BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

BMJ Open

Estimation and Predictors of Hospitalization Expenses and in-hospital Mortality for Stroke Patients in a Low-Middle Income Country: Evidence from a Nationwide Study in Iranian Hospitals

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-067573
Article Type:	Original research
Date Submitted by the Author:	30-Aug-2022
Complete List of Authors:	Kazemi, Zohreh; Tehran University of Medical Sciences, Department of Health Management and Economics; National Center for Health Insurance Research Emamgholipour, Sara; Tehran University of Medical Sciences, Department of Health Management and Economics Daroudi, Rajabali ; Tehran University of Medical Sciences, Department of Health Management and Economics; National Center for Health Insurance Research Ghorbani, Askar ; Tehran University of Medical Sciences School of Medicine, Department of Neurology Yunesian, Masud; Tehran University of Medical Sciences, Department of Environmental Health Engineering; TUMS, Department of Research Methodology and Data Analysis Hassanvand, Mohammad Sadegh; Tehran University of Medical Sciences, Department of Environmental Health Engineering; Tehran University of Medical Sciences Shahali , Zahra ; National Center for Health Insurance Research
Keywords:	HEALTH ECONOMICS, Stroke < NEUROLOGY, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, EPIDEMIOLOGY

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Title: Estimation and Predictors of Hospitalization Expenses and in-hospital Mortality for Stroke Patients in a Low-Middle Income Country: Evidence from a Nationwide Study in Iranian Hospitals

Author names: Zohreh Kazemi[1,8], Sara Emamgholipour Sefiddashti*[2], Rajabali Daroudi[3,8], Askar Ghorbani[4], Masud Yunesian[5,6], Mohammad Sadegh Hassanvand[5,7], Zahra Shahali[8]

Author affiliations:

[1] PhD Student of Health Economics, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran;

[2] Professor of Health Economics, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran;

[3] Associate Professor of Health Economics, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran;

[4] Associate Professor of Stroke and Cerebrovascular Disorders, Neurointerventionist Shariati Hospital, Department of Neurology, School of Medicine Tehran University of Medical Sciences;

[5] Department of Environmental Health Engineering, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran;

[6] Professor of Epidemiology, Department of Research Methodology and Data Analysis, Institute for Environmental Research, TUMS;

[7] Associate Professor Center for Air Pollution Research, Institute for Environmental Research, Tehran University of Medical Sciences, Tehran, Iran;

[8] National Center for Health Insurance Research (Iran Health Insurance Organization)

***Corresponding author:** Sara Emamgholipour Sefiddashti, Professor of Health Economics, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. Email: s-emamgholipour@tums.ac.ir

Contact information:

- Zohreh Kazemi: zohkazemi2020@gmail.com; 09151641747
- Dr. Sara Emamgholipour Sefiddashti: s-emamgholipour@tums.ac.ir; 09124799674
- Dr. Rajabali Daroudi: rdaroudi@sina.tums.ac.ir; 09158088846
- Dr. Askar Ghorbani: aghorbani@razi.tums.ac.ir; 09120224119
- Dr. Masud Yunesian: yunesian@tums.ac.ir; 09122019571
- Dr. Mohammad Sadegh Hassanvand: hassanvand@tums.ac.ir; 09127305125
- Zahra Shahali: z.shahali3000@ihio.gov.ir; 09127179169, 09914020661

Keywords: Hospital, Hospitalization Expenses, Mortality, Stroke, Generalized Linear Models, Logistic Regression.

Word count: The submitted manuscripts include 4797 words excluding the title page, abstract, references, tables, and acknowledgments. If the number of words is reduced to 4,000 words, some important results may be lost. We thus request that this limit be waived.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Estimation and Predictors of Direct Hospitalization Expenses and in-hospital Mortality for Stroke Patients in a Low-Middle Income Country: Evidence from a Nationwide Study in Iranian Hospitals

Abstract

Objective: Stroke is the second most prevalent cardiovascular disease in Iran. The present study investigates the estimation and predictors of hospitalization expenses and in-hospital mortality for stroke patients in Iranian hospitals.

Setting: Stroke patients in Iran between 2019–2020 were identified, through the data collected from the Iran Health Insurance Organization and the Ministry of Health and Medical Education. This study is the first to conduct a pervasive, nationwide investigation.

Design: This is a cross-sectional, prevalence-based study. Generalized linear models and a multiple logistic regression model were used to determine the predictors of hospitalization expenses and in-hospital mortality for stroke patients.

Participants: A total of 19,150 patients suffering from stroke were studied.

Results: Mean hospitalization expenses per stroke patient in Iran amounted to $590.91 ± 974.44 (mean ± SD). Mean daily hospitalization expenses per stroke patient were $55.18 ± 37.89. The in-hospital mortality for stroke patients was 18.80%. Younger people (aged <=49 years) had significantly higher expenses than older patients. The in-hospital mortality odds ratio was significantly 1.539 times (95% CI, 1.401—1.691) higher in hemorrhagic stroke compared to ischemic and unspecified strokes. Patients under the Iranian Fund health insurance coverage had significantly 1.14 times (95% CI, 1.097—1.186) higher expenses and 1.319 times (95% CI, 1.099—1.582) higher mortality compared to those under the Rural Fund coverage. The in-hospital mortality odds ratio was significantly 1.539 times (95% CI, 1.401—1.691) higher in hemorrhagic stroke compared to ischemic and unspecified strokes. There were also significant geographic variations in expenses and mortality rates of stroke patients.

Conclusion: Applying cost-effective stroke prevention strategies among the younger population (<= 49 years old) is strongly recommended. Migration to universal health insurance can be an effective step in reducing the inequality gap among all insured patients.

Keywords: Hospital, Hospitalization Expenses, Mortality, Stroke, Generalized Linear Models, Logistic Regression.

Strengths and limitations of this study

- Nationally representative samples were used to generate nationwide estimates.
- Outcome determinants are presented in the form of average cost ratio and odds ratio (OR) for comparability and usability by policy makers worldwide.
- This study is limited by the absence of stroke comorbidities and severity data.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Introduction

Cardiovascular disease (CVD) is a non-communicable disease, frequently identified as a leading cause of premature death and increased health care expenses (1, 2). In general, CVD incidences and mortality rates vary across regions because of such factors as appropriate and adequate health care accessibility, dietary habits, lifestyle, etc. For instance, less educated patients in low and middle-income countries (LMICs) suffer higher rates of CVD incidence and mortality (3, 4).

Patients from LMICs, mostly in the Eastern Mediterranean Region (EMR), suffer 50% of all CVD mortalities and bear 80% of global CVD burden. CVD has been a progressive, epidemic problem during the recent years (5, 6). Iran suffers the highest CVD burden in the EMR (6, 7), as CVDs account for the third most important contributor to the burden of disease in Iran (8).

Stroke is the primary cause of cardiovascular disease. Globally, stroke is the second most common cause of mortality, and the stroke burden in terms of disability-adjusted life years (DALYs) is increasing. Between 1990 to 2019, the total number of prevalent cases, deaths, and disability adjusted life years (DALYs) because of stroke has increased steadily, reaching 101 million (85.3% increase), 6.55 million (43.3% increase), and 143 million (32.4% increase) respectively by 2019. The global increases in stroke burden can been largely attributed to population growth and aging (9).

Likewise, LMICs bear the majority of the CVD burden. Not only is stroke more prevalent in LMICs, but it also poses a larger risk of mortality, disability, and recurrence (10-12). Stroke is the second most prevalent type of CVD in Iran; more prevalent than in western countries (6).

Stroke complications are not limited to physical and psychological effects on the patient, as they also affect the patient's family and the society economically (13). Despite resources spent on its treatment, the cost component of stroke, as well as the difference in expenses based on patient characteristics and health care providers, remain unclear. Most LMICs do not have a comprehensive disease registration system or accurate financial records, the absence of which impede disease-specific expense analysis (14). The numerous studies conducted on the expenses and burden of diseases in Iran have been limited to datasets from one or a few local hospitals. This study is the first to conduct a nationwide investigation, because for the first time, Iran Health Insurance Organization (IHIO) has provided access to nationwide data.

Objectives

Increasing social expectations and scarcity of resources have made resource prioritization necessary to meet health care needs (13). A Stroke affects not only the survivors' physical, psychological and social well-being but also their financial aspects of their lives. Therefore, identifying the components and determinants of hospitalization expenses is essential for the further development of socio-economic intervention strategies targeting stroke survivors (15).

Analysis of hospitalization expenses provides valuable information on such various healthcare decision-making processes as planning, prioritizing, and allocating resources; economic evaluation of health interventions; evaluation of funding distribution inefficiencies; as well as identification of cost reduction opportunities for policymakers, insurance organizations, and health care providers (14, 16, 17). Therefore, this study aims to identify: (1) hospitalization expenses of strokes in Iran and their components; (2) predictors of stroke hospitalization expenses in Iran; and (3) predictors of in-hospital mortality in Iran.

For peer review only

Methods

Study design and setting

A prevalence-based, cross-sectional survey was conducted on the population of the people covered by the IHIO. There are three types of basic health insurance in Iran. IHIO covers more than half of the Iranian population. This organization maintains a database that gathers patient files (containing diagnosis and treatment data), as well as financial records from Iranian hospital information systems (HIS). For this study, IHIO database was queried, extracting data for the period between 23 August 2019 and 21 June 2020.

A healthcare system perspective with a bottom-up (micro-costing) approach was used to determine hospitalization expenses of stroke patients, in which patient-specific data were collected based on their utilization of valuated hospital services (18).

Data, participants, and eligibility criteria

Hospitalized cerebrovascular patients with the ICD-10 diagnosis code I60–I64 were included in the study and their afflictions were classified as hemorrhagic strokes (ICD-10: I60–I62), ischemic strokes (ICD-10: I63), or unspecified strokes (ICD-10: I64). Ischemic and unspecified strokes were combined, in accordance with a neurologist's opinion, that some physicians may have used the unspecified code for ischemic stroke cases.

A predesigned, structured, case report form (CRF) was used to collect data from medical records on patient demographics (14 items); cost components, and resource consumption (55 items); disease and patient hospitalization processes (36 items); and hospital characteristics (7 items). Patient data were obtained from IHIO information records extracted by experts at the Iranian National Center for Health Insurance Research (NCHIR), while information about hospitals was obtained from the accreditation sources of the hospitals of the Ministry of Health and Medical Education (MHME). The two datasets were combined and cost components, were summarized and categorized into eight groups: Medical examination and consultation, accommodation and nursing, laboratory tests, medical imaging, medicine and medical materials, rehabilitation, surgery, and medical interventions.

The present study was carried out via a complete enumeration method, also known as census. This is thus a pervasive study, encompassing all hospitalized stroke patients under IHIO coverage at the affiliated hospitals across Iran. Herein 30,615 medical records were reviewed, of which 11,465 cases were excluded because they did not meet the required criteria elaborated below, leaving this study with 19,150 records to analyze. The participants were not directly involved in this study. The study population was limited to the unidentified records in the IHIO database.

Grounds for elimination include: (1) Persistent and temporary emergency room patients, as they were not considered hospitalized (2) Patients with a LoS of one and two days were excluded because according to the neurologist's opinion, Suspected cases of stroke should be excluded, and only confirmed cases of stroke should be included in the study. (4) Medical records lacking critical data such as LoS, and medical records of newly established hospitals that MHME had not accredited at the time.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Variables

Hospitalization expenses and in-hospital mortality were the two outcome variables studied in this research. Hospitalization expenses are the direct expenses incurred by stroke patient during their hospitalization period. Hospitalization expenses were recorded in Iranian rials (IRR) before being converted to and expressed in United States dollars (USD) for comparability purposes (1 USD = 149,000 Rials, as of 19 March 2020). The second outcome variable, in-hospital mortality, is an important index in measuring clinical quality (19). It is used in this study to evaluate the health outcome of patients.

Independent predictor variables in this study include age, gender, marital status, the insurance fund covering the patient, province of residence, Lengths of stay in intensive care unit (ICU LoS), LoS in other ward for patients without injury or critical conditions, stroke subtype, surgery reception, outcome of hospitalization, hospital accreditation grade, hospital ownership, and hospital size.

Hospital accreditation is a 'systematic, external evaluation of a hospital's structure, processes and outcomes by an independent, professional, accreditation body, using published optimum, evidence-based and achievable standards' (20). MHME defines different tariffs depending on the hospital accreditation grade, such that grade 1 hospitals have higher tariffs and thus charge their patients more (21).

In terms of ownership, there are four groups of Iranian hospitals: governmental, private sector, social security, and special (military, charity, and other organizations). While their tariffs depends on their accreditation grade, governmental hospitals have subsidized tariffs while private sector hospitals are more expensive (22). Social security and special hospitals have a mixture of the two tariff levels.

Statistical analysis

All collected data were imported into Microsoft Excel spreadsheet CRFs, where randomly selected entries were double-checked for accuracy and consistency. The data were then cleaned-up for export into Stata version 14.1, (Stata Corp, College Station, TX, USA) for statistical analysis.

Cost distributions reported in this study possess a positive, intense skewness and are non-negative. This is in concordance with commonly reported observations in previous health datasets. Generalized linear models (GLM) with gamma family distribution and the log link function was used to determine the predictors for hospitalization expenses of stroke patients.

The dependent variable of in-hospital mortality was a binary parameter expressed as either zero or one. Thus, to investigate determinants of in-hospital mortality, multiple logistic regression (LR) was used to model potential predictors.

Skewness and Kurtosis normality tests were used to check for normality of continuous data. Descriptive statistics were used to summarize expenses, patient demographics, disease, hospitalization process, and hospital characteristics. Categorical variables were summarized as count and percentage, while continuous variables were presented as mean with standard deviation (SD), or median with lower and upper quadrille, (i.e., 25th and 75th percentiles). To estimate daily hospitalization expenses, total expenses, and cost components (each of our eight cost groups), both means and medians for central tendency, SD with 25th and 75th percentiles (upper and lower quadrilles) for variability and dispersion were reported, yielding a comprehensive sense of cost distribution data. Hospitalization expenses refers to the sum of all medical and nonmedical expenses incurred upon stroke patients during hospitalization (19).

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

The GLM with gamma distribution has been shown to closely predict mean expenses, as well as total hospitalization expenses More so, the log link function has the advantage of guaranteeing non-negative outcomes while maintaining the original scale of the data, as opposed to the log transformation(16, 23).

The Box-Cox approach was used to find the appropriate functional form and the linkage function, while the modified Park test was used to select the distribution family. In addition, non-nested selections from six different patterns of gamma, Gaussian, and Poisson distribution families with log and the second root linkage functions were iterated 40 times, and their Akaike and Bayesian criteria were compared. The log link and gamma family distributions had the smallest Akaike and Bayesian criteria, which confirms the decency of the fitting model. P-values less than 0.05 were considered statistically significant. Multivariate analysis was used to eliminate the effect of confounders.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Results

A total of 19,150 stroke patients were included in the study, of which 14,234 (74.33%; mean age: 71±15; gender: 51.5% male) had suffered from an ischemic and unspecified stroke (I&US) and 4,916 (25.67%; mean age: 64±18; gender: 54.5% male) had endured a hemorrhagic stroke (HS). Table 1 displays the demographic and hospitalization characteristics of the studied population.

The mean LoS was 8.62 ± 11.7 days (mean ± SD) for I&US, 12.33 ± 14.48 days for HS, and 9.57 ± 12.62 days overall. The mean ICU LoS and other ward LoS were 3.87 ± 10.43 days and 5.70 ± 7.30 days respectively. The 30-day in-hospital case-fatality ratio was 13.38% (1,824 / 13,637) for IS patients, 29.33% (1,320 / 4,501) for HS patients, and 17.33% (3,144 / 18,138) overall.

