et al.</i> , 2022)	N/A
12	Vyas, <i>et al.</i> (Vyas <i>et al.</i> , 2023)	Immigrants, younger patients, and residents of low-income neighborhoods
13	Zhu, <i>et al.</i> (Zhu <i>et al.</i> , 2022)	N/A

Table 2 shows that, based on the 13 studies analyzed, some studies identified factors influencing the magnitude of stroke care costs, although not all studies reported specific analyses of cost determinants. Several clinical variables were consistently reported to have a significant association with increased costs. Stroke type, particularly the comparison between strokes with atrial fibrillation (AF) and non-AF, stroke severity, and discharge status were found to significantly influence cost ($p < 0.05$) (Azahar et al., 2022). In addition, a higher disability score based on the modified Rankin Scale (mRS) was significantly associated with increased hospitalization costs ($p < 0.001$) (Canciu et al., 2025).

Other clinical severity indicators, such as the National Institutes of Health Stroke Scale (NIHSS) score at hospital admission, have also been reported to be independently associated with increased direct medical costs, indirect costs, and total costs (Lv et al., 2023). This suggests that the more severe a patient's clinical condition at admission, the greater the resulting financial burden. In addition to severity, stroke subtype, length of hospital stay, risk factors, and the patient's functional status also contribute to cost variations in several studies (18–20).

In addition to clinical factors, several studies have also identified sociodemographic determinants, such as age (Omari, Mohammed et al., 2023), immigrant status (23), and residence in low-income areas (Vyas et al., 2023), that are associated with variations in stroke costs. However, more than half of the studies did not report a detailed analysis of the factors influencing costs (Dobe et al., 2025; Ma et al., 2024b; Marques et al., 2021; Su et al., 2022; Tan et al., 2022; Zhu et al., 2022). These findings suggest that clinical severity, length of hospital stay, and sociodemographic factors contribute to the magnitude of the economic burden associated with stroke treatment.

This review identifies clinical severity as a key determinant of stroke treatment costs. Indicators such as the NIHSS score at admission and the mRS disability score are consistently associated with increased costs. These findings suggest that patients with more severe clinical conditions require greater healthcare resources, whether in the form of medical interventions, medication use, or long-term rehabilitation. Additionally, other factors such as stroke subtype, length of hospital stay, and the patient's functional status also contribute to cost variations. This aligns with the concept that the economic burden of chronic diseases is heavily influenced by the complexity of the patient's clinical condition (Bloom et al., 2020).

The results of this review also indicate that direct medical costs are a major component in nearly all studies. This component is primarily dominated by inpatient costs, which are closely linked to Length Of Stay (LOS). Although not all studies report LOS in detail, several studies suggest that the longer a patient is hospitalized, the higher the costs incurred. This can be explained by the fact that extended hospital stays are usually associated with higher severity, complications, and the need for more complex medical interventions. Thus, the efficiency of hospital services, including LOS management, is a critical factor in stroke cost containment (Lu et al., 2025).

In addition to clinical factors, several sociodemographic determinants such as age, socioeconomic status, and geographic location also contribute to variations in costs. Patients living in areas with limited resources or low incomes tend to have different access to healthcare services, which can ultimately influence financing patterns and total costs incurred (Feigin et al., 2025). However, not all studies include these variables in their analyses, so there remain limitations in comprehensively understanding the non-clinical factors that influence stroke costs.