***Table 1**: Demographic and hospitalization characteristics of the studied population*

Characteristics	Ischemic & unspecified n=14,234 (Proportion=74.33%)	Hemorrhagic stroke n=4,916 (Proportion =25.67%)	Total n=19,150, (Proportion =100%)
Age, years, mean ± SD (min-max)	71 ± 15(1-119)	64±18(1–106)	69±16(1–119)
Gender			
Male	7,330(51.50)	2,679(54.50)	10,009(52.27)
Female	6,904(48.50)	2,237(47.50)	9,141(47.73)
Marital status			
Married	5,470(38.43)	1,899(38.63)	7,369(38.48)
Single	8,659(60.83)	2,986(60.74)	11,645(60.81)
Unspecified	105(0.74)	31(0.63)	136(0.71)
Health insurance coverage			
Rural Fund	6,472(45.47)	2,234(45.44)	8,706(45.46)
Others	1,230(8.64)	376(7.65)	1,606(8.39)
Civil Servants Fund	2,835(19.91)	885(18.00)	3,720(19.42)
Iranian Fund	687(4.83)	343(6.98)	1,030(5.38)
Universal health insurance	1,933(13.58)	776(15.79)	2,709(14.15)
Imam Khomeini Relief Committee	1,077(7.57)	302(6.14)	1,379(7.20)
Other ward LoS (mean ± SD)	5.72±6.99	5.64±8.13	5.70±7.30
ICU LoS (mean ± SD)	2.90±9.45	6.68±12.44	3.87±10.43
Total LoS (mean ± SD)	8.62±11.76	12.33±14.48	9.57±12.62
Hospital accreditation grade			
Grade 1	13,223(93.50)	4,677(95.96)	17,900(94.12)
Grade 2	836(5.91)	173(3.55)	1,009(5.31)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Grade 3&4	84(0.59)	24(0.49)	108(0.57)
Hospital ownership			
Governmental	14,021(98.50)	4866(98.98)	18887(98.63)
Private	69(0.48)	24(0.49)	93(0.49)
Military, charity, other organizations	123(0.86)	22(0.45)	145(0.76)
Social security	21(0.15)	4(0.80)	25(0.13)
Hospital size			
<=100 Bed or S	713(5.04)	113(2.32)	826(4.35)
100–320 Bed or M	8,244(58.33)	2,523(51.75)	10,767(56.64)
320–600 Bed or L	3,210(22.71)	1,260(25.85)	4,470(23.52)
600–1000 Bed or XL	1,903(13.46)	976(20.02)	2,879(15.15)
>1000 Bed or HC	63(0.45)	3(0.06)	66(0.35)
Outcome of treatment			
Full recovery	4,199(29.50)	1,183(24.06)	5,382(28.10)
Partial recovery	6,977(49.02)	1,874(38.12)	8,851(46.22)
Death	2,122(14.91)	1,479(30.09)	3,601(18.80)
Discharge against medical advice	792(5.56)	254(5.17)	1,046(5.46)
Referral to another hospital	144(1.01)	126(2.56)	270(1.41)
Surgery reception			
Yes	2,486(17.47)	2,248(45.73)	4,734(24.72)
No	1,1748(82.53)	2,668(54.27)	14,416(75.28)
30-day hospital case-fatality rates	1,824(13.38)	1,320(29.33)	3,144(17.33)

Total and daily hospitalization expenses per stroke patient

Mean hospitalization expenses per stroke patient was $482.59 (SD ± $844.53) for I&US, $904.41 (SD ± $1,225.34) for HS, and $590.91 (SD ± $974.44) overall. Mean daily hospitalization expenses per stroke patient was $49.91 (SD ± $33.01) for I&US, $70.43 (SD ± $46.09) for HS, and $55.18 (SD ± $37.89) for stroke. HS patients had higher mean hospitalization expenses per patient, compared to I&US patients. This was also higher in all age groups for patients with HS than I&US. Supplementary table 1 illustrates total and daily hospitalization expenses, for stroke patients, stratified by LoS and stroke type. Supplementary table 2 displays hospitalization expenses for stroke patients, stratified by age, gender, and stroke type.

Table 2 presents the different hospitalization cost components for the stroke patients studied. Accommodation and nursing (55.11%) represent the main component of hospitalization expenses for stroke patients. Medicine and medical materials (17.16%), medical examination and consultation (11.72%), medical imaging services (6.76%), laboratory tests (4.23%), surgery (3.93%), and rehabilitation (0.81%) are the next components in severity. On the contrary, medical interventions (0.29%) represent the lowest proportion of hospitalization expenses per patient.

***Table 2**: Hospitalization expenses for stroke patients, stratified by resource utilization and stroke type*

Cost component	Ischemic & unspecified stroke	Hemorrhagic stroke	Total
Accommodation and nursing			
Mean(SD)	208.42(481.85)	410.61(637.50)	260.14(533.40)
Median(25^{th}–75^{th} percentile)	70.15(46.77–151.90)	175.37(76.71–460.87)	81.84(46.77–217.49)
Sum(% of total hospital costs)	3,808,553.87(53.61)	2,644,728.39(57.49)	6,450,576.38(55.10)
Medicine and medical materials			
Mean(SD)	65.83(153.89)	125.03(212.48)	80.98(172.74)
Median(25^{th}–75^{th} percentile)	17.63(7.92–54.95)	46.68(19.73–134.70)	22.85(9.33–74.23)
Sum(% of total hospital costs)	1,203,534.78(16.94)	805,978.98(17.53)	2,009,109.79(17.16)
Visit and consultation			
Mean(SD)	54.21(70.39)	60.20(75.90)	55.73(71.87)
Median(25^{th}–75^{th} percentile)	34.79(23.00–57.22)	38.09(21.85–69.30)	35.42(22.71–60.44)
Sum(% of total hospital costs)	987,736.96(13.90)	380,181.35(8.26)	1,371,848.09(11.72)
Medical imaging services			
Mean(SD)	32.46(30.24)	30.98(31.21)	32.08(30.50)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Median(25th–75th percentile)	26.06(16.35–39.34)	22.98(13.09–38.28)	25.39(15.40–39.08)
Sum(% of total hospital costs)	590,264.49(8.31)	197,880.09(4.30)	790,937.07(6.76)
Laboratory tests			
Mean(SD)	17.23(30.19)	28.07(41.96)	20.00(33.93)
Median(25th–75th percentile)	7.92(4.44–17.05)	13.65(5.98–32.80)	8.88(4.70–20.69)
Sum(% of total hospital costs)	314,328.42(4.42)	180,324.38(3.92)	495,004.43(4.23)
Surgery			
Mean(SD)	38.42(68.64)	114.77(122.33)	74.67(105.03)
Median(25th–75th percentile)	11.64(5.64–36.55)	85.14(18.29–166.21)	27.30(8.05–108.26)
Sum(% of total hospital costs)	122,959.70(1.73)	340,604.95(7.40)	459,610.82(3.93)
Rehabilitation			
Mean(SD)	10.75(26.38)	21.60(36.01)	13.84(29.85)
Median(25th–75th percentile)	4.01(2.41–8.63)	8.42(3.61–25.00)	4.81(2.41–12.34)
Sum(% of total hospital costs)	51,850.42(0.73)	42,513.29(0.92)	94,228.28(0.81)
Medical interventions			
Mean(SD)	11.41(18.25)	10.81(18.71)	11.26(18.37)
Median(25th–75th percentile)	8.03(4.86–11.14)	8.03(4.86–10.98)	8.03(4.86–11.03)
Sum(% of total hospital costs)	25,518.65(0.36)	8,259.71(0.18)	33,903.56(0.29)
Total hospital cost			
Mean(SD)	482.59(844.53)	904.41(1225.34)	590.91(974.44)
Median(25th–75th percentile)	214.62(137.94–436.62)	457.96(230.71–1031.14)	252.93(148.84–564.98)
Sum(% of total hospital costs)	7,104,747.29(60.70)	4,600,471.15(39.30)	11,705,218.44(100)

All prices are in United States dollars (USD)

Predictors of hospitalization expenses for stroke patients

Table 3 displays the predictors of hospitalization expenses for stroke patients in Iran. Independent predictor variables for the GLM model were age, gender, insurance funds, province of residence, ICU LoS, other ward LoS, stroke subtype, surgery reception, outcome of hospitalization, hospital accreditation grade, hospital ownership, and hospital size.

This study has found no significant differences in average expenses by gender, or between the reference group and patients covered by other insurance institutions. However, significant differences were observed between hospitalization expenses among various age groups, such that 0—49 years old patients had the highest average hospitalization expenses. The average hospitalization expenses for the 50—59, 60—69, 70—79, and over 80 years old patients were respectively 0.934, 0.930, 0.940, and 0.921 times smaller than that of the 0—49 years old patients. There was a significant difference between the average expenses for people under the Civil Servants Fund and the Iranians Fund insurance coverage, compared to the people covered by the Rural Fund; such that their average expenses were respectively 1.03 and 1.14 times higher than that of the Rural Fund reference group.

The average hospitalization expenses of Alborz, Fars, Kohkiluyeh and Boyer-Ahmad, Markazi, Sistan and Baluchestan, and Zanjan provinces showed no significant differences from that of the Tehran province (the reference group). The expenses in the Hamadan province were 1.075 times higher than Tehran. All other provinces had significantly lower hospitalization expenses than Tehran. The lowest average belongs to the Kermanshah province.

Both ICU and other ward LoS had a significant positive association with the average hospitalization expenses for stroke patients, such that LoS longer than 7 days were 3.098 times higher, compared to other ward LoS of 1–3 days, and 7.689 times higher than single-day ICU LoS.

No significant differences were observed in average hospitalization expenses between HS and I&US patients. However, mean hospitalization expenses of stroke patients who underwent surgery was significantly 1.602 times higher than the reference group, members of which had no surgery. However, significant differences of respectively 1.599 and 2.442 times higher average hospitalization expenses for

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

stroke patients were observed at special (military, charity, other organizations) and private hospitals, compared to public hospitals.

With the increase in size and number of hospital beds, the average hospitalization expenses for stroke patients were significantly raised above small hospitals (S), by 1.046 times in medium hospitals (M), 1.116 times in large hospitals (L), 1.176 times in very large hospitals (XL), and 1.347 times in hospital complexes (HC).

Analyzing hospitalization outcomes such as death, discharge against medical advice, and referral to another hospital, compared to full recovery (designated as a reference group) revealed significant differences in mean hospitalization expenses of stroke patients with such outcomes for patients. Therefore, their average hospitalization expenses were respectively 1.361, 1.108, and 1.278 times higher compared to the full recovery reference group.

Table 3: *Predictors of hospitalization expenses for stroke patients in Iran*

Variables		N	%	Coefficient	Lower	Upper	P-value
Age	<=49	2081	10.87	1			
	50–59	2496	13.03	0.934	0.903	0.967	0.000
	60–69	4440	23.19	0.935	0.903	0.968	0.000
	70–79	4510	23.55	0.940	0.912	0.970	0.000
	>=80	5623	29.36	0.921	0.934	0.950	0.000
Gender	Female	9,141	47.73	1			
	Male	10,009	52.27	1.016	0.049	1.000	1.034
Health insurance coverage	Rural Fund	8,706	45.46	1			
	Others	1,606	8.39	1.031	0.999	1.064	0.054
	Civil Servants Fund	3,720	19.43	1.033	1.009	1.057	0.006
	Iranian Fund	1,030	5.38	1.140	1.097	1.186	0.000
	Universal health insurance	2,709	14.15	0.987	0.962	1.013	0.332
	Imam Khomeini Relief Committee	1,379	7.20	0.978	0.946	1.011	0.193
Province	Tehran	788	4.11	1			
	Alborz	302	1.58	1.024	0.947	1.107	0.546
	Ardabil	436	2.28	0.806	0.751	0.865	0.000
	Bushehr	215	1.12	0.885	0.809	0.967	0.007
	East Azarbaijan	1,063	5.55	0.875	0.828	0.925	0.000
	Fars	1,768	9.23	0.957	0.909	1.008	0.094
	Qazvin	336	1.75	0.768	0.713	0.828	0.000
	Qom	335	1.75	0.836	0.775	0.902	0.000
	Gilan	676	3.53	0.751	0.704	0.802	0.000
	Golestan	619	3.23	0.770	0.723	0.820	0.000
	Hamadan	493	2.57	1.075	1.005	1.149	0.034
	Chaharmahal and Bakhtiari	295	1.54	0.865	0.799	0.937	0.000
	Hormozgan	412	2.15	0.804	0.749	0.864	0.000
	Ilam	163	0.85	0.780	0.703	0.865	0.000
	Isfahan	1,298	6.78	0.912	0.864	0.962	0.001
	Kerman	677	3.54	0.863	0.812	0.918	0.000
	Kermanshah	527	2.75	0.712	0.665	0.762	0.000
	Razavi Khorasan	1,806	9.43	0.768	0.729	0.809	0.000
	Khuzestan	1,143	5.97	0.832	0.788	0.880	0.000
	Kohkiluyeh and Boyer-Ahmad	187	0.98	0.987	0.899	1.084	0.793
	Kurdistan	438	2.29	0.889	0.830	0.953	0.001
	Lorestan	667	3.48	0.767	0.721	0.817	0.000
	Markazi	336	1.75	0.928	0.860	1.001	0.054
	Mazandaran	1,224	6.39	0.842	0.798	0.888	0.000
	North Khorasan	293	1.53	0.787	0.727	0.852	0.000
	Semnan	117	0.61	0.789	0.704	0.883	0.000

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

	Sistan and Baluchestan	571	2.98	0.971	0.911	1.036	0.378
	West Azerbaijan	969	5.06	0.862	0.814	0.912	0.000
	Yazd	235	1.23	0.852	0.781	0.930	0.000
	Zanjan	523	2.73	0.983	0.918	1.051	0.613
	South Khorasan	238	1.24	0.768	0.705	0.837	0.000
Other ward LoS	**0–3 Days**	7,688	40.33	1			
	4–5 Days	5,008	26.27	1.247	1.219	1.275	0.000
	6–7 Days	2,550	13.38	1.633	1.589	1.679	0.000
	> 7 Days	3,816	20.02	3.098	3.022	3.176	0.000
ICU LoS	**0–1 Days**	13,169	69.09	1			
	2–4 Days	1,952	10.24	2.016	1.957	2.077	0.000
	5–7 Days	1,213	6.36	3.072	2.962	3.187	0.000
	> 7 Days	2,728	14.31	7.689	7.471	7.915	0.000
Stroke type	**Ischemic & unspecified**	14,234	74.33	1			
	Hemorrhagic	4,916	25.67	1.015	0.994	1.036	0.151
Surgery	**No**	14,416	75.28	1			
	Yes	4,734	24.72	1.602	1.566	1.639	0.000
Hospital accreditation grade	**Grade 3&4**	108	0.57	1			
	Grade 1	17,900	94.12	0.968	0.863	1.086	0.580
	Grade 2	1,009	5.31	0.963	0.854	1.087	0.545
Hospital ownership	**Governmental**	18,887	98.62	1			
	Military, charity, other organizations	145	0.76	1.599	1.450	1.762	0.000
	Social security	25	0.13	1.134	0.903	1.425	0.279
	Private	93	0.49	2.442	2.145	2.780	0.000
Hospital size	**<=100 Bed (S)**	826	4.35	1			
	100–320 Bed (M)	10,767	56.64	1.046	1.000	1.093	0.048
	321–600 Bed (L)	4,470	23.51	1.116	1.063	1.172	0.000
	601–1000 Bed (XL)	2,879	15.15	1.176	1.116	1.239	0.000
	>1000 Bed (HC)	66	0.35	1.347	1.161	1.563	0.000
Outcome of hospitalization	**Full recovery**	5,382	28.10	1			
	Partial recovery	8,851	46.22	1.013	0.991	1.036	0.236
	Death	3,601	18.80	1.361	1.325	1.399	0.000
	Discharge against medical advice	1046	5.46	1.108	1.064	1.153	0.000
	Referral to another hospital	270	1.41	1.278	1.189	1.375	0.000

Predictors of in-hospital mortality for stroke patients

Table 4 presents predictors of in-hospital mortality for stroke patients. Independent predictor variables in the multiple logistic regression model include age, gender, marital status, insurance fund, province of residence, ICU LoS, other ward LoS, stroke subtype, surgery reception, hospital accreditation grade, and hospital ownership. Where the other variables were constant, the odds ratio (OR) of in-hospital mortality for 60–69, 70–79, and over 80 years old patients were 1.538, 2.119, and 3.233 times higher than the 0–49 years old patients, respectively. There were no significant differences in the chance of in-hospital mortality between men and women. But there was a significant difference between single and married patients. Thus, the chance of mortality for single patients was 1.332 times higher than for married patients. There was also a significant difference in hospital mortality rates of patients under Civil Servants Fund and Iranians Fund insurance coverage, compared to that of the patients covered by the Rural Fund insurance, such that their ORs were respectively 0.886 and 1.319 times higher.

The ORs of in-hospital mortality in Alborz (1.753), East Azerbaijan (1.965), Fars (1.329), Gilan (2.135), Golestan (1.651), Khorasan Razavi (1.451), Khuzestan (1.942), Sistan and Baluchestan (1.662) and Zanjan (1.415) were significantly higher than Tehran. The lowest and highest chances of mortality were

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

found in Fars and Gilan provinces, respectively. The ORs in Kermanshah and Kohkiluyeh Boyer-Ahmad provinces were 0.613 and 0.444 times lower than Tehran, respectively.

The in-hospital mortality OR for stroke patients with more than three days LoS in other ward was significantly lower than those in the reference group. This ratio was significantly higher for ICU patients, compared to the reference group, such that chances of in-hospital mortality in patients with a 2–4, 5–7, and over 7 days LoS, were 2.556, 4.206 and 4.629 times higher than that of the reference group, respectively.

At 2.616 times, the in-hospital mortality OR for stroke patients who received surgery was significantly different from patients who did not undergo surgery. At about 1.539 times, this ratio was significantly higher in HS compared to I&US.

There were no significant differences in hospital mortality OR for stroke patients across hospitals with different accreditation grades. At about 2.374 times, mortality OR was significantly higher in governmental hospitals, compared to private hospitals.

Table 4: *Predictors of in-hospital mortality for stroke patients in Iran*

Variables		Died (Person)	Discharged (Person)	Mortality (%)	OR	Lower	Upper	P-value
Age	<=49	302	1,779	14.51	1			
	50–59	311	2,185	12.46	1.0429	0.861	1.263	0.667
	60–69	722	3,718	16.26	1.538	1.301	1.818	0.000
	70–79	864	3,646	19.16	2.119	1.794	2.502	0.000
	>=80	1,402	4,221	24.93	3.233	2.751	3.800	0.000
Gender	Female	1,729	7,412	18.91	1			
	Male	1,872	8,137	18.70	0.988	0.909	1.074	0.776
Marital status	Married	1,157	6,212	11.16	1			
	Single	2,393	9,252	20.55	1.332	1.213	1.463	0.000
Insurance funds	Rural Fund	1,590	7,116	18.26	1			
	Others	319	1,287	19.86	1.074	0.920	1.253	0.365
	Civil Servants Fund	730	2,990	19.62	0.886	0.789	0.995	0.042
	Iranian Fund	249	781	24.17	1.319	1.099	1.582	0.003
	Universal health insurance	457	2,252	16.87	0.985	0.861	1.128	0.833
	Imam Khomeini Relief Committee	256	1,123	18.56	0.999	0.843	1.182	0.988
Province	Tehran	150	638	19.04	1			
	Alborz	67	235	22.19	1.753	1.290	2.542	0.003
	Ardabil	74	362	16.97	1.222	0.853	1.752	0.274
	Bushehr	43	172	20.00	1.270	0.820	1.968	0.285
	East Azarbaijan	249	814	23.42	1.965	1.507	2.561	0.000
	Fars	339	1429	19.17	1.329	1.037	1.704	0.025
	Qazvin	57	279	16.96	1.443	0.986	2.113	0.059
	Qom	66	269	19.70	1.333	0.916	1.940	0.133
	Gilan	151	525	22.34	2.135	1.572	2.900	0.000
	Golestan	146	473	23.59	1.651	1.223	2.228	0.001
	Hamadan	81	412	16.43	1.094	0.779	1.537	0.602
	Chaharmahal and Bakhtiari	41	254	13.90	0.756	0.495	1.156	0.197
	Hormozgan	75	337	18.20	1.078	0.756	1.537	0.679
	Ilam	19	144	11.66	0.717	0.387	1.328	0.290
	Isfahan	224	1074	17.26	0.929	0.712	1.211	0.586
	Kerman	135	542	19.94	1.220	0.901	1.653	0.199
	Kermanshah	71	456	13.47	0.613	0.433	0.868	0.006
	Razavi Khorasan	370	1436	20.49	1.451	1.133	1.857	0.003
	Khuzestan	234	909	20.47	1.942	1.482	2.544	0.000
	Kohgiluyeh and Boyer-Ahmad	17	170	9.09	0.444	0.241	0.819	0.009
	Kurdistan	69	369	15.75	0.774	0.542	1.107	0.161
	Lorestan	141	526	21.14	1.332	0.981	1.809	0.066
	Markazi	61	275	18.15	1.060	0.723	1.556	0.764

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

	Mazandaran	167	1057	13.64	0.834	0.629	1.104	0.205
	North Khorasan	65	228	22.18	1.425	0.973	2.088	0.069
	Semnan	22	95	18.80	0.705	0.404	1.230	0.218
	Sistan and Baluchestan	113	458	19.79	1.662	1.212	2.279	0.002
	West Azerbaijan	187	782	19.30	1.182	0.892	1.568	0.245
	Yazd	38	197	16.17	0.640	0.405	1.012	0.056
	Zanjan	88	435	16.83	1.415	1.011	1.981	0.043
	South Khorasan	41	197	17.23	0.923	0.599	1.420	0.714
Other ward LoS	**0~3 Days**	2,080	5,608	27.06	1			
	4~5 Days	477	4,531	9.52	0.526	0.465	0.594	0.000
	6~7 Days	267	2,283	10.47	0.515	0.443	0.600	0.000
	> 7 Days	761	3,055	19.94	0.823	0.736	0.921	0.001
ICU LoS	**0~1 Days**	1,289	11,880	9.79	1			
	2~4 Days	527	1,425	27.00	2.556	2.240	2.916	0.000
	5~7 Days	479	734	39.49	4.206	3.633	4.869	0.000
	>7 Days	1,290	1,438	47.29	4.629	4.127	5.193	0.000
Stroke type	**Ischemic & unspecified**	2,122	12,112	14.91	1			
	Hemorrhagic	1,479	3,437	30.09	1.539	1.401	1.691	0.000
Surgery	**No**	1,787	12,629	12.40	1			
	Yes	1,814	2,920	38.32	2.616	2.378	2.878	0.000
Hospital accreditation grade	**Grade 1**	3,353	14,547	18.73	1			
	Grade 2	191	818	18.93	0.865	0.709	1.055	0.151
	Grade 3&4	28	85	24.78	0.924	0.559	1.529	0.759
Hospital ownership	**Private**	11	82	11.83	1			
	Governmental	3,575	15,312	18.93	2.374	1.130	4.987	0.022
	Military, charity, other organizations	13	132	8.97	1.399	0.535	3.656	0.494
	Social security	2	23	8.00	0.740	0.135	4.065	0.729

Discussion

This study found mean hospitalization expenses per stroke patient in Iran ($590.91) to be lower than Philippines ($781.42) and China ($2,008); the former is an Asian LMIC while the latter is a developed country (17, 24). A root cause of this difference is the lower prevalence of traditional medical technologies in Iran compared to modern, expensive ones (25). Furthermore, the difference in mean expenses is likely because of the differences in standards of care, payment systems, modern medical technologies and services, sanctions against Iran, and the steep fall in the value of Iranian Rial, the national currency. In Iran, public hospitals are subsidized by the state; rendering their therapy costs lower than the actual cost of services. As such, these prices don't reflect the true value of their services.

Estimates for the hospitalization expenses of stroke patients demonstrate that average expenses per HS patient were higher than I&US patients. Moreover, obtaining overall estimates regarding hospitals revealed more than half of the hospitalization expenses of stroke patients (60%) to be related to IS. These findings are consistent with similar, relevant studies (16, 24, 26). Patients suffering HS have a longer average other ward LoS compared to other ward I&US patients (12.33 ± 14.48 days) and significantly longer ICU LoS (6.68 ± 12.44 days). In addition, HS patients undergo more brain surgery compared to IS patients, adding to their expenses, which may partly explain some of the differences.

In a study, Alene showed that the overall in-hospital mortality of stroke in Ethiopia was 18%. The pooled result of her systematic review and meta-analysis study revealed that nearly one-fifth of the stroke patients studied had died during hospitalization(27). This is very close to our in-hospital mortality rate (18%). This measurement is lower than that of previous studies conducted in such LMICs as Kenya (21.6%) and Burkina Faso (28.7%) (28, 29), but higher compared to such developing countries as China

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

(2.30%) and Germany (9.50%) (30, 31). The disparity is likely caused by improvements in stroke care and prevention in developed countries. Furthermore, the lack of intermediate care departments such as specialized stroke care units (SCU), and neurology ICU, as well as the lack of trained manpower in hospital wards for care, transportation, and rehabilitation of stroke patients is another factor affecting the in-hospital mortality of stroke patients in Iran. Thus, LMICs, including Iran, are in need of improvements, both in terms of care and treatment of stroke patients, and in terms of acute stroke care service accessibility, to ensure a reliable and effective stroke care (30-33).

In concordance with previous studies, this study found significant differences in hospitalization expenses by age (24, 26, 34). Also consistent with previous studies was the observation that younger people (0–49 years) had significantly higher expenses than older patients (26). This may be because of their higher use of rehabilitation services, medical interventions, surgery, and more invasive diagnostic and therapeutic methods. Therefore, it is economically rational to emphasize the use of cost-effective prevention strategies in the 0–49 years old population (26, 35).

Increasing age was associated with higher expenses in 50–79 years old patients and with higher in-hospital mortality for 60 years old patients and above according to the age- and gender-adjusted models. The age-related patterns of increase in stroke mortality was similar among developed and developing countries (36). Several studies confirm advanced age as a risk factor for death and poor prognosis of stroke (28).

Patients under the Civil Servants Fund insurance coverage had significantly higher expenses (1.033 times) and lower mortality OR (0.886 times) than the reference group, probably because they can afford better services and care. These patients are government employees who enjoy supplemental health insurance, allowing them to afford starred and VIP beds. This can explain the cost increase and mortality decrease in this group. In contrast, patients under the Iranian Fund coverage have significantly higher expenses (1.140 times) and higher mortality OR (1.319 times) than the reference group. They are often in poor socioeconomic conditions, and thus in financially justified need of special attention by the government and health insurance policymakers. In this regard, migration to universal health insurance can be an effective step in reducing the inequality gap across health insurance plans.

Differences in expenses between provinces could be because of variations in physicians' fees, the cost of medicine and medical materials, and the use of VIP or starred beds. Other factors include prices of specialized services, as well as complexities associated with patient conditions in different provinces. The most plausible explanation for the higher mortality in the eleven mentioned provinces may be demographic differences, socio-economic status, the level of risk factors (such as hypertension, hypercholesterolemia, obesity, and diabetes), stroke complications, service quality flaws, ineffectiveness of treatments, and the lack of health care facilities and budget in the geographic area (4).

With increasing LoS, the average hospitalization expenses for stroke patient increases. This is consistent with the findings of other studies (17, 19). On the other hand, patients with more than four days LoS had less mortality than that of stroke patient with one to three days LoS; whereas the death rate for patients admitted to the ICU increases with their length of stay. Liu C, et al. has showed that with increasing LoS, the mortality rate among patients decreases (19). Because of the fact that LoS is adjustable, it can be used as a target to control hospitalization expenses and improve hospitalization care.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Surgical intervention significantly increases the average expenses and mortality for stroke patients. This finding is similar to that of another study (37).Patients who undergo surgery have the possibility of perioperative stroke, which, along with the physiological conditions of the patient, other comorbidities, and the difference in the surgical and treatment procedures, can increase the risk of death after surgery (38, 39). A suitable interpretation for this increase in expenses and mortality rate in correlation with surgery, could not be found, either in this study or in others. It was also not possible to access further clinical information. We thus suggest subsequent studies to identify predictor factors of stroke mortality for patients who undergo surgery among the Iranian population, so that high-risk surgical patients can be identified, and the necessary arrangements can be made for effective surgical management and post-operative care.

No significant differences were found in the average hospitalization expenses among patients suffering various types of strokes. This finding is inconsistent with the findings of Diestro et al. in the Philippines (40). On the other hand, there are significant differences in hospital mortality based on stroke type, which is similar to the findings of Pucciarelli et al. (41).

Based on our estimates, the average hospitalization expenses in private hospitals are 2.449 times higher than that of public hospitals. Other studies have estimated that mean expenses of ischemic stroke, primary intracerebral hemorrhage, and subarachnoid hemorrhage patients in Brazilian private hospitals are 1.94, 6.28, and 3.75 times higher than that of Brazilian public hospitals, respectively. These figures are slightly higher than our estimates. Fundamental differences in health systems and pricing could explain some of these observed differences (42, 43).

We have further observed an increase in the average hospitalization expenses of stroke patients in conjunction with increase in the hospital size. One potential reason is the slow adoption of new treatments and technologies in smaller hospitals with fewer resources, as they lack access to specialty care and advanced therapies for stroke. Another possibility is the lack of clinical expertise in many small and medium hospitals because of the difficulties of attracting and retaining specialist physicians. These hospitals may also lack the infrastructure for rapid imaging procedures or such highly specialized clinical support services as neurocritical care and dedicated stroke units (44). These factors can lead to the accommodation of patients with higher stroke severity, and consequently higher expenses, to larger hospitals.

A surprising observation in our study was that treatments ending in death had the highest expenses relative to treatments with other outcomes. This is in contrast to the findings of Liu C, et al. in China, which posits the hospitalization expenses of surviving patients to be nearly five times higher than that of the patients who perished (19). The discrepancy could stem from the use of more complex procedures, specialized therapies because of the acute condition of dying patients or their stay in the ICU, and the difference in accommodation tariffs for ICU beds.

Suggestions and future research

It was not possible to extract comorbidity and stroke severity data from the IHIO databases. As such, we advise policymakers to encourage physicians to reflect on stroke severity indices, as well as comorbidity data in electronic patient files.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

More research is needed to solve the knowledge gaps in our study. Future studies may benefit from taking clinical variables such as disease severity and comorbidities into account. Socio-economic indicators, such as patient income and education level, can also be considered as determinants of hospitalization costs and in-hospital mortality in future studies.

According to the study results, reducing the length of stay along with encouraging reasonable prescription and consumption of drugs are effective strategies for policymakers and healthcare authorities to control hospitalization expenses.

Conclusion

Hospitalization expenses and mortality rates can be associated with numerous factors, many of which may be helpful in developing evidence-based policies. Populations of stroke patients insured by the Iranian Fund, as well as regions with higher hospitalization expenses and in-hospital mortality should be a priority target for policymakers to improve effective medical care outreach and increase access to affordable hospitalization and medications. Migration to universal health insurance can be an effective step in reducing the inequality gap between all insured patients. Applying cost-effective stroke prevention strategies in the younger population (Aged 0–49 years) is strongly recommended.

Author contributions

- Study concept and design: ZK, SE, RD, AG, MU, MH.
- Collection and assembly of data: ZS, ZK
- Acquisition, analysis or interpretation of data: ZK
- Statistical analysis: ZK
- Drafting of the manuscript: ZK
- Critical revision of the manuscript for important intellectual content: ZK, SE, RD, AG, MU, MH
- Study supervision: SE
- Final approval of manuscript: all authors.

Funding

This work was supported by Iran National Science Foundation (Gran No. 98029140).

Disclosure statement

No potential conflict of interest was reported by the author(s).

Ethics and consent

This research was part of a PhD thesis approved by the Ethics Committee of Tehran University of Medical Sciences (code: IR.TUMS.SPH.REC.1398.229). This study does not involve human participants and research ethics approval for human participants not applicable.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Article summary

Globally, stroke is the second most common cause of mortality, and the stroke burden is increasing. This study shows hospitalization expenses, in-hospital mortality, and their determinants in Iran. Stroke patients under the Iranian Fund insurance coverage, as well as those residing in regions with higher hospitalization expenses and mortality, should be priority target populations for policymakers for effective medical care. Migration to universal health insurance and applying stroke prevention strategies to the younger population are strongly recommended.

Availability of data and materials

The datasets used and analyzed during the current study are available via the corresponding author.

Supplemental material

Supplementary table 1

Supplementary table 2

References

1. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, et al. 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. The Lancet. 2020;396(10258):1204-22.
2. Mensah George A, Roth Gregory A, Fuster V. The Global Burden of Cardiovascular Diseases and Risk Factors. Journal of the American College of Cardiology. 2019;74(20):2529-32.
3. Rosengren A, Smyth A, Rangarajan S, Ramasundarahettige C, Bangdiwala SI, AlHabib KF, et al. Socioeconomic status and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study. The Lancet Global Health. 2019;7(6):e748-e60.
4. Amini M, Zayeri F, Salehi M. Trend analysis of cardiovascular disease mortality, incidence, and mortality-to-incidence ratio: results from global burden of disease study 2017. BMC Public Health. 2021;21(1):401.
5. Alwan A. Global status report on noncommunicable diseases 2010: World Health Organization; 2011.
6. Sarrafzadegan N, Mohammmadifard N. Cardiovascular disease in Iran in the last 40 years: prevalence, mortality, morbidity, challenges and strategies for cardiovascular prevention. Archives of Iranian medicine. 2019;22(4):204-10.
7. Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A. Growing Epidemic of Coronary Heart Disease in Low- and Middle-Income Countries. Current Problems in Cardiology. 2010;35(2):72-115.
8. Eisavi M, Mazaheri E, Rezapour A, Vahedi S, Hadian M, Jafari A. The cost-effectiveness and cost-utility of statin drug for the treatment of patients with cardiovascular disease, a systematic review. International Journal of Preventive Medicine. 2021;12(1):39.
9. Roth Gregory A, Mensah George A, Johnson Catherine O, Addolorato G, Ammirati E, Baddour Larry M, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. Journal of the American College of Cardiology. 2020;76(25):2982-3021.
10. Farzadfard MT, Thrift AG, Amiri A, Kapral MK, Hashemi P, Sposato LA, et al. Five-Year Case Fatality Following First-Ever Stroke in the Mashhad Stroke Incidence Study: A Population-Based

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Study of Stroke in the Middle East. Journal of Stroke and Cerebrovascular Diseases. 2018;27(4):1085-9.
11. Salehi M, Amiri A, Thrift AG, Kapral MK, Sposato L, Behrouz R, et al. Five-Year Recurrence Rate and the Predictors Following Stroke in the Mashhad Stroke Incidence Study: A Population-Based Cohort Study of Stroke in the Middle East. Neuroepidemiology. 2018;50(1-2):18-22.
12. Morovatdar N, Thrift AG, Stranges S, Kapral M, Behrouz R, Amiri A, et al. Socioeconomic Status and Long-Term Stroke Mortality, Recurrence and Disability in Iran: The Mashhad Stroke Incidence Study. Neuroepidemiology. 2019;53(1-2):27-31.
13. Darba S, Safaei N, Mahboub-Ahari A, Nosratnejad S, Alizadeh G, Ameri H, et al. Direct and Indirect Costs Associated with Coronary Artery (Heart) Disease in Tabriz, Iran. Risk Manag Healthc Policy. 2020;13:969-78.
14. Hendriks ME, Kundu P, Boers AC, Bolarinwa OA, te Pas MJ, Akande TM, et al. Step-by-step guideline for disease-specific costing studies in low- and middle-income countries: a mixed methodology. Global Health Action. 2014;7(1):23573.
15. Pucciarelli G, Rebora P, Arisido MW, Ausili D, Simeone S, Vellone E, et al. Direct Cost Related to Stroke A Longitudinal Analysis of Survivors After Discharge From a Rehabilitation Hospital. Journal of Cardiovascular Nursing. 2020;35(1):86-94.
16. Aminde LN, Dzudie A, Mapoure YN, Tantchou JC, Veerman JL. Estimation and determinants of direct medical costs of ischaemic heart disease, stroke and hypertensive heart disease: evidence from two major hospitals in Cameroon. Bmc Health Services Research. 2021;21(1):13.
17. Diestro JDB, Omar AT, Sarmiento RJC, Enriquez CAG, Castillo LLC-D, Ho BL, et al. Cost of hospitalization for stroke in a low–middle-income country: Findings from a public tertiary hospital in the Philippines. International Journal of Stroke. 2021;16(1):39-42.
18. Jo C. Cost-of-illness studies: concepts, scopes, and methods. Clin Mol Hepatol. 2014;20(4):327-37.
19. Liu C, Luo L, Duan L, Hou S, Zhang B, Jiang Y. Factors affecting in-hospital cost and mortality of patients with stroke: Evidence from a case study in a tertiary hospital in China. The International Journal of Health Planning and Management. 2021;36(2):399-422.
20. Mosadeghrad AM. Iran: Hospital Accreditation: Future Directions. Healthcare Systems:: CRC Press; 2018. p. 297-303.
21. Yousefinezhadi T, Mosadeghrad AM, Arab M, Ramezani M, Sari AA. An Analysis of Hospital Accreditation Policy in Iran. Iran J Public Health. 2017;46(10):1347-58.
22. Mehraban S, Raghfar H. The Place of Health Insurance in Reducing Catastrophic Health Expenditure. Iranian Journal of Economic Studies. 2018;7(2):239-54.
23. Dodd S, Bassi A, Bodger K, Williamson P. A comparison of multivariable regression models to analyse cost data. Journal of evaluation in clinical practice. 2006;12(1):76-86.
24. Zhu D, Xuefeng S, Nicholas S, Chen S, Ding R, Huang L, et al. Medical Service Utilization and Direct Medical Cost of Stroke in Urban China. International Journal of Health Policy and Management. 2020:-.
25. Schroeck FR, Jacobs BL, Bhayani SB, Nguyen PL, Penson D, Hu J. Cost of New Technologies in Prostate Cancer Treatment: Systematic Review of Costs and Cost Effectiveness of Robotic-assisted Laparoscopic Prostatectomy, Intensity-modulated Radiotherapy, and Proton Beam Therapy. European Urology. 2017;72(5):712-35.
26. Wang G, Zhang Z, Ayala C, Dunet DO, Fang J, George MG. Costs of hospitalization for stroke patients aged 18-64 years in the United States. Journal of Stroke and Cerebrovascular Diseases. 2014;23(5):861-8.
27. Alene M, Assemie MA, Yismaw L, Ketema DB. Magnitude of risk factors and in-hospital mortality of stroke in Ethiopia: a systematic review and meta-analysis. BMC Neurology. 2020;20(1):309.
28. Kaduka L, Muniu E, Oduor C, Mbui J, Gakunga R, Kwasa J, et al. Stroke Mortality in Kenya's Public Tertiary Hospitals: A Prospective Facility-Based Study. Cerebrovascular Diseases Extra. 2018;8(2):70-9.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