Table 3. Results of cost conversion due to stroke

No	Author	Country	Method	Calculated Indicator	Result					
					Direct Medical Cost		Direct non-medical cost		Indirect Cost	
					Research Result	USD in 2026	Research Result	USD in 2026	Research Result	USD in 2026
1	Azahar, <i>et al.</i> (Azahar et al., 2022)	Malaysia	Cost of illness (COI)	Direct medical cost	MYR 2.269,79 (2018)	739,63	N/A	N/A	N/A	N/A
2	Canciu, <i>et al.</i> (Canciu et al., 2025)	Romania	Cost of illness (COI)	Direct medical cost	RON 5295.33 thousand (2024)	1.301,54	N/A	N/A	N/A	N/A
3	Dobe, <i>et al.</i> (Dobe et al., 2025)	Mozambique	Cost of illness (COI)	Direct medical cost and direct non-medical cost	\$721.45 (2019)	887,29	\$13,62	16,75	N/A	N/A
4	Lv, <i>et al.</i> (Lv et al., 2023)	China	Health Expenditure (HE)	Direct medical cost, direct non-medical cost, and indirect costs per year	26.612,67 CNY (2018)	4915,8	2.787,56 CNY	514,86	28.167,25 CNY	5202,5
5	Ma, <i>et al.</i> (Ma et al., 2024b)	China	Health Expenditure (HE)	Direct medical cost and indirect cost	\$58.6 billion (2018)	74,23 billion	N/A	N/A	\$166.5 billion (2018)	210,91 billion
6	Marques, <i>et al.</i> (Marques et al., 2021)	Portugal	Health Expenditure (HE)	Indirect cost	N/A	N/A	N/A	N/A	€8726 (2017)	13435,97
7	Mohammed, <i>et al.</i> (Mohammed et al., 2025)	Malaysia	Cost of illness (COI)	Direct medical cost	MYR 1.970,7 (2020)	605,3	N/A	N/A	N/A	N/A
8	Omari, <i>et al.</i> (Omari, Mohammed et al., 2023)	Morocco	Cost of illness (COI)	Direct medical cost	\$3674,32 per patient per year (2019)	4518,95	N/A	N/A	N/A	N/A
9	Santoso, <i>et al.</i> (Santoso et al., 2024)	Indonesia	Cost of illness (COI)	Direct medical cost	Rp 8,487,531 per person (2022)	569,23	N/A	N/A	N/A	N/A
10	Su, <i>et al.</i> (Su et al., 2022)	China	Cost of illness (COI)	Direct medical cost	\$1020 for ischemic stroke and 2813	1217,93 for ischemic	N/A	N/A	N/A	N/A

No	Author	Country	Method	Calculated Indicator	Result					
					Direct Medical Cost		Direct non-medical cost		Indirect Cost	
					Research Result	USD in 2026	Research Result	USD in 2026	Research Result	USD in 2026
					for hemorrhagic stroke (2020)	stroke and 3358,86 for hemorrhagic stroke				
11	Tan, <i>et al.</i> (Tan et al., 2022)	Australia	Cost of illness (COI)	Direct medical cost	\$149,180 (2022)	167903,4	N/A	N/A	N/A	N/A
12	Vyas, <i>et al.</i> (Vyas et al., 2023)	Canada	Cost of illness (COI)	Direct medical cost	Canadian dollars 33 522 per year (2018)	31055,05	N/A	N/A	N/A	N/A
13	Zhu, <i>et al.</i> (Zhu et al., 2022)	China	Cost of illness (COI)	Direct medical cost	RMB 10.637 per year (2016)	2084,3	RMB3. 093 per year (2016)	606,07	N/A	N/A

Table 3 presents the results of the conversion of stroke-related costs from each study, adjusted to 2026 USD values to enhance comparability across countries. In general, most studies reported direct medical costs as the primary component of the economic burden of stroke, while only a few studies also accounted for direct non-medical costs and indirect costs. Of the 13 articles, 3 analyzed the economic burden of stroke based on health expenditures (Lv et al., 2023; Ma et al., 2024b; Marques et al., 2021), while the remaining 10 analyzed the economic burden of stroke based on disease costs (Azahar et al., 2022; Canciu et al., 2025; Dobe et al., 2025; Mohammed et al., 2025; Omari, Mohammed et al., 2023; Santoso et al., 2024; Su et al., 2022; Tan et al., 2022; Vyas et al., 2023; Zhu et al., 2022).

The Cost-Of-Illness (COI) method is relatively easy to apply, but it has limitations because it fails to capture the loss of utility resulting from a disease (Gochi et al., 2018). In contrast, the HEALTH EXPENDITURE (HE) method can capture total health expenditures, which reflect all costs incurred for health care services and related activities, such as insurance administration. Nevertheless, the HE method requires more detailed and specific data, particularly regarding household expenditures and indirect cost components (Persson et al., 2017).

COI studies aim to estimate the economic burden caused by a disease in a specific population (Forsyth & Hogendoorn, 2022). Generally, this approach encompasses two main components: direct costs and indirect costs. Direct costs represent the value of resources used in the treatment and rehabilitation of patients with the condition under study. This component includes all goods, services, and resources consumed during the implementation of health interventions, such as hospitalization costs, medical services, medications, medical equipment, and rehabilitation services (İçağasıoğlu et al., 2017).