29. Labodi LD, Kadri C, Valentin YN, Christian N, Jean KB. Intra-hospital mortality of stroke and its predictive factors in a reference hospital in Ouagadougou, Burkina Faso. Brain. 2017;1(3):1-6.
30. Nimptsch U, Mansky T. Trends in acute inpatient stroke care in Germany--an observational study using administrative hospital data from 2005-2010. Dtsch Arztebl Int. 2012;109(51-52):885-92.
31. He Q, Wu C, Luo H, Wang Z-Y, Ma X-Q, Zhao Y-F, et al. Trends in In-Hospital Mortality among Patients with Stroke in China. PLOS ONE. 2014;9(3):e92763.
32. Ovbiagele B. Nationwide Trends in In-Hospital Mortality Among Patients With Stroke. Stroke. 2010;41(8):1748-54.
33. 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.
34. Buisman LR, Tan SS, Nederkoorn PJ, Koudstaal PJ, Redekop WK. Hospital costs of ischemic stroke and TIA in the Netherlands. Neurology. 2015;84(22):2208-15.
35. Brown DL, Boden-Albala B, Langa KM, Lisabeth LD, Fair M, Smith MA, et al. Projected costs of ischemic stroke in the United States. Neurology. 2006;67(8):1390.
36. Feigin VL, Krishnamurthi RV, Parmar P, Norrving B, Mensah GA, Bennett DA, et al. Update on the global burden of ischemic and hemorrhagic stroke in 1990-2013: the GBD 2013 study. Neuroepidemiology. 2015;45(3):161-76.
37. Diestro JD, Omar A, Sarmiento RJ, Enriquez CA, Chua-De Castillo LL, Ho BL, et al. Cost of Hospitalization for Stroke in a Low-Middle Income Country: Findings from a Public Tertiary Hospital in the Philippines. Neurology. 2020;94(15).
38. Patel BM, Reinert NJ, Sridharan ND, Thirumala PD. Predictive Factors of Perioperative Stroke-Related Mortality Following Vascular Surgery: A Retrospective Analysis. Journal of Stroke and Cerebrovascular Diseases. 2021;30(7):105833.
39. Woo SH, Marhefka GD, Cowan SW, Ackermann L. Development and Validation of a Prediction Model for Stroke, Cardiac, and Mortality Risk After Non‐Cardiac Surgery. Journal of the American Heart Association. 2021;10(4):e018013.
40. Yin X, Huang L, Man X, Jiang Y, Zhao X, Zhao L, et al. Inpatient cost of stroke in Beijing: a descriptive analysis. Neuroepidemiology. 2018;51(3-4):115-22.
41. Namale G, Kamacooko O, Makhoba A, Mugabi T, Ndagire M, Ssanyu P, et al. Predictors of 30-day and 90-day mortality among hemorrhagic and ischemic stroke patients in urban Uganda: a prospective hospital-based cohort study. BMC Cardiovascular Disorders. 2020;20(1):442.
42. Vieira LGD, Safanelli J, de Araujo T, Schuch HA, Kuhlhoff MHR, Nagel V, et al. The cost of stroke in private hospitals in Brazil: a one-year prospective study. Arquivos De Neuro-Psiquiatria. 2019;77(6):393-403.
43. Safanelli J, Vieira LGD, de Araujo T, Manchope LFS, Kuhlhoff MHR, Nagel V, et al. The cost of stroke in a public hospital in Brazil: a one-year prospective study. Arquivos De Neuro-Psiquiatria. 2019;77(6):404-11.
44. Hammond G, Luke AA, Elson L, Towfighi A, Joynt Maddox KE. Urban-rural inequities in acute stroke care and in-hospital mortality. Stroke. 2020;51(7):2131-8.

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Supplementary Table 1: *Total and daily hospitalization expenses for stroke patients, stratified by LoS and stroke type*

Cost title	Length of stay	Ischemic and unspecified stroke			Hemorrhagic stroke			Total		
		Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)
Daily	3–4 Days	5,966 (41.91)	47.39 (38.74)	38.89 (32.47–50.45)	1,207 (24.55)	69.81 (53.11)	53.88 (35.72–87.43)	7173 (37.46)	51.16 (42.34)	39.82 (32.74–54.52)
	5–7 Days	3,939 (27.67)	45.88 (26.42)	37.40 (30.69–51.92)	1,291 (26.26)	66.75 (54.33)	53.19 (33.85–85.29)	5230 (27.31)	51.03 (36.54)	39.01 (31.17–59.65)
	8–14 Days	2,653 (18.64)	51.77 (28.71)	43.71 (32.48–64.51)	1,243 (25.28)	68.19 (40.60)	60.91 (37.98–86.54)	3896 (20.34)	57.01 (33.84)	47.83 (33.75–71.80)
	+15 Days	1,676 (11.77)	65.47 (25.66)	64.34 (45.17–83.13)	1,175 (23.90)	77.48 (30.62)	77.28 (56.97–94.42)	2851 (14.89)	70.43 (28.43)	69.78 (48.96–87.82)
	Total	14,234 (100)	49.91 (33.01)	40.55 (32.45–58.56)	4,916 (100)	70.43 (46.09)	62.84 (38.12–89.11)	19150 (100)	55.18 (37.89)	43.59 (33.28–68.42)
Total	3–4 Days	5,966 (41.91)	162.20 (139.71)	132.48 (107.92–172.84)	1,207 (24.55)	242.30 (179.14)	187.38 (124.32–306.27)	7173 (37.46)	175.68 (150.09)	137.11 (109.73–189.96)
	5–7 Days	3,939 (27.67)	265.98 (155.88)	217.63 (172.82–304.83)	1,291 (26.26)	392.65 (322.52)	307.06 (202.75–488.36)	5230 (27.31)	297.25 (216.67)	230.17 (177.02–351.16)
	8–14 Days	2,653 (18.64)	529.59 (330.42)	437.23 (315.24–658.01)	1,243 (25.28)	703.41 (438.76)	615.61 (382.24–897.54)	3896 (20.34)	585.05 (377.21)	476.74 (327.85–738.70)
	+15 Days	1,676 (11.77)	2,064.65 (1,672.31)	1,550.01 (966.96–2,569.02)	1,175 (23.90)	2,359.48 (1,741.98)	1,933.03 (1,245.50–2,938.63)	2851 (14.89)	2,186.46 (1,707.32)	1,712.48 (1,065.78–2,737.02)
	Total	14,234 (100)	482.59 (844.53)	214.62 (137.94–436.62)	4,916 (100)	904.41 (1,225.34)	457.96 (230.71–1,031.14)	19150 (100)	590.91 (974.44)	252.93 (148.84–564.98)

All prices are in United States dollars (USD)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Supplementary Table 2: *Hospitalization expenses of stroke patients, stratified by age, gender, and stroke type*

Gender and age	Ischemic & unspecified stroke			Hemorrhagic stroke			Total		
	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)
Female									
<= 49	563 (8.15)	456.62 (906.75)	198.82 (133.56 – 428.98)	352 (15.74)	995.71 (1261.70)	572.56 (256.87 – 1,211.20)	915	664.01 (1088.92)	277.98 (149.71 – 676.39)
50-59	724 (10.49)	442.64 (881.36)	189.96 (125.29 – 360.61)	357 (15.96)	1,000.84 (1313.37)	504.39 (231.29 – 1,186.64)	1081	627.16 (1076.06)	245.68 (142.10 – 554.24)
60-69	1488 (21.55)	402.85 (687.18)	192.45 (128.68 – 364.44)	561 (25.08)	897.96 (1220.08)	469.04 (214.79 – 1,124.72)	2,049	538.48 (893.77)	229.92 (138.31 – 497.03)
70-79	1888 (27.35)	443.90 (706.97)	216.00 (138.42 – 434.51)	517 (23.11)	865.73 (1215.32)	397.12 (218.10 – 883.55)	2,405	534.62 (859.93)	242.72 (146.42 – 511.87)
>=80	2,241(32.46)	555.94 (952.02)	243.80 (1,48.71 – 501.09)	450 (20.12)	777.03 (1019.16)	428.45 (222.21 – 932.71)	2,691	592.91 (966.90)	267.05 (154.36 – 558.26)
Total	6,904 (100)	472.35 (827.31)	214.50 (137.17 – 429.76)	2237 (100)	897.98 (1205.46)	464.40 (223.74 – 1,061.53)	9,141	576.54 (951.83)	248.78 (147.21 – 548.24)
Male									
<= 49	638 (8.70)	483.86 (802.50)	224.67 (147.09 – 439.71)	528 (19.71)	921.90 (1182.40)	490.04 (258.64 – 1,124.66)	1,166	682.22 (1,015.95)	321.18 (171.21 – 713.06)
50-59	998 (13.62)	420.51 (774.66)	195.58 (136.48 – 369.83)	417 (15.57)	786.23 (1070.87)	407.45 (208.33 - 843.83)	1,415	528.36 (887.94)	233.97 (144.53 – 487.07)
60-69	1745 (23.81)	464.32 (817.73)	197.94 (134.52 – 408.41)	646 (24.11)	993.32 (1349.58)	487.30 (248.01 – 1,129.69)	2,391	607.25 (1,017.19)	244.44 (146.69 – 562.82)
70-79	1,587 (21.65)	530.91 (986.53)	212.87 (136.80 – 439.23)	518 (19.34)	1,024.30 (1493.00)	430.39 (244.68 – 1,126.28)	2,105	652.38 (1,151.83)	251.50 (148.60 – 594.44)
>=80	2,362 (32.22)	519.47 (847.65)	237.55 (144.44 – 515.68)	570 (21.28)	790.20 (995.06)	427.48 (224.92 – 907.96)	2,932	572.12 (884.59)	262.89 (151.02 – 589.50)
Total	7,330 (100)	492.24 (860.37)	214.81 (138.73 – 442.42)	2,679 (100)	909.78 (1241.90)	450.83 (236.76 – 998.03)	10,009	604.04 (994.50)	257.22 (150.45 – 583.32)
Male and female									
<= 49	1,201 (8.44)	471.09 (852.71)	212.25 (140.17 – 429.76)	880	951.42 (1214.57)	529.70 (257.41 – 1,160.20)	2,081	674.21 (1,048.44)	304.06 (160.26 – 693.46)
50-59	1,722 (12.10)	429.81 (821.02)	194.27 (131.41 – 362.57)	774	885.22 (1192.90)	437.79 (218.01 – 973.65)	2,496	571.15 (974.90)	239.34 (143.99 – 522.35)
60-69	3,233 (22.71)	436.04 (760.96)	194.83 (131.70 – 383.88)	1,207	948.99 (1291.36)	481.02 (229.98 – 1,127.90)	4,440	575.52 (962.72)	236.24 (143.18 – 533.64)
70-79	3,475 (24.41)	483.64 (847.15)	215.09 (137.56 – 434.71)	1,035	945.09 (1363.05)	409.51 (230.25 – 987.57)	4,510	589.58 (1,008.35)	246.88 (147.54 – 541.56)
>=80	4,603 (32.34)	537.23 (900.07)	240.22 (145.99 – 507.95)	1,020	784.39 (1005.29)	428.45 (222.43 – 912.99)	5,623	582.07 (924.88)	265.47 (152.46 – 575.93)
Total	14,234 (100)	482.59 (844.53)	214.62 (137.94 – 436.62)	4,916	904.41 (1225.34)	457.96 (230.71 – 1,031.14)	1,9150	590.91 (974.44)	252.93 (148.54 – 564.98)

All prices are in United States dollars (USD)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cross sectionalreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

For peer review only

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1

Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	#3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	#4	Present key elements of study design early in the paper	4
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	4
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	4-5

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Bias	#9	Describe any efforts to address potential sources of bias	NA
Study size	#10	Explain how the study size was arrived at	4
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	4-5
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	4-6
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	5-6
Statistical methods	#12c	Explain how missing data were addressed	4-5
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	5-6
Statistical methods	#12e	Describe any sensitivity analyses	NA
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	6
Participants	#13b	Give reasons for non-participation at each stage	NA

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

For peer review only

Participants	#13c	Consider use of a flow diagram	
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	6
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	4
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	6-7
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-8
Main results	#16b	Report category boundaries when continuous variables were categorized	6-8
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-8
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	6-8
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8-10

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	8-10
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	8-10
Generalisability	#21	Discuss the generalisability (external validity) of the study results	2
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

None The STROBE checklist is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist can be completed online using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

BMJ Open

Estimation and Predictors of Direct Hospitalization Expenses and in-hospital Mortality for Stroke Patients in a Low-Middle Income Country: Evidence from a Nationwide Cross-Sectional Study in Iranian Hospitals

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-067573.R1
Article Type:	Original research
Date Submitted by the Author:	30-Oct-2022
Complete List of Authors:	Kazemi, Zohreh; Tehran University of Medical Sciences, Department of Health Management and Economics; National Center for Health Insurance Research Emamgholipour, Sara; Tehran University of Medical Sciences, Department of Health Management and Economics Daroudi, Rajabali ; Tehran University of Medical Sciences, Department of Health Management and Economics; National Center for Health Insurance Research Ghorbani, Askar ; Tehran University of Medical Sciences School of Medicine, Department of Neurology Yunesian, Masud; Tehran University of Medical Sciences, Department of Environmental Health Engineering; TUMS, Department of Research Methodology and Data Analysis Hassanvand, Mohammad Sadegh; Tehran University of Medical Sciences, Department of Environmental Health Engineering; Tehran University of Medical Sciences Shahali , Zahra ; National Center for Health Insurance Research
Primary Subject Heading:	Neurology
Secondary Subject Heading:	Epidemiology
Keywords:	HEALTH ECONOMICS, Stroke < NEUROLOGY, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Estimation and Predictors of Direct Hospitalization Expenses and in-hospital Mortality for Stroke Patients in a Low-Middle Income Country: Evidence from a Nationwide Cross-Sectional Study in Iranian Hospitals

Author names: Zohreh Kazemi[1,8], Sara Emamgholipour Sefiddashti*[2], Rajabali Daroudi[3,8], Askar Ghorbani[4], Masud Yunesian[5,6], Mohammad Sadegh Hassanvand[5,7], Zahra Shahali[8]

Author affiliations:

[1] PhD Student of Health Economics, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran;

[2] Professor of Health Economics, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran;

[3] Associate Professor of Health Economics, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran;

[4] Associate Professor of Stroke and Cerebrovascular Disorders, Neurointerventionist Shariati Hospital, Department of Neurology, School of Medicine Tehran University of Medical Sciences;

[5] Department of Environmental Health Engineering, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran;

[6] Professor of Epidemiology, Department of Research Methodology and Data Analysis, Institute for Environmental Research, TUMS;

[7] Associate Professor Center for Air Pollution Research, Institute for Environmental Research, Tehran University of Medical Sciences, Tehran, Iran;

[8] National Center for Health Insurance Research (Iran Health Insurance Organization)

***Corresponding author:** Sara Emamgholipour Sefiddashti, Professor of Health Economics, Department of Health Management and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. Email: s-emamgholipour@tums.ac.ir

Contact information:

- Zohreh Kazemi: zohkazemi2020@gmail.com; 09151641747
- Dr. Sara Emamgholipour Sefiddashti: s-emamgholipour@tums.ac.ir; 09124799674
- Dr. Rajabali Daroudi: rdaroudi@sina.tums.ac.ir; 09158088846
- Dr. Askar Ghorbani: aghorbani@razi.tums.ac.ir; 09120224119
- Dr. Masud Yunesian: yunesian@tums.ac.ir; 09122019571
- Dr. Mohammad Sadegh Hassanvand: hassanvand@tums.ac.ir; 09127305125
- Zahra Shahali: z.shahali3000@ihio.gov.ir; 09127179169, 09914020661

Keywords: Hospital, Hospitalization Expenses, Mortality, Stroke, Generalized Linear Models, Logistic Regression.

Word count: The submitted manuscripts include 4797 words excluding the title page, abstract, references, tables, and acknowledgments. If the number of words is reduced to 4,000 words, some important results may be lost. We thus request that this limit be waived.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Abstract

Objective: Stroke is the second most prevalent cardiovascular disease in Iran. The present study investigates the estimation and predictors of hospitalization expenses and in-hospital mortality for stroke patients in Iranian hospitals.

Setting: Stroke patients in Iran between 2019–2020 were identified through the data collected from the Iran Health Insurance Organization and the Ministry of Health and Medical Education. This study is the first to conduct a pervasive, nationwide investigation.

Design: This is a cross-sectional, prevalence-based study. Generalized linear models and a multiple logistic regression model were used to determine the predictors of hospitalization expenses and in-hospital mortality for stroke patients.

Participants: A total of 19,150 patients suffering from stroke were studied.

Results: Mean hospitalization expenses per stroke patient in Iran amounted to $590.91 ± 974.44 (mean ± SD). Mean daily hospitalization expenses per stroke patient were $55.18 ± 37.89. The in-hospital mortality for stroke patients was 18.80%. Younger people (aged <=49 years) had significantly higher expenses than older patients. The odds ratio of in-hospital mortality in hemorrhagic stroke was significantly higher by 1.539 times (95% CI, 1.401-1.691) compared with ischemic and unspecified strokes. Compared to patients covered by the rural fund, patients covered by Iranian health insurance had significantly higher costs by 1.14 times (95% confidence interval, 1.186-1.097) and 1.319 times (95% confidence interval, 1.099-1.582) higher mortality. There were also significant geographic variations in stroke patients' expenses and mortality rates.

Conclusion: Applying cost-effective stroke prevention strategies among the younger population (<= 49 years old) is strongly recommended. Migration to universal health insurance can effectively reduce the inequality gap among all insured patients.

Keywords: Hospital, Hospitalization Expenses, Mortality, Stroke, Generalized Linear Models, Logistic Regression.

Strengths and limitations of this study

- Nationally representative samples were used to generate nationwide estimates.
- Outcome determinants are presented as an average cost ratio and odds ratio (OR) for comparability and usability by policymakers worldwide.
- This study is limited by the absence of stroke comorbidities and severity data.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Introduction

Cardiovascular disease (CVD) is a non-communicable disease frequently identified as a leading cause of premature death and increased healthcare expenses (1, 2). In general, CVD incidences and mortality rates vary across regions because of appropriate and adequate healthcare accessibility, dietary habits, lifestyle, etc. For instance, less educated patients in low and middle-income countries (LMICs) suffer higher rates of CVD incidence and mortality (3, 4).

Patients from LMICs, mostly in the Eastern Mediterranean Region (EMR), suffer 50% of all CVD mortalities and bear 80% of the global CVD burden. CVD has been a progressive epidemic problem in recent years (5, 6). Iran suffers the highest CVD burden in the EMR (6, 7), as CVDs account for the third most important contributor to the burden of disease in Iran (8).

Stroke is the primary cause of cardiovascular disease. Globally, stroke is the second most common cause of mortality, and the stroke burden in terms of disability-adjusted life years (DALYs) is increasing. Between 1990 to 2019, the total number of prevalent cases, deaths, and disability-adjusted life years (DALYs) because of stroke has increased steadily, reaching 101 million (85.3% increase), 6.55 million (43.3% increase), and 143 million (32.4% increase) respectively by 2019. The global stroke burden increases can be largely attributed to population growth and aging (9).

Likewise, LMICs bear the majority of the CVD burden. Stroke is more prevalent in LMICs and poses a larger mortality risk, disability, and recurrence (10-12). Stroke is the second most prevalent type of CVD in Iran, more prevalent than in western countries (6).

Stroke complications are not limited to physical and psychological effects on the patient; they also affect the patient's family and society economically (13). Despite resources spent on its treatment, the cost component of stroke and the difference in expenses based on patient characteristics and healthcare providers remain unclear. Most LMICs do not have a comprehensive disease registration system or accurate financial records, the absence of which impedes disease-specific expense analysis (14). The numerous studies conducted on the expenses and burden of diseases in Iran have been limited to datasets from one or a few local hospitals. This study is the first to conduct a nationwide investigation because Iran Health Insurance Organization (IHIO) has provided access to nationwide data for the first time.

Objectives

Increasing social expectations and scarcity of resources have made resource prioritization necessary to meet healthcare needs (13). A Stroke affects the survivors' physical, psychological and social well-being and the financial aspects of their lives. Therefore, identifying the components and determinants of hospitalization expenses is essential for further developing socioeconomic intervention strategies targeting stroke survivors (15).

Analysis of hospitalization expenses provides valuable information on such various healthcare decision-making processes as planning, prioritizing, and allocating resources; economic evaluation of health interventions; evaluation of funding distribution inefficiencies; as well as identification of cost reduction opportunities for policymakers, insurance organizations, and health care providers (14, 16, 17). Therefore, this study aims to identify: (1) hospitalization expenses of strokes in Iran and their components, (2) predictors of stroke hospitalization expenses in Iran, and (3) predictors of in-hospital mortality in Iran.

For peer review only

Methods

Study design and setting

A prevalence-based, cross-sectional survey was conducted on the population of the people covered by the IHIO. There are three types of basic health insurance in Iran. The IHIO and the Iranian Social Security Organization (ISSO) are the largest insurance institutions in Iran. IHIO covers about half of the Iranian population (over 42 million people) that includes rural and urban residents, employees, and non-employees. These institutions are covered by the Supreme Council of Health Insurance (SCHI) and because they follow the policies and decisions of the SCHI Insurance, they have the same benefits package according to article 2 of Iran's health universal Insurance Law. The demographic structure and gender age distribution of the population covered by IHIO are similar to Iran population structure(18). Therefore, the study of the population covered by IHIO can be generalized to the whole population of Iran.

IHIO maintains a database that gathers patient files (containing diagnosis and treatment data) and financial records from Iranian hospital information systems (HIS). The IHIO database was queried for this study, extracting data between 23 August 2019 and 21 June 2020.

A healthcare system perspective with a bottom-up (micro-costing) approach was used to determine hospitalization expenses of stroke patients, in which patient-specific data were collected based on their utilization of evaluated hospital services (19).

Data, participants, and eligibility criteria

Hospitalized cerebrovascular patients with the ICD-10 diagnosis code I60–I64 were included in the study, and their afflictions were classified as hemorrhagic strokes (ICD-10: I60–I62), ischemic strokes (ICD-10: I63), or unspecified strokes (ICD-10: I64). Under a neurologist's opinion, ischemic and unspecified strokes were combined so that some physicians may have used the unspecified code for ischemic stroke cases.

A predesigned, structured case report form (CRF) was used to collect data from medical records on patient demographics (14 items), cost components and resource consumption (55 items), disease and patient hospitalization processes (36 items), and hospital characteristics (7 items). Patient data were obtained from IHIO information records extracted by experts at the Iranian National Center for Health Insurance Research (NCHIR). In contrast, information about hospitals was obtained from the accreditation sources of the hospitals of the Ministry of Health and Medical Education (MHME). The two datasets were combined, and cost components were summarized and categorized into eight groups: Medical examination and consultation, hospital accommodation and nursing, laboratory tests, medical imaging, medicine, and medical materials, rehabilitation, surgery, and medical interventions.

The present study was carried out via a complete enumeration method, also known as the census. This is thus a pervasive study, encompassing all hospitalized stroke patients under IHIO coverage at the affiliated hospitals across Iran. Herein 30,615 medical records were reviewed, of which 11,465 cases were excluded because they did not meet the criteria elaborated below, leaving this study with 19,150 records to analyze. The participants were not directly involved in this study. The study population was limited to the unidentified records in the IHIO database.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Grounds for elimination include (1) Persistent and temporary emergency room patients, as they were not considered hospitalized[n=85] (2) Patients with a LoS of one [n=4306] and two days [n=4368] were excluded because, according to the neurologist's opinion, Suspected cases of stroke should be excluded, and only confirmed cases of stroke should be included in the study. (3) Medical records lacking critical data such as LoS[n=2702] and medical records of newly established hospitals that MHME had not accredited at the time [n=4], and we could not find hospital characteristics.

Variables

Hospitalization expenses and in-hospital mortality were the two outcome variables studied in this research. Hospitalization expenses are the direct expenses incurred by stroke patients during their hospitalization period. Hospitalization expenses were recorded in Iranian rials (IRR) before being converted to and expressed in United States dollars (USD) for comparability purposes (1 USD = 149,000 Rials, as of 19 March 2020). The second outcome variable, in-hospital mortality, is an important index in measuring clinical quality (20). It is used in this study to evaluate the health outcome of patients.

Independent predictor variables in this study include age, gender, marital status, the insurance fund covering the patient, province of residence, Lengths of stay in the intensive care unit (ICU LoS), LoS in another ward for patients without injury or critical conditions, stroke subtype, surgery reception, the outcome of hospitalization, hospital accreditation grade, hospital ownership, and hospital size.

Hospital accreditation is a 'systematic, external evaluation of a hospital's structure, processes, and outcomes by an independent, professional, accreditation body, using published optimum, evidence-based and achievable standards' (21). MHME defines different tariffs depending on the hospital accreditation grade, such that grade 1 hospitals have higher tariffs and thus charge their patients more (22).

In ownership, there are four groups of Iranian hospitals: governmental, private sector, social security, and special (military, charity, and other organizations). While their tariffs depend on their accreditation grade, governmental hospitals have subsidized tariffs, while private sector hospitals are more expensive (23). Social security and special hospitals have a mixture of the two tariff levels.

Statistical analysis

All collected data were imported into Microsoft Excel spreadsheet CRFs, where randomly selected entries were double-checked for accuracy and consistency. The data were then cleaned up for export into Stata version 14.1 (Stata Corp, College Station, TX, USA) for statistical analysis.

Cost distributions reported in this study possess a positive, intense skewness and are non-negative. This is in concordance with commonly reported observations in previous health datasets. Generalized linear models (GLM) with gamma family distribution and the log link function were used to determine the predictors for hospitalization expenses of stroke patients.

The dependent variable of in-hospital mortality was a binary parameter expressed as either zero or one. Thus, multiple logistic regression (LR) was used to model potential predictors and investigate in-hospital mortality determinants.

Skewness and Kurtosis normality tests were used to check for the normality of continuous data. Descriptive statistics were used to summarize expenses, patient demographics, disease, hospitalization

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

process, and hospital characteristics. Categorical variables were summarized as count and percentage, while continuous variables were presented as mean with standard deviation (SD) or median with a lower and upper quadrille (i.e., 25th and 75th percentiles). To estimate daily hospitalization expenses, total expenses, and cost components (each of our eight cost groups), both means and medians for central tendency, SD with 25th and 75th percentiles (upper and lower quadrilles) for variability and dispersion were reported, yielding a comprehensive sense of cost distribution data. Hospitalization expenses are the sum of all medical and nonmedical expenses incurred by stroke patients during hospitalization (20).

GLM with gamma distribution has been shown to predict mean costs as well as total hospitalization costs closely. In addition, the log link function has the advantage of ensuring non-negative results by preserving the original scale of the data, as opposed to log transformation(16, 24).

The Box-Cox approach was used to find the appropriate functional form and the linkage function, while the modified Park test was used to select the distribution family. In addition, non-nested selections from six different patterns of gamma, Gaussian, and Poisson distribution families with log and the second root linkage functions were iterated 40 times, and their Akaike and Bayesian criteria were compared. The log link and gamma family distributions had the smallest Akaike and Bayesian criteria, confirming the fitting model's decency. P-values less than 0.05 were considered statistically significant. Multivariate analysis was used to eliminate the effect of confounders.

Patient and public involvement

Patients and/or the public were not involved in this research's design, conduct, reporting, or dissemination plans.

Results

A total of 19,150 stroke patients were included in the study, of which 14,234 (74.33%; mean age: 71±15; gender: 51.5% male) had suffered from an ischemic and unspecified stroke (I&US), and 4,916 (25.67%; mean age: 64±18; gender: 54.5% male) had endured a hemorrhagic stroke (HS). Table 1 displays the demographic and hospitalization characteristics of the studied population.

The mean LoS was 8.62 ± 11.7 days (mean ± SD) for I&US, 12.33 ± 14.48 days for HS, and 9.57 ± 12.62 days overall. The mean ICU LoS and other ward LoS were 3.87 ± 10.43 days and 5.70 ± 7.30 days, respectively. The in-hospital mortality ratio was 14.91% for IS patients, 30.21% for HS patients, and 18.83% overall.

***Table 1**: Demographic and hospitalization characteristics of the studied population*

Characteristics	Ischemic & unspecified n=14,234 (Proportion=74.33%)	Hemorrhagic stroke n=4,916 (Proportion =25.67%)	Total n=19,150, (Proportion =100%)
Age, years, mean ± SD (min-max)	71 ± 15(1-119)	64±18(1–106)	69±16(1–119)
Gender			
Male	7,330(51.50)	2,679(54.50)	10,009(52.27)
Female	6,904(48.50)	2,237(47.50)	9,141(47.73)
Marital status			
Married	5,470(38.43)	1,899(38.63)	7,369(38.48)
Single	8,659(60.83)	2,986(60.74)	11,645(60.81)
Unspecified	105(0.74)	31(0.63)	136(0.71)
Health insurance coverage			

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Rural Fund	6,472(45.47)	2,234(45.44)	8,706(45.46)
Others	1,230(8.64)	376(7.65)	1,606(8.39)
Civil Servants Fund	2,835(19.91)	885(18.00)	3,720(19.42)
Iranian Fund	687(4.83)	343(6.98)	1,030(5.38)
Universal health insurance	1,933(13.58)	776(15.79)	2,709(14.15)
Imam Khomeini Relief Committee	1,077(7.57)	302(6.14)	1,379(7.20)
ICU LoS (mean ± SD)	2.90±9.45	6.68±12.44	3.87±10.43
Other ward LoS (mean ± SD)	5.72±6.99	5.64±8.13	5.70±7.30
Total LoS (mean ± SD)	8.62±11.76	12.33±14.48	9.57±12.62
Hospital accreditation grade			
Grade 1	13,223(93.50)	4,677(95.96)	17,900(94.12)
Grade 2	836(5.91)	173(3.55)	1,009(5.31)
Grade 3&4	84(0.59)	24(0.49)	108(0.57)
Hospital ownership			
Governmental	14,021(98.50)	4866(98.98)	18887(98.63)
Private	69(0.48)	24(0.49)	93(0.49)
Military, charity, other organizations	123(0.86)	22(0.45)	145(0.76)
Social security	21(0.15)	4(0.80)	25(0.13)
Hospital size			
<=100 Bed or S	713(5.04)	113(2.32)	826(4.35)
100–320 Bed or M	8,244(58.33)	2,523(51.75)	10,767(56.64)
320–600 Bed or L	3,210(22.71)	1,260(25.85)	4,470(23.52)
600–1000 Bed or XL	1,903(13.46)	976(20.02)	2,879(15.15)
>1000 Bed or HC	63(0.45)	3(0.06)	66(0.35)
Outcome of treatment			
Full recovery	4,199(29.50)	1,183(24.06)	5,382(28.10)
Partial recovery	6,977(49.02)	1,874(38.12)	8,851(46.22)
Death	2,122(14.91)	1,479(30.09)	3,601(18.80)
Discharge against medical advice	792(5.56)	254(5.17)	1,046(5.46)
Referral to another hospital	144(1.01)	126(2.56)	270(1.41)
Surgery reception			
Yes	2,486(17.47)	2,248(45.73)	4,734(24.72)
No	1,1748(82.53)	2,668(54.27)	14,416(75.28)
In-hospital mortality ratio	2121(14.91)	1485(30.17)	3606(18.83)

Total and daily hospitalization expenses per stroke patient

Mean hospitalization expenses per stroke patient was $482.59 (SD ± $844.53) for I&US, $904.41 (SD ± $1,225.34) for HS, and $590.91 (SD ± $974.44) overall. Mean daily hospitalization expenses per stroke patient was $49.91 (SD ± $33.01) for I&US, $70.43 (SD ± $46.09) for HS, and $55.18 (SD ± $37.89) for stroke. HS patients had higher mean hospitalization expenses per patient than I&US patients. This was also higher in all age groups for patients with HS than I&US. Supplementary table 1 illustrates total and daily hospitalization expenses for stroke patients, stratified by LoS and stroke type. Supplementary table 2 displays hospitalization expenses for stroke patients, stratified by age, gender, and stroke type.

Table 2 presents the different hospitalization cost components for the stroke patients studied. Hospital accommodation and nursing (55.11%) represent the main component of hospitalization expenses for stroke patients. Medicine and medical materials (17.16%), medical examination and consultation (11.72%), medical imaging services (6.76%), laboratory tests (4.23%), surgery (3.93%), and rehabilitation (0.81%) are the next components in severity. On the contrary, medical interventions (0.29%) represent the lowest proportion of hospitalization expenses per patient.