Meanwhile, HE studies are used to calculate the total expenditures incurred as a result of a disease. In this systematic review, seven articles employing the HE method primarily focused on direct non-medical costs and indirect costs, including the costs of informal

caregivers and lost productivity. Informal caregivers are defined as individuals, typically family members, who provide care either with or without compensation. This care includes assistance with activities of daily living and instrumental activities of daily living (Joo et al., 2017). Costs associated with caregivers include time spent traveling to visit patients and various other expenses incurred during the care process (Martín-gutiérrez et al., 2026).

Direct costs are the value of the resources used for the treatment and rehabilitation of people with the condition under study. Direct costs refer to all goods, services, and other resources consumed during the provision of health interventions for a specific disease. This includes money spent on hospital care, services provided by doctors and other medical professionals, medications, equipment, and rehabilitation. Direct medical costs per patient vary significantly across countries. In upper-middle-income countries such as Malaysia (Azahar et al., 2022; Mohammed et al., 2025) and Indonesia (Santoso et al., 2024), estimated direct medical costs per patient after conversion range from USD 569.23 to USD 739.63. In Morocco (Omari, Mohammed et al., 2023), direct medical costs are reported at USD 4,518.95 per patient per year, while in China (Lv et al., 2023; Ma et al., 2024b; Su et al., 2022; Zhu et al., 2022) the range is quite wide, ranging from approximately USD 1,217.93 for ischemic stroke to USD 4,915.80 per year in another study. High-income countries show relatively higher estimates, such as Canada (Vyas et al., 2023) with costs of approximately USD 31,055.05 per patient per year and Australia (Tan et al., 2022) at USD 167,903.4, reflecting differences in healthcare system structures and medical service prices between countries.

In addition to direct medical costs, only a small fraction of studies report direct non-medical costs, such as transportation costs or informal care, which are relatively smaller in magnitude compared to direct medical costs. These results indicate substantial heterogeneity in stroke cost estimates across countries, both in terms of nominal amounts and the cost components calculated. This variation is likely influenced by differences in analytical perspectives, calculation methods, the scope of cost components, and the characteristics of each country's health financing system.

The variation in costs across countries in this review is striking. High-income countries show significantly higher estimated costs compared to middle-income countries. This difference reflects not only variations in the prices of health services but also differences in financing systems, the availability of medical technology, and service standards (Strlicuc et al., 2021). Furthermore, converting costs into a common currency, even when adjusted, remains limited because it cannot fully account for differences in purchasing power and the economic structures of each country. Therefore, cross-country comparisons must be made with caution (Lorenzoni, 2022).

Another key finding is that indirect costs, particularly those related to lost productivity and premature death, can contribute significantly to the total economic burden of stroke. In fact, in some population-based studies, indirect costs exceed direct medical costs (Girotra et al., 2020). This underscores that the impact of stroke is not limited to the healthcare system but also has far-reaching effects on the social and economic aspects of society. Unfortunately, not all studies include these components, so it is highly likely that estimates of the economic burden of stroke remain underestimated (Ma et al., 2024a). Additionally, direct non-medical costs such as transportation and informal care have not been reported in detail. In fact, informal care provided by families is a crucial component, particularly in developing countries with limited access to formal rehabilitation facilities. The lack of reporting on these cost components indicates a gap in the comprehensive measurement of the economic burden of stroke.

This review also has several limitations. First, the heterogeneity of methods, perspectives, and cost components across studies complicates the process of synthesizing and comparing results. Second, some studies did not report in detail the analytical methods or cost determinants, thereby limiting further interpretation. Third, differences in the years of data

collection and cost conversion methods may affect the accuracy of comparisons across studies. Finally, the absence of utility-based outcome measures such as QALYs or DALYs in the analyzed studies indicates that the burden of stroke has not been comprehensively evaluated from a quality-of-life perspective.

CONCLUSION

This systematic review shows that the economic burden of stroke is substantial and varies across countries, methods, and analytical perspectives. Most studies use the Cost of Illness (COI) approach because it is more practical, although it does not fully capture the full economic impact, such as loss of utility, whereas the Health Expenditure (HE) approach is more comprehensive but requires more complex data. Direct medical costs, particularly inpatient care, are the primary component influenced by clinical severity, length of hospital stay, and sociodemographic factors. High-income countries tend to have higher cost estimates compared to middle-income countries, reflecting differences in healthcare systems and service prices. Additionally, indirect costs such as lost productivity contribute significantly to the total economic burden, yet are often not fully accounted for.

COMPETING INTEREST

The authors declare no conflict of interest.

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