***Table 2**: Hospitalization expenses for stroke patients, stratified by resource utilization and stroke type*

Cost component	Ischemic & unspecified stroke	Hemorrhagic stroke	Total
Accommodation and nursing			
Mean(SD)	208.42(481.85)	410.61(637.50)	260.14(533.40)
Median(25^{th}–75^{th} percentile)	70.15(46.77–151.90)	175.37(76.71–460.87)	81.84(46.77–217.49)
Sum(% of total hospital costs)	3,808,553.87(53.61)	2,644,728.39(57.49)	6,450,576.38(55.10)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Medicine and medical materials			
Mean(SD)	65.83(153.89)	125.03(212.48)	80.98(172.74)
Median(25th–75th percentile)	17.63(7.92–54.95)	46.68(19.73–134.70)	22.85(9.33–74.23)
Sum(% of total hospital costs)	1,203,534.78(16.94)	805,978.98(17.53)	2,009,109.79(17.16)
Visit and consultation			
Mean(SD)	54.21(70.39)	60.20(75.90)	55.73(71.87)
Median(25th–75th percentile)	34.79(23.00–57.22)	38.09(21.85–69.30)	35.42(22.71–60.44)
Sum(% of total hospital costs)	987,736.96(13.90)	380,181.35(8.26)	1,371,848.09(11.72)
Medical imaging services			
Mean(SD)	32.46(30.24)	30.98(31.21)	32.08(30.50)
Median(25th–75th percentile)	26.06(16.35–39.34)	22.98(13.09–38.28)	25.39(15.40–39.08)
Sum(% of total hospital costs)	590,264.49(8.31)	197,880.09(4.30)	790,937.07(6.76)
Laboratory tests			
Mean(SD)	17.23(30.19)	28.07(41.96)	20.00(33.93)
Median(25th–75th percentile)	7.92(4.44–17.05)	13.65(5.98–32.80)	8.88(4.70–20.69)
Sum(% of total hospital costs)	314,328.42(4.42)	180,324.38(3.92)	495,004.43(4.23)
Surgery			
Mean(SD)	38.42(68.64)	114.77(122.33)	74.67(105.03)
Median(25th–75th percentile)	11.64(5.64–36.55)	85.14(18.29–166.21)	27.30(8.05–108.26)
Sum(% of total hospital costs)	122,959.70(1.73)	340,604.95(7.40)	459,610.82(3.93)
Rehabilitation			
Mean(SD)	10.75(26.38)	21.60(36.01)	13.84(29.85)
Median(25th–75th percentile)	4.01(2.41–8.63)	8.42(3.61–25.00)	4.81(2.41–12.34)
Sum(% of total hospital costs)	51,850.42(0.73)	42,513.29(0.92)	94,228.28(0.81)
Medical interventions			
Mean(SD)	11.41(18.25)	10.81(18.71)	11.26(18.37)
Median(25th–75th percentile)	8.03(4.86–11.14)	8.03(4.86–10.98)	8.03(4.86–11.03)
Sum(% of total hospital costs)	25,518.65(0.36)	8,259.71(0.18)	33,903.56(0.29)
Total hospital cost			
Mean(SD)	482.59(844.53)	904.41(1225.34)	590.91(974.44)
Median(25th–75th percentile)	214.62(137.94–436.62)	457.96(230.71–1031.14)	252.93(148.84–564.98)
Sum(% of total hospital costs)	7,104,747.29(60.70)	4,600,471.15(39.30)	11,705,218.44(100)

All prices are in United States dollars (USD)

Predictors of hospitalization expenses for stroke patients

Table 3 displays the predictors of hospitalization expenses for stroke patients in Iran. Independent predictor variables for the GLM model were age, gender, insurance funds, province of residence, ICU LoS, other ward LoS, stroke subtype, surgery reception, outcome of hospitalization, hospital accreditation grade, hospital ownership, and hospital size.

This study has found no significant difference in average expenses between the patients insured by other insurance institutions and reference groups. However, significant differences were observed between hospitalization expenses among various age groups, such that 0—49 years old patients had the highest average hospitalization expenses. The average hospitalization expenses for the 50—59, 60—69, 70—79, and over 80 years old patients were respectively 0.934, 0.930, 0.940, and 0.921 times smaller than that of the 0—49 years old patients. Hospitalization costs for men were significantly higher than for women (1.017 times).

There was a significant difference between the average expenses for people under the Civil Servants Fund and the Iranians Fund insurance coverage, compared to those covered by the Rural Fund; such that their average expenses were 1.03 and 1.14 times higher respectively than that of the Rural Funds reference group.

The average hospitalization expenses of Alborz, Fars, Kohkiluyeh and Boyer-Ahmad, Markazi, Sistan and Baluchestan, and Zanjan provinces showed no significant differences from the Tehran province (the reference group). The expenses in the Hamadan province were 1.075 times higher than in Tehran. All

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

other provinces had significantly lower hospitalization expenses than Tehran. The lowest average belongs to the Kermanshah province.

ICU and other ward LoS had a significant positive association with the average hospitalization expenses for stroke patients, such that LoS longer than 7 days were 3.098 times higher, compared to other ward LoS of 1–3 days and 7.689 times higher than single-day ICU LoS.

No significant differences were observed in average hospitalization expenses between HS and I&US patients. However, the mean hospitalization expenses of stroke patients who underwent surgery were significantly 1.602 times higher than that of the reference group members who had no surgery. However, significant differences of respectively 1.599 and 2.442 times higher average hospitalization expenses for stroke patients were observed at special (military, charity, other organizations) and private hospitals, compared to public hospitals.

With the increase in size and number of hospital beds, the average hospitalization expenses for stroke patients were significantly raised above small hospitals (S) by 1.046 times in medium hospitals (M), 1.116 times in large hospitals (L), 1.176 times in very large hospitals (XL), and 1.347 times in hospital complexes (HC).

Analyzing hospitalization outcomes such as death, discharge against medical advice, and referral to another hospital, compared to full recovery (designated as a reference group), revealed significant differences in mean hospitalization expenses of stroke patients with such outcomes. Therefore, their average hospitalization expenses were 1.361, 1.108, and 1.278 times higher compared to the full recovery reference group.

Table 3: *Predictors of hospitalization expenses for stroke patients in Iran*

Variables		N	%	Coefficient	Lower	Upper	P-value
Age	<=49	2081	10.87	1			
	50–59	2496	13.03	0.934	0.903	0.967	<.001
	60–69	4440	23.19	0.935	0.903	0.968	<.001
	70–79	4510	23.55	0.940	0.912	0.970	<.001
	>=80	5623	29.36	0.921	0.934	0.950	<.001
Gender	Female	9,141	47.73	1			
	Male	10,009	52.27	1.017	1.000	1.034	0.049
Health insurance coverage	Rural Fund	8,706	45.46	1			
	Others	1,606	8.39	1.031	0.999	1.064	0.054
	Civil Servants Fund	3,720	19.43	1.033	1.009	1.057	0.006
	Iranian Fund	1,030	5.38	1.140	1.097	1.186	<.001
	Universal health insurance	2,709	14.15	0.987	0.962	1.013	0.332
	Imam Khomeini Relief Committee	1,379	7.20	0.978	0.946	1.011	0.193
Province	Tehran	788	4.11	1			
	Alborz	302	1.58	1.024	0.947	1.107	0.546
	Ardabil	436	2.28	0.806	0.751	0.865	<.001
	Bushehr	215	1.12	0.885	0.809	0.967	0.007
	East Azarbaijan	1,063	5.55	0.875	0.828	0.925	<.001
	Fars	1,768	9.23	0.957	0.909	1.008	0.094
	Qazvin	336	1.75	0.768	0.713	0.828	<.001
	Qom	335	1.75	0.836	0.775	0.902	<.001
	Gilan	676	3.53	0.751	0.704	0.802	<.001
	Golestan	619	3.23	0.770	0.723	0.820	<.001
	Hamadan	493	2.57	1.075	1.005	1.149	0.034

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

	Chaharmahal and Bakhtiari	295	1.54	0.865	0.799	0.937	<.001
	Hormozgan	412	2.15	0.804	0.749	0.864	<.001
	Ilam	163	0.85	0.780	0.703	0.865	<.001
	Isfahan	1,298	6.78	0.912	0.864	0.962	0.001
	Kerman	677	3.54	0.863	0.812	0.918	<.001
	Kermanshah	527	2.75	0.712	0.665	0.762	<.001
	Razavi Khorasan	1,806	9.43	0.768	0.729	0.809	<.001
	Khuzestan	1,143	5.97	0.832	0.788	0.880	<.001
	Kohkiluyeh and Boyer-Ahmad	187	0.98	0.987	0.899	1.084	0.793
	Kurdistan	438	2.29	0.889	0.830	0.953	0.001
	Lorestan	667	3.48	0.767	0.721	0.817	<.001
	Markazi	336	1.75	0.928	0.860	1.001	0.054
	Mazandaran	1,224	6.39	0.842	0.798	0.888	<.001
	North Khorasan	293	1.53	0.787	0.727	0.852	<.001
	Semnan	117	0.61	0.789	0.704	0.883	<.001
	Sistan and Baluchestan	571	2.98	0.971	0.911	1.036	0.378
	West Azerbaijan	969	5.06	0.862	0.814	0.912	<.001
	Yazd	235	1.23	0.852	0.781	0.930	<.001
	Zanjan	523	2.73	0.983	0.918	1.051	0.613
	South Khorasan	238	1.24	0.768	0.705	0.837	<.001
ICU LoS	0–1 Days	13,169	69.09	1			
	2–4 Days	1,952	10.24	2.016	1.957	2.077	<.001
	5–7 Days	1,213	6.36	3.072	2.962	3.187	<.001
	> 7 Days	2,728	14.31	7.689	7.471	7.915	<.001
Other ward LoS	0–3 Days	7,688	40.33	1			
	4–5 Days	5,008	26.27	1.247	1.219	1.275	<.001
	6–7 Days	2,550	13.38	1.633	1.589	1.679	<.001
	> 7 Days	3,816	20.02	3.098	3.022	3.176	<.001
Stroke type	Ischemic & unspecified	14,234	74.33	1			
	Hemorrhagic	4,916	25.67	1.015	0.994	1.036	0.151
Surgery	No	14,416	75.28	1			
	Yes	4,734	24.72	1.602	1.566	1.639	<.001
Hospital accreditation grade	Grade 3&4	108	0.57	1			
	Grade 1	17,900	94.12	0.968	0.863	1.086	0.580
	Grade 2	1,009	5.31	0.963	0.854	1.087	0.545
Hospital ownership	Governmental	18,887	98.62	1			
	Military, charity, other organizations	145	0.76	1.599	1.450	1.762	<.001
	Social security	25	0.13	1.134	0.903	1.425	0.279
	Private	93	0.49	2.442	2.145	2.780	<.001
Hospital size	<=100 Bed (S)	826	4.35	1			
	100–320 Bed (M)	10,767	56.64	1.046	1.000	1.093	0.048
	321–600 Bed (L)	4,470	23.51	1.116	1.063	1.172	<.001
	601–1000 Bed (XL)	2,879	15.15	1.176	1.116	1.239	<.001
	>1000 Bed (HC)	66	0.35	1.347	1.161	1.563	<.001
Outcome of hospitalization	Full recovery	5,382	28.10	1			
	Partial recovery	8,851	46.22	1.013	0.991	1.036	0.236
	Death	3,601	18.80	1.361	1.325	1.399	<.001
	Discharge against medical advice	1046	5.46	1.108	1.064	1.153	<.001
	Referral to another hospital	270	1.41	1.278	1.189	1.375	<.001

Predictors of in-hospital mortality for stroke patients

Table 4 presents predictors of in-hospital mortality for stroke patients. Independent predictor variables in the multiple logistic regression model include age, gender, marital status, insurance fund, province of residence, ICU LoS, other ward LoS, stroke subtype, surgery reception, hospital accreditation grade, and hospital ownership. Where the other variables were constant, the odds ratio (OR) of in-hospital mortality

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

for 60–69, 70–79, and over 80 years old patients were 1.538, 2.119, and 3.233 times higher than the 0–49 years old patients, respectively. There were no significant differences in the chance of in-hospital mortality between men and women. But there was a significant difference between single and married patients. Thus, the chance of mortality for single patients was 1.332 times higher than for married patients. There was also a significant difference in hospital mortality rates of patients under Civil Servants Fund and Iranians Fund insurance coverage, compared to patients covered by the rural fund insurance, so that their OR was 0.886 and 1.319 times higher, respectively.

The ORs of in-hospital mortality in Alborz (1.753), East Azerbaijan (1.965), Fars (1.329), Gilan (2.135), Golestan (1.651), Khorasan Razavi (1.451), Khuzestan (1.942), Sistan and Baluchestan (1.662) and Zanjan (1.415) were significantly higher than Tehran. The lowest and highest chances of mortality were found in Fars and Gilan provinces, respectively. The ORs in Kermanshah and Kohkiluyeh Boyer-Ahmad provinces were 0.613 and 0.444 times lower than in Tehran, respectively.

The in-hospital mortality OR for stroke patients with more than three days LoS in other ward was significantly lower than those in the reference group. This ratio was significantly higher for ICU patients, compared to the reference group, such that chances of in-hospital mortality in patients with a 2–4, 5–7, and over 7 days LoS, were 2.556, 4.206, and 4.629 times higher than that of the reference group, respectively.

At 2,616 times, in-hospital mortality for stroke patients who underwent surgery was significantly different from that of patients who did not undergo surgery. At about 1.539 times, this ratio was significantly higher in HS compared to I&US.

There were no significant differences in hospital mortality OR for stroke patients across hospitals with different accreditation grades. At about 2.374 times, mortality OR was significantly higher in governmental hospitals than in private hospitals. Supplementary Table 3 shows hospitalization costs of stroke patients by death/life, gender, and type of stroke.

Table 4: Predictors of in-hospital mortality for stroke patients in Iran

Variables		Died (Person)	Discharged (Person)	Mortality (%)	OR	Lower	Upper	P-value
Age	<=49	302	1,779	14.51	1			
	50–59	311	2,185	12.46	1.0429	0.861	1.263	0.667
	60–69	722	3,718	16.26	1.538	1.301	1.818	<.001
	70–79	864	3,646	19.16	2.119	1.794	2.502	<.001
	>=80	1,402	4,221	24.93	3.233	2.751	3.800	<.001
Gender	Female	1,729	7,412	18.91	1			
	Male	1,872	8,137	18.70	0.988	0.909	1.074	0.776
Marital status	Married	1,157	6,212	11.16	1			
	Single	2,393	9,252	20.55	1.332	1.213	1.463	<.001
Insurance funds	Rural Fund	1,590	7,116	18.26	1			
	Others	319	1,287	19.86	1.074	0.920	1.253	0.365
	Civil Servants Fund	730	2,990	19.62	0.886	0.789	0.995	0.042
	Iranian Fund	249	781	24.17	1.319	1.099	1.582	0.003
	Universal health insurance	457	2,252	16.87	0.985	0.861	1.128	0.833
	Imam Khomeini Relief Committee	256	1,123	18.56	0.999	0.843	1.182	0.988
Province	Tehran	150	638	19.04	1			
	Alborz	67	235	22.19	1.753	1.290	2.542	0.003
	Ardabil	74	362	16.97	1.222	0.853	1.752	0.274
	Bushehr	43	172	20.00	1.270	0.820	1.968	0.285
	East Azarbaijan	249	814	23.42	1.965	1.507	2.561	<.001

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

	Fars	339	1429	19.17	1.329	1.037	1.704	0.025
	Qazvin	57	279	16.96	1.443	0.986	2.113	0.059
	Qom	66	269	19.70	1.333	0.916	1.940	0.133
	Gilan	151	525	22.34	2.135	1.572	2.900	<.001
	Golestan	146	473	23.59	1.651	1.223	2.228	0.001
	Hamadan	81	412	16.43	1.094	0.779	1.537	0.602
	Chaharmahal and Bakhtiari	41	254	13.90	0.756	0.495	1.156	0.197
	Hormozgan	75	337	18.20	1.078	0.756	1.537	0.679
	Ilam	19	144	11.66	0.717	0.387	1.328	0.290
	Isfahan	224	1074	17.26	0.929	0.712	1.211	0.586
	Kerman	135	542	19.94	1.220	0.901	1.653	0.199
	Kermanshah	71	456	13.47	0.613	0.433	0.868	0.006
	Razavi Khorasan	370	1436	20.49	1.451	1.133	1.857	0.003
	Khuzestan	234	909	20.47	1.942	1.482	2.544	<.001
	Kohgiluyeh and Boyer-Ahmad	17	170	9.09	0.444	0.241	0.819	0.009
	Kurdistan	69	369	15.75	0.774	0.542	1.107	0.161
	Lorestan	141	526	21.14	1.332	0.981	1.809	0.066
	Markazi	61	275	18.15	1.060	0.723	1.556	0.764
	Mazandaran	167	1057	13.64	0.834	0.629	1.104	0.205
	North Khorasan	65	228	22.18	1.425	0.973	2.088	0.069
	Semnan	22	95	18.80	0.705	0.404	1.230	0.218
	Sistan and Baluchestan	113	458	19.79	1.662	1.212	2.279	0.002
	West Azerbaijan	187	782	19.30	1.182	0.892	1.568	0.245
	Yazd	38	197	16.17	0.640	0.405	1.012	0.056
	Zanjan	88	435	16.83	1.415	1.011	1.981	0.043
	South Khorasan	41	197	17.23	0.923	0.599	1.420	0.714
Other ward LoS	0~3 Days	2,080	5,608	27.06	1			
	4~5 Days	477	4,531	9.52	0.526	0.465	0.594	<.001
	6~7 Days	267	2,283	10.47	0.515	0.443	0.600	<.001
	> 7 Days	761	3,055	19.94	0.823	0.736	0.921	0.001
ICU LoS	0~1 Days	1,289	11,880	9.79	1			
	2~4 Days	527	1,425	27.00	2.556	2.240	2.916	<.001
	5~7 Days	479	734	39.49	4.206	3.633	4.869	<.001
	>7 Days	1,290	1,438	47.29	4.629	4.127	5.193	<.001
Stroke type	Ischemic & unspecified	2,122	12,112	14.91	1			
	Hemorrhagic	1,479	3,437	30.09	1.539	1.401	1.691	<.001
Surgery	No	1,787	12,629	12.40	1			
	Yes	1,814	2,920	38.32	2.616	2.378	2.878	<.001
Hospital accreditation grade	Grade 1	3,353	14,547	18.73	1			
	Grade 2	191	818	18.93	0.865	0.709	1.055	0.151
	Grade 3&4	28	85	24.78	0.924	0.559	1.529	0.759
Hospital ownership	Private	11	82	11.83	1			
	Governmental	3,575	15,312	18.93	2.374	1.130	4.987	0.022
	Military, charity, other organizations	13	132	8.97	1.399	0.535	3.656	0.494
	Social security	2	23	8.00	0.740	0.135	4.065	0.729

Discussion

This study found mean hospitalization expenses per stroke patient in Iran ($590.91) to be lower than Philippines ($781.42) and China ($2,008); the former is an Asian LMIC while the latter is a developed country (17, 25). A root cause of this difference is the lower prevalence of traditional medical technologies in Iran compared to modern, expensive ones (26). Furthermore, the difference in mean expenses is likely because of the differences in standards of care, payment systems, modern medical technologies and services, sanctions against Iran, and the steep fall in the value of the Iranian Rial, the national currency. In Iran, public hospitals are subsidized by the state, rendering their therapy costs are

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

lower than the actual cost of services. As such, these prices don not reflect the true value of their services.

Estimates for the hospitalization expenses of stroke patients demonstrate that average expenses per HS patient were higher than I&US patients. Moreover, obtaining overall hospital estimates revealed that more than half of the hospitalization expenses of stroke patients (60%) are related to IS. These findings are consistent with similar, relevant studies (16, 25, 27). Patients suffering from HS have a longer average other ward LoS compared to other ward I&US patients (12.33 ± 14.48 days) and significantly longer ICU LoS (6.68 ± 12.44 days). In addition, HS patients undergo more brain surgery than IS patients, adding to their expenses, which may partly explain some differences.

In a study, Alene showed that Ethiopia's overall in-hospital stroke mortality was 18%. The pooled result of her systematic review and meta-analysis study revealed that nearly one-fifth of the stroke patients studied had died during hospitalization(28). This is very close to the mortality rate in our hospital (18.83%).This measurement is lower than that of previous studies conducted in such LMICs as Kenya (21.6%) and Burkina Faso (28.7%) (29, 30) but higher compared to such developing countries as China (2.30%) and Germany (9.50%) (31, 32). The disparity is likely caused by improved stroke care and prevention in developed countries. Furthermore, the lack of intermediate care departments such as specialized stroke care units (SCU) and neurology ICU, as well as the lack of trained human resources in hospital wards for care, transportation, and rehabilitation of stroke patients, is another factor affecting the in-hospital mortality of stroke patients in Iran. Thus, LMICs, including Iran, need improvements, both in terms of care and treatment of stroke patients and in terms of acute stroke care service accessibility, to ensure a reliable and effective stroke care (31-34).

In concordance with previous studies, this study found significant differences in hospitalization expenses by age (25, 27, 35). Also consistent with previous studies was the observation that younger people (0–49 years) had significantly higher expenses than older patients (27). This may be because of their higher use of rehabilitation services, medical interventions, surgery, and more invasive diagnostic and therapeutic methods. Therefore, it is economically rational to emphasize using cost-effective prevention strategies in the 0–49 years old population (27, 36).

Increasing age was associated with higher expenses for 50–79 years old patients and higher in-hospital mortality for 60 and above patients, according to the age- and gender-adjusted models. The age-related increase in stroke mortality patterns was similar among developed and developing countries (37). Several studies confirm advanced age as a risk factor for death and poor prognosis of stroke (29).

Hospitalization expenses in men are 1.017 times higher than in women. This difference may depend on factors such as stroke severity and co-morbidities. Evidence from hospital studies show that a significant percentage of stroke patients suffer from high blood pressure, diabetes, blood cholesterol level, and other cardiovascular problems. Therefore, the management and treatment of stroke may require the treatment of other comorbidities too; In addition, patients in advanced stages and with higher stroke severity may have more costs than those in the early stages. Failure to account for these factors can lead to bias in the results(38, 39). Despite the power of the present study to obtain information at the national level compared to Aminde et al.'s study in 2 hospitals in Cameroon or Diestro et al.'s study in 1 hospital in the Philippines (16, 17), there is also a limitation in obtaining information on the severity of the disease and comorbidities in the IHIO data similar to other LMICs countries, which is due to the incomplete

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

registration of diseases(14). On the other hand, there was no significant difference in in-hospital mortality between women and men. The combination of these data with epidemiological data of stroke in Iran shows that the incidence, prevalence, and age-standardized death of men compared to women, respectively (134.02 vs. 143.73), (1159.26 vs. 1349.66), and (64.78 vs. 68.16), indicating a lower ratio in men(40). Therefore, based on the results of this study, gender differentiation cannot be considered for stroke prevention strategies, and it seems that health policymakers should consider both sex groups of Iranian -men and women-, while more studies are needed in this regard.

Patients covered by the Civil Servants Fund insurance coverage had significantly higher expenses (1.033 times) and lower mortality OR (0.886 times) than the reference group, probably because they could afford better services and care. These patients are government employees who enjoy supplemental health insurance, allowing them to afford starred and VIP beds. This can explain the cost increase and mortality decrease in this group. In contrast, the Iranian Fund coverage patients have significantly higher expenses (1.140 times) and higher mortality OR (1.319 times) than the reference group. The highest in-hospital mortality ratio in these patients might be attributed to failure to receive high-quality care on time due to discrimination in the behavior of service providers based on their socioeconomic status(41, 42), which requires further research to address this ambiguity. Patients insured by the Iranian Fund, are often in poor socioeconomic conditions, thus in financially justified need of special attention by the government and health insurance policymakers. In this regard, migration to universal health insurance can effectively reduce the inequality gap across health insurance plans.

Differences in expenses between provinces could be because of variations in physicians' fees, the cost of medicine and medical materials, and the use of VIP or starred beds. Other factors include the prices of specialized services and complexities associated with patient conditions in different provinces. The most plausible explanation for the higher mortality in the eleven mentioned provinces may be demographic differences, socioeconomic status, the level of risk factors (such as hypertension, hypercholesterolemia, obesity, and diabetes), stroke complications, service quality flaws, the ineffectiveness of treatments, and the lack of health care facilities and budget in the geographic area (4).

With increasing LoS, the average hospitalization expenses for stroke patient increases. This is consistent with the findings of other studies (17, 20). On the other hand, patients with more than four days LoS had less mortality than a stroke patient with one to three days of LoS; the death rate for patients admitted to the ICU increases with their length of stay. Liu C et al. showed that with increasing LoS, the mortality rate among patients decreases (20). Because LoS is adjustable, it can be used as a target to control hospitalization expenses and improve hospitalization care.

The surgical intervention significantly increases the average expenses and mortality for stroke patients. This finding is similar to that of another study (43). Patients who undergo surgery have the possibility of perioperative stroke, which increases the risk of death after surgery, along with the patient's physiological conditions, other comorbidities, and differences in surgical and treatment methods (44, 45). A suitable interpretation for this increase in expenses and mortality rate in correlation with surgery could not be found, either in this study or in others. It was also not possible to access further clinical information. Therefore, we suggest subsequent studies to identify predictor factors of stroke mortality for patients who undergo surgery among the Iranian population so that high-risk surgical patients can be identified and the necessary arrangements can be made for effective surgical management and post-operative care.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

There were no significant differences in the average hospitalization expenses among patients suffering various strokes. This finding is inconsistent with the findings of Diestro et al. in the Philippines (46). On the other hand, there are significant differences in hospital mortality based on stroke type, which is similar to the findings of Pucciarelli et al. (47).

Based on our estimates, the average hospitalization expenses in private hospitals are 2.449 times higher than in public hospitals. Other studies have estimated that mean expenses of ischemic stroke, primary intracerebral hemorrhage, and subarachnoid hemorrhage patients in Brazilian private hospitals are 1.94, 6.28, and 3.75 times higher, respectively, than in Brazilian public hospitals.These figures are slightly higher than our estimates. Fundamental differences in health systems and pricing could explain some of these observed differences (48, 49).

We have further observed an increase in the average hospitalization expenses of stroke patients in conjunction with an increase in hospital size. One potential reason is the slow adoption of new treatments and technologies in smaller hospitals with fewer resources, as they lack access to specialty care and advanced therapies for stroke. Another possibility is the lack of clinical expertise in many small and medium hospitals because of the difficulties of attracting and retaining specialist physicians. These hospitals may also lack the infrastructure for rapid imaging procedures or highly specialized clinical support services such as neurocritical care and dedicated stroke units (50). These factors can lead to the hospital accommodation of patients with higher stroke severity and, consequently, higher expenses to larger hospitals.

A surprising observation in our study was that treatments ending in death had the highest expenses relative to treatments with other outcomes. This is in contrast to the findings of Liu Xie et al. in China, who found that hospitalization costs for surviving patients were approximately five times higher than for patients who died(20). The discrepancy could stem from more complex procedures and specialized therapies because of the acute condition of dying patients or their stay in the ICU and the difference in hospital Accommodation and nursing tariffs for ICU beds.

Compared to other studies, one of the weaknesses of this study is that ischemic and unspecified strokes were combined in one category. By reviewing patients' files with a neurologist, we found that the number of unspecified strokes is more than ischemic strokes, and the proportion of ischemic strokes is unacceptable and does not match with other studies (15, 16, 24, 47, 48). Therefore, we recommend policymakers use practical measures to sensitize physicians to record medical diagnoses and correct stroke related coding accurately.

Suggestions and future research

It was impossible to extract comorbidity and stroke severity data from the IHIO databases. As such, we advise policymakers to encourage physicians to detailed registration of stroke and reflect on stroke severity indices and comorbidity data in electronic patient files.

More research is needed to solve the knowledge gaps in our study. Future studies may benefit from taking into account clinical variables such as disease severity and comorbidities. In future studies, socioeconomic indicators such as patient income and education level can also be considered determinants of hospitalization costs and in-hospital mortality.

For peer review only

According to the study results, reducing the length of stay and encouraging reasonable prescription and consumption of drugs are effective strategies for policymakers and healthcare authorities to control hospitalization expenses.

Conclusion

Hospitalization expenses and mortality rates can be associated with numerous factors, many of which may help develop evidence-based policies. Populations of stroke patients insured by the Iranian Fund and regions with higher hospitalization expenses and in-hospital mortality should be a priority target for policymakers to improve effective medical care outreach and increase access to affordable hospitalization and medications. Migration to universal health insurance can effectively reduce the inequality gap between all insured patients. Applying cost-effective stroke prevention strategies in the younger population (Aged 0–49 years) is strongly recommended.

Acknowledgements

We thank Dr. Ali Shojaee and his colleagues at NCHIR and IHIO for their cooperation in collecting research data

Author contributions

ZK, SE, RD, AG, MY, and M.S.H contributed to the study design. ZS and ZK contributed to data collection. ZK analyzed, interpreted the data and produced the initial manuscript. SE is the Study supervision. ZK, SE, RD, AG, MY, and M.S.H made critical revisions to the manuscript. All authors have read and approved the final version of the manuscript.

Funding

This work was supported by Iran National Science Foundation (Gran No. 98029140).

Competing Interest

No potential conflict of interest was reported by the author(s).

Ethics and consent

This research was part of a PhD thesis approved by the Ethics Committee of Tehran University of Medical Sciences (code: IR.TUMS.SPH.REC.1398.229).

Article summary

Globally, stroke is the second most common cause of mortality, and the stroke burden is increasing. This study shows hospitalization expenses, in-hospital mortality, and their determinants in Iran. Stroke patients under the Iranian Fund insurance coverage and those residing in regions with higher hospitalization expenses and mortality should be priority target populations for policymakers for effective medical care. Migration to universal health insurance and stroke prevention strategies to the younger population are strongly recommended.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Availability of data and materials

Data are available upon reasonable request.

Supplemental material

Supplementary table 1

Supplementary table 2

Supplementary table 3

Refrences:

1. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, et al. 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. The Lancet. 2020;396(10258):1204-22.
2. Mensah George A, Roth Gregory A, Fuster V. The Global Burden of Cardiovascular Diseases and Risk Factors. Journal of the American College of Cardiology. 2019;74(20):2529-32.
3. Rosengren A, Smyth A, Rangarajan S, Ramasundarahettige C, Bangdiwala SI, AlHabib KF, et al. Socioeconomic status and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study. The Lancet Global Health. 2019;7(6):e748-e60.
4. Amini M, Zayeri F, Salehi M. Trend analysis of cardiovascular disease mortality, incidence, and mortality-to-incidence ratio: results from global burden of disease study 2017. BMC Public Health. 2021;21(1):401.
5. Alwan A. Global status report on noncommunicable diseases 2010: World Health Organization; 2011.
6. Sarrafzadegan N, Mohammmadifard N. Cardiovascular disease in Iran in the last 40 years: prevalence, mortality, morbidity, challenges and strategies for cardiovascular prevention. Archives of Iranian medicine. 2019;22(4):204-10.
7. Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A. Growing Epidemic of Coronary Heart Disease in Low- and Middle-Income Countries. Current Problems in Cardiology. 2010;35(2):72-115.
8. Eisavi M, Mazaheri E, Rezapour A, Vahedi S, Hadian M, Jafari A. The cost-effectiveness and cost-utility of statin drug for the treatment of patients with cardiovascular disease, a systematic review. International Journal of Preventive Medicine. 2021;12(1):39.
9. Roth Gregory A, Mensah George A, Johnson Catherine O, Addolorato G, Ammirati E, Baddour Larry M, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. Journal of the American College of Cardiology. 2020;76(25):2982-3021.
10. Farzadfard MT, Thrift AG, Amiri A, Kapral MK, Hashemi P, Sposato LA, et al. Five-Year Case Fatality Following First-Ever Stroke in the Mashhad Stroke Incidence Study: A Population-Based Study of Stroke in the Middle East. Journal of Stroke and Cerebrovascular Diseases. 2018;27(4):1085-9.
11. Salehi M, Amiri A, Thrift AG, Kapral MK, Sposato L, Behrouz R, et al. Five-Year Recurrence Rate and the Predictors Following Stroke in the Mashhad Stroke Incidence Study: A Population-Based Cohort Study of Stroke in the Middle East. Neuroepidemiology. 2018;50(1-2):18-22.
12. Morovatdar N, Thrift AG, Stranges S, Kapral M, Behrouz R, Amiri A, et al. Socioeconomic Status and Long-Term Stroke Mortality, Recurrence and Disability in Iran: The Mashhad Stroke Incidence Study. Neuroepidemiology. 2019;53(1-2):27-31.
13. Darba S, Safaei N, Mahboub-Ahari A, Nosratnejad S, Alizadeh G, Ameri H, et al. Direct and Indirect Costs Associated with Coronary Artery (Heart) Disease in Tabriz, Iran. Risk Manag Healthc Policy. 2020;13:969-78.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

14. Hendriks ME, Kundu P, Boers AC, Bolarinwa OA, te Pas MJ, Akande TM, et al. Step-by-step guideline for disease-specific costing studies in low- and middle-income countries: a mixed methodology. Global Health Action. 2014;7(1):23573.
15. Pucciarelli G, Rebora P, Arisido MW, Ausili D, Simeone S, Vellone E, et al. Direct Cost Related to Stroke A Longitudinal Analysis of Survivors After Discharge From a Rehabilitation Hospital. Journal of Cardiovascular Nursing. 2020;35(1):86-94.
16. Aminde LN, Dzudie A, Mapoure YN, Tantchou JC, Veerman JL. Estimation and determinants of direct medical costs of ischaemic heart disease, stroke and hypertensive heart disease: evidence from two major hospitals in Cameroon. Bmc Health Services Research. 2021;21(1):13.
17. Diestro JDB, Omar AT, Sarmiento RJC, Enriquez CAG, Castillo LLC-D, Ho BL, et al. Cost of hospitalization for stroke in a low–middle-income country: Findings from a public tertiary hospital in the Philippines. International Journal of Stroke. 2021;16(1):39-42.
18. Shojaee A. Estimated pharmaceutical costs of the Iran Health Insurance Organization until 2030 to achieving universal health coverage [Ph.D. thesis in health policy]: Tehran University of Medical Sciences, School of Public Health, Department of Health Management and Economics, Tehran, Iran; 2022.
19. Jo C. Cost-of-illness studies: concepts, scopes, and methods. Clin Mol Hepatol. 2014;20(4):327-37.
20. Liu C, Luo L, Duan L, Hou S, Zhang B, Jiang Y. Factors affecting in-hospital cost and mortality of patients with stroke: Evidence from a case study in a tertiary hospital in China. The International Journal of Health Planning and Management. 2021;36(2):399-422.
21. Mosadeghrad AM. Iran: Hospital Accreditation: Future Directions. Healthcare Systems:: CRC Press; 2018. p. 297-303.
22. Yousefinezhadi T, Mosadeghrad AM, Arab M, Ramezani M, Sari AA. An Analysis of Hospital Accreditation Policy in Iran. Iran J Public Health. 2017;46(10):1347-58.
23. Mehraban S, Raghfar H. The Place of Health Insurance in Reducing Catastrophic Health Expenditure. Iranian Journal of Economic Studies. 2018;7(2):239-54.
24. Dodd S, Bassi A, Bodger K, Williamson P. A comparison of multivariable regression models to analyse cost data. Journal of evaluation in clinical practice. 2006;12(1):76-86.
25. Zhu D, Xuefeng S, Nicholas S, Chen S, Ding R, Huang L, et al. Medical Service Utilization and Direct Medical Cost of Stroke in Urban China. International Journal of Health Policy and Management. 2020:-.
26. Schroeck FR, Jacobs BL, Bhayani SB, Nguyen PL, Penson D, Hu J. Cost of New Technologies in Prostate Cancer Treatment: Systematic Review of Costs and Cost Effectiveness of Robotic-assisted Laparoscopic Prostatectomy, Intensity-modulated Radiotherapy, and Proton Beam Therapy. European Urology. 2017;72(5):712-35.
27. Wang G, Zhang Z, Ayala C, Dunet DO, Fang J, George MG. Costs of hospitalization for stroke patients aged 18-64 years in the United States. Journal of Stroke and Cerebrovascular Diseases. 2014;23(5):861-8.
28. Alene M, Assemie MA, Yismaw L, Ketema DB. Magnitude of risk factors and in-hospital mortality of stroke in Ethiopia: a systematic review and meta-analysis. BMC Neurology. 2020;20(1):309.
29. Kaduka L, Muniu E, Oduor C, Mbui J, Gakunga R, Kwasa J, et al. Stroke mortality in Kenya's public tertiary hospitals: a prospective facility-based study. Cerebrovascular diseases extra. 2018;8(2):70-9.
30. Labodi LD, Kadri C, Valentin YN, Christian N, Jean KB. Intra-hospital mortality of stroke and its predictive factors in a reference hospital in Ouagadougou, Burkina Faso. Brain. 2017;1(3):1-6.
31. Nimptsch U, Mansky T. Trends in acute inpatient stroke care in Germany--an observational study using administrative hospital data from 2005-2010. Dtsch Arztebl Int. 2012;109(51-52):885-92.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

32. He Q, Wu C, Luo H, Wang Z-Y, Ma X-Q, Zhao Y-F, et al. Trends in In-Hospital Mortality among Patients with Stroke in China. PLOS ONE. 2014;9(3):e92763.
33. Ovbiagele B. Nationwide Trends in In-Hospital Mortality Among Patients With Stroke. Stroke. 2010;41(8):1748-54.
34. 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.
35. Buisman LR, Tan SS, Nederkoorn PJ, Koudstaal PJ, Redekop WK. Hospital costs of ischemic stroke and TIA in the Netherlands. Neurology. 2015;84(22):2208-15.
36. Brown DL, Boden-Albala B, Langa KM, Lisabeth LD, Fair M, Smith MA, et al. Projected costs of ischemic stroke in the United States. Neurology. 2006;67(8):1390.
37. Feigin VL, Krishnamurthi RV, Parmar P, Norrving B, Mensah GA, Bennett DA, et al. Update on the global burden of ischemic and hemorrhagic stroke in 1990-2013: the GBD 2013 study. Neuroepidemiology. 2015;45(3):161-76.
38. Matizirofa L, Chikobvu D. Analysing and quantifying the effect of predictors of stroke direct costs in South Africa using quantile regression. BMC Public Health. 2021;21(1):1560.
39. Boachie MK, Thsehla E, Immurana M, Kohli-Lynch C, Hofman KJ. Estimating the healthcare cost of overweight and obesity in South Africa. Global health action. 2022;15(1):2045092.
40. GBD Compare. Accessed June 1, 2022.2019 [Available from: https://vizhub.healthdata.org/gbd-compare/].
41. Hunt P, MacNaughton G. Impact assessments, poverty and human rights: a case study using the right to the highest attainable standard of health. 2006.
42. Nygren-Krug H. questions and answers on health and human rights. Geneva: World Health Organization. 2002.
43. Diestro JD, Omar A, Sarmiento RJ, Enriquez CA, Chua-De Castillo LL, Ho BL, et al. Cost of Hospitalization for Stroke in a Low-Middle Income Country: Findings from a Public Tertiary Hospital in the Philippines. Neurology. 2020;94(15).
44. Patel BM, Reinert NJ, Sridharan ND, Thirumala PD. Predictive Factors of Perioperative Stroke-Related Mortality Following Vascular Surgery: A Retrospective Analysis. Journal of Stroke and Cerebrovascular Diseases. 2021;30(7):105833.
45. Woo SH, Marhefka GD, Cowan SW, Ackermann L. Development and Validation of a Prediction Model for Stroke, Cardiac, and Mortality Risk After Non‐Cardiac Surgery. Journal of the American Heart Association. 2021;10(4):e018013.
46. Yin X, Huang L, Man X, Jiang Y, Zhao X, Zhao L, et al. Inpatient cost of stroke in Beijing: a descriptive analysis. Neuroepidemiology. 2018;51(3-4):115-22.
47. Namale G, Kamacooko O, Makhoba A, Mugabi T, Ndagire M, Ssanyu P, et al. Predictors of 30-day and 90-day mortality among hemorrhagic and ischemic stroke patients in urban Uganda: a prospective hospital-based cohort study. BMC Cardiovascular Disorders. 2020;20(1):442.
48. Vieira LGD, Safanelli J, de Araujo T, Schuch HA, Kuhlhoff MHR, Nagel V, et al. The cost of stroke in private hospitals in Brazil: a one-year prospective study. Arquivos De Neuro-Psiquiatria. 2019;77(6):393-403.
49. Safanelli J, Vieira LGD, de Araujo T, Manchope LFS, Kuhlhoff MHR, Nagel V, et al. The cost of stroke in a public hospital in Brazil: a one-year prospective study. Arquivos De Neuro-Psiquiatria. 2019;77(6):404-11.
50. Hammond G, Luke AA, Elson L, Towfighi A, Joynt Maddox KE. Urban-rural inequities in acute stroke care and in-hospital mortality. Stroke. 2020;51(7):2131-8.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Supplementary Table 1: *Total and daily hospitalization expenses for stroke patients, stratified by LoS and stroke type*

Cost title	Length of stay	Ischemic and unspecified stroke			Hemorrhagic stroke			Total		
		Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)
Daily	3–4 Days	5,966 (41.91)	47.39 (38.74)	38.89 (32.47–50.45)	1,207 (24.55)	69.81 (53.11)	53.88 (35.72–87.43)	7173 (37.46)	51.16 (42.34)	39.82 (32.74–54.52)
	5–7 Days	3,939 (27.67)	45.88 (26.42)	37.40 (30.69–51.92)	1,291 (26.26)	66.75 (54.33)	53.19 (33.85–85.29)	5230 (27.31)	51.03 (36.54)	39.01 (31.17–59.65)
	8–14 Days	2,653 (18.64)	51.77 (28.71)	43.71 (32.48–64.51)	1,243 (25.28)	68.19 (40.60)	60.91 (37.98–86.54)	3896 (20.34)	57.01 (33.84)	47.83 (33.75–71.80)
	+15 Days	1,676 (11.77)	65.47 (25.66)	64.34 (45.17–83.13)	1,175 (23.90)	77.48 (30.62)	77.28 (56.97–94.42)	2851 (14.89)	70.43 (28.43)	69.78 (48.96–87.82)
	Total	14,234 (100)	49.91 (33.01)	40.55 (32.45–58.56)	4,916 (100)	70.43 (46.09)	62.84 (38.12–89.11)	19150 (100)	55.18 (37.89)	43.59 (33.28–68.42)
Total	3–4 Days	5,966 (41.91)	162.20 (139.71)	132.48 (107.92–172.84)	1,207 (24.55)	242.30 (179.14)	187.38 (124.32–306.27)	7173 (37.46)	175.68 (150.09)	137.11 (109.73–189.96)
	5–7 Days	3,939 (27.67)	265.98 (155.88)	217.63 (172.82–304.83)	1,291 (26.26)	392.65 (322.52)	307.06 (202.75–488.36)	5230 (27.31)	297.25 (216.67)	230.17 (177.02–351.16)
	8–14 Days	2,653 (18.64)	529.59 (330.42)	437.23 (315.24–658.01)	1,243 (25.28)	703.41 (438.76)	615.61 (382.24–897.54)	3896 (20.34)	585.05 (377.21)	476.74 (327.85–738.70)
	+15 Days	1,676 (11.77)	2,064.65 (1,672.31)	1,550.01 (966.96–2,569.02)	1,175 (23.90)	2,359.48 (1,741.98)	1,933.03 (1,245.50–2,938.63)	2851 (14.89)	2,186.46 (1,707.32)	1,712.48 (1,065.78–2,737.02)
	Total	14,234 (100)	482.59 (844.53)	214.62 (137.94–436.62)	4,916 (100)	904.41 (1,225.34)	457.96 (230.71–1,031.14)	19150 (100)	590.91 (974.44)	252.93 (148.84–564.98)

All prices are in United States dollars (USD)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Supplementary Table 2: *Hospitalization expenses of stroke patients, stratified by age, gender, and stroke type*

Gender and age	Ischemic & unspecified stroke			Hemorrhagic stroke			Total		
	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)
Female									
<= 49	563 (8.15)	456.62 (906.75)	198.82 (133.56 – 428.98)	352 (15.74)	995.71 (1261.70)	572.56 (256.87 – 1,211.20)	915	664.01 (1088.92)	277.98 (149.71 – 676.39)
50-59	724 (10.49)	442.64 (881.36)	189.96 (125.29 – 360.61)	357 (15.96)	1,000.84 (1313.37)	504.39 (231.29 – 1,186.64)	1081	627.16 (1076.06)	245.68 (142.10 – 554.24)
60-69	1488 (21.55)	402.85 (687.18)	192.45 (128.68 – 364.44)	561 (25.08)	897.96 (1220.08)	469.04 (214.79 – 1,124.72)	2,049	538.48 (893.77)	229.92 (138.31 – 497.03)
70-79	1888 (27.35)	443.90 (706.97)	216.00 (138.42 – 434.51)	517 (23.11)	865.73 (1215.32)	397.12 (218.10 – 883.55)	2,405	534.62 (859.93)	242.72 (146.42 – 511.87)
>=80	2,241(32.46)	555.94 (952.02)	243.80 (1,48.71 – 501.09)	450 (20.12)	777.03 (1019.16)	428.45 (222.21 – 932.71)	2,691	592.91 (966.90)	267.05 (154.36 – 558.26)
Total	6,904 (100)	472.35 (827.31)	214.50 (137.17 – 429.76)	2237 (100)	897.98 (1205.46)	464.40 (223.74 – 1,061.53)	9,141	576.54 (951.83)	248.78 (147.21 – 548.24)
Male									
<= 49	638 (8.70)	483.86 (802.50)	224.67 (147.09 – 439.71)	528 (19.71)	921.90 (1182.40)	490.04 (258.64 – 1,124.66)	1,166	682.22 (1,015.95)	321.18 (171.21 – 713.06)
50-59	998 (13.62)	420.51 (774.66)	195.58 (136.48 – 369.83)	417 (15.57)	786.23 (1070.87)	407.45 (208.33 - 843.83)	1,415	528.36 (887.94)	233.97 (144.53 – 487.07)
60-69	1745 (23.81)	464.32 (817.73)	197.94 (134.52 – 408.41)	646 (24.11)	993.32 (1349.58)	487.30 (248.01 – 1,129.69)	2,391	607.25 (1,017.19)	244.44 (146.69 – 562.82)
70-79	1,587 (21.65)	530.91 (986.53)	212.87 (136.80 – 439.23)	518 (19.34)	1,024.30 (1493.00)	430.39 (244.68 – 1,126.28)	2,105	652.38 (1,151.83)	251.50 (148.60 – 594.44)
>=80	2,362 (32.22)	519.47 (847.65)	237.55 (144.44 – 515.68)	570 (21.28)	790.20 (995.06)	427.48 (224.92 – 907.96)	2,932	572.12 (884.59)	262.89 (151.02 – 589.50)
Total	7,330 (100)	492.24 (860.37)	214.81 (138.73 – 442.42)	2,679 (100)	909.78 (1241.90)	450.83 (236.76 – 998.03)	10,009	604.04 (994.50)	257.22 (150.45 – 583.32)
Male and female									
<= 49	1,201 (8.44)	471.09 (852.71)	212.25 (140.17 – 429.76)	880	951.42 (1214.57)	529.70 (257.41 – 1,160.20)	2,081	674.21 (1,048.44)	304.06 (160.26 – 693.46)
50-59	1,722 (12.10)	429.81 (821.02)	194.27 (131.41 – 362.57)	774	885.22 (1192.90)	437.79 (218.01 – 973.65)	2,496	571.15 (974.90)	239.34 (143.99 – 522.35)
60-69	3,233 (22.71)	436.04 (760.96)	194.83 (131.70 – 383.88)	1,207	948.99 (1291.36)	481.02 (229.98 – 1,127.90)	4,440	575.52 (962.72)	236.24 (143.18 – 533.64)
70-79	3,475 (24.41)	483.64 (847.15)	215.09 (137.56 – 434.71)	1,035	945.09 (1363.05)	409.51 (230.25 – 987.57)	4,510	589.58 (1,008.35)	246.88 (147.54 – 541.56)
>=80	4,603 (32.34)	537.23 (900.07)	240.22 (145.99 – 507.95)	1,020	784.39 (1005.29)	428.45 (222.43 – 912.99)	5,623	582.07 (924.88)	265.47 (152.46 – 575.93)
Total	14,234 (100)	482.59 (844.53)	214.62 (137.94 – 436.62)	4,916	904.41 (1225.34)	457.96 (230.71 – 1,031.14)	1,9150	590.91 (974.44)	252.93 (148.54 – 564.98)

All prices are in United States dollars (USD)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Supplementary Table 3: *Hospitalization expenses of stroke patients, stratified by death/life, gender, and stroke type*

Gender and age	Ischemic & unspecified stroke			Hemorrhagic stroke			Total		
	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)	Number (percent)	Mean (SD)	Median (25^{th} – 75^{th} percentile)
Female									
Life	5835 (84.55)	350.56 (570.56)	188.31(128.98-331.17)	1575 (70.41)	789.02 (1168.02)	373.11(192-854.05)	7410 (81.06)	443.75 (760.49)	210.02(134.96-411.68)
Death	1066 (15.45)	1138.98 (1457.76)	569.11(322.81-1351.50)	665 (29.69)	1157.22 (1253.54)	720.05(359.21-1395.45)	1731 (18.94)	1145.96 (1382.74)	615.81(335.59-1367.67)
Total	6,901 (100)	472.35 (827.31)	214.50(137.17-429.76)	2240 (100)	897.98 (1205.46)	464.40(223.74-1061.53)	9,141 (100)	576.54 (951.83)	248.78(147.21-548.24)
Male									
Life	6272 (85.60)	372.59 (626.53)	189.17(131.76-341.63)	1862 (69.43)	762.07 (1053.46)	377.38 (204.67-820.38)	8134 (81.27)	461.75 (763.80)	215.19(138.68-423.95)
Death	1055 (14.40)	1203.59 (1489.29)	683.92(352.82-1429.33)	820 (30.57)	1246.43 (1538.64)	694.95(359.49-1504.62)	1875 (18.73)	1222.28 (1510.77)	689.55(355.70-1460.08)
Total	7327 (100)	492.24 (860.37)	214.81(138.73-442.42)	2682 (100)	909.78 (1241.90)	450.83(236.76-998.03)	10009 (100)	604.04 (994.50)	257.22(150.45-583.32)
Male and female									
Life	12107 (85.09)	361.97 (600.28)	188.76(130.19-335.48)	3437 (69.83)	774.42 (1107.35)	374.53(196.88-834.00)	15544 (81.17)	453.17 (762.25)	212.49(137.11-418.69)
Death	2121 (14.91)	1171.11 (1473.53)	629.47(335.90-1392.40)	1485 (30.17)	1206.49 (1418.36)	699.47(359.21-1472.28)	3606 (18.83)	1185.65 (1451.03)	654.33(344.63-1410.20)
Total	14228 (100)	482.59 (844.53)	214.62(137.94-436.62)	4922 (100)	904.41 (1225.34)	457.96(230.71-1031.14)	19150 (100)	590.91 (974.44)	252.93(148.84-564.98)

All prices are in United States dollars (USD)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cross sectionalreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	#3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	#4	Present key elements of study design early in the paper	4
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	4
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	4-5

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Bias	#9	Describe any efforts to address potential sources of bias	NA
Study size	#10	Explain how the study size was arrived at	4
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	4-5
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	4-6
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	5-6
Statistical methods	#12c	Explain how missing data were addressed	4-5
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	5-6
Statistical methods	#12e	Describe any sensitivity analyses	NA
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	6
Participants	#13b	Give reasons for non-participation at each stage	NA

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

For peer review only

Participants	#13c	Consider use of a flow diagram	
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	6
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	4
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	6-7
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-8
Main results	#16b	Report category boundaries when continuous variables were categorized	6-8
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-8
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	6-8
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8-10

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.

Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	8-10
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	8-10
Generalisability	#21	Discuss the generalisability (external validity) of the study results	2
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

None The STROBE checklist is distributed under the terms of the Creative Commons Attribution License CC-BY. This checklist can be completed online using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2022-067573 on 13 December 2022. Downloaded from http://bmjopen.bmj.com/ on April 18, 2024 by guest. Protected by copyright.