



BMJ Open Comparison of health service use and costs in stroke with and without comorbidities: a cross-sectional analysis using China urban medical claims data

Ruoxi Ding ¹, Dawei Zhu,¹ Yong Ma,² Xuefeng Shi ³, Ping He¹

To cite: Ding R, Zhu D, Ma Y, *et al.* Comparison of health service use and costs in stroke with and without comorbidities: a cross-sectional analysis using China urban medical claims data. *BMJ Open* 2020;**10**:e037032. doi:10.1136/bmjopen-2020-037032

► Prepublication history and additional material for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2020-037032>).

RD and DZ contributed equally.

Received 20 January 2020

Revised 08 November 2020

Accepted 17 November 2020



© Author(s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹China Center for Health Development Studies, Peking University, Beijing, China

²China Health Insurance Research Association, Beijing, China

³School of Management, Beijing University of Chinese Medicine, Beijing, China

Correspondence to

Dr Ping He;
phe@pku.edu.cn and
Dr Xuefeng Shi;
shixuefeng981206@163.com

ABSTRACT

Objectives Stroke is the leading cause of death and disability in China, but there is scarce of evidence on whether and to what extent comorbidity affects the stroke-related costs in health system. We examined the association between comorbidity and stroke-related health service utilisation and costs in urban China.

Settings The data used in this study were extracted by a 5% random sampling from claims data of China Urban Employees' Basic Medical Insurance and Urban Residents' Basic Medical Insurance from 2013 to 2016, which covered more than 93% of residents in urban China. The data included 89 cities and contained beneficiaries' demographic information, medical diagnoses and expenditures of outpatient and inpatients services.

Participants 382 906 patients with stroke were identified as the study population in this study.

Primary and secondary outcome measures The information on health service utilisation and cost was extracted based on the condition that stroke was claimed as the index disease.

Results Among 382 906 patients with stroke, 41.0% had a comorbidity. The estimated number of annual outpatient visits among patients with 0, 1, 2 and 3 or more comorbidities were 1.97, 2.30, 2.34 and 2.37, respectively. The annual outpatient expenditure increased from 762.4 (95% CI 746.9 to 777.8) RMB among patients without any comorbidities to 1156.4 (1132.7 to 1180.2) RMB among patients with three or more comorbidities. The increased utilisation and costs among patients with comorbidity were also observed for inpatient services. Stroke-related services utilisation and costs were significantly increased among patients who comorbid conditions like hypertension or chronic pulmonary diseases.

Conclusion Comorbidity among patients with stroke was associated with increased healthcare utilisation and cost. It poses an extra substantial healthcare burden in China. Our study provides information for both clinical management and health service planning and financing for patients with stroke.

INTRODUCTION

Stroke remains the leading cause of death and disability. According to the estimation based on Global Burden of Disease 2016 study, stroke caused 5.5 million deaths and

Strengths and limitations of this study

- This study, using the claims data of urban medical insurance, provided the most recent situation on comorbidity and its association with health service utilisation and costs among patients with stroke in urban China.
- This study employed the Elixhauser Index, which has been demonstrated to be a more comprehensive and better predictive tool for outcomes of people with stroke, to examine the association between comorbidity and stroke-related health service utilisation and costs in urban China.
- Our study quantified the extra burden of comorbidity on major types of health service utilisation and costs, which allows the governments to estimate the medical budget, optimise resource allocation and enhance modelling of the potential return on prevention investment.
- Extrapolation from our findings to the comorbid situation of patients with stroke in China should be cautious because the claims database we used was restricted to the urban population.
- The lack of related information on the time of occurrence of comorbidity and the cross-sectional data excluded the possibility to determine the sequence of comorbidities and stroke events for further analysis.

116 million disability-adjusted life years (DALYs) worldwide, and the proportional contribution of stroke-related DALYs and deaths to all diseases had increased to 5.28% and 10.11%, respectively.^{1 2} In China, the mortality rate of stroke has been reported to be four times greater than that in western developed nations.³ Every year approximately 1.6 million deaths and 2.5 million new cases occurred in this country, which made stroke exceed heart disease to become the leading cause of morbidity and mortality.⁴⁻⁶ The economic burden of stroke has also risen sharply, with annual increase rate higher than 110% during the first decade of the 21st

century, and the cost of stroke care has reached approximately ¥40 billion since 2011.⁷ As the population ageing, the stroke expenditure will become more burdensome to the entire society.

The majority of patients with stroke are diagnosed at an advanced age and often have concomitant chronic diseases. Stroke shared several potential risk factors with other chronic conditions like diabetes, hypertension, renal diseases and cancer, which further increase the prevalence of comorbidity among patients with stroke.⁸ Comorbidity was associated with exposure to complex pharmacological treatment and increased risk of adverse events, which has substantial impacts on both short-term and long-term health outcomes.^{9 10} Previous studies suggested that comorbidity in the general population incurred extra healthcare utilisation and expenditures.¹¹ Therefore, assessing the prevalence of comorbidity and the composite impact of comorbidity on stroke-related health service utilisation and costs in China would improve the financial predictability and prioritised prevention efforts.¹²

Currently, it is unknown that to what extent comorbidity, in terms of types and numbers, affects the stroke-related costs on health system in China. Previous research mainly focused on health outcomes of patients with stroke using the Charlson Comorbidity Index.¹³ In this study, we employed the Elixhauser Index, which has been demonstrated to be a more comprehensive and better predictive tool for outcomes of people with stroke,¹⁴ to examine the association between comorbidity and stroke-related health service utilisation and costs in urban China, using medical insurance claims data.

METHODS

Data source and study population

The data used in this study were extracted by a 5% random sampling from claims data of China Urban Employees' Basic Medical Insurance (UEBMI) and Urban Residents' Basic Medical Insurance (URBMI) from 2013 to 2016, which covered more than 93% of residents in urban China.¹⁵ The number of beneficiaries of UEBMI and URBMI in these 4 years had summed up to 2578 million (644.5 million per year on average). The data, which were collected and sampled by China Health Insurance Research Association, included 89 cities and contained beneficiaries' demographic information, medical diagnoses and expenditures of outpatient and inpatient services. The sample was drawn using systematic random sampling strategy with a random start. In brief, every K th record from a population of size N was selected, with the first sample record picked from a random number table. In such a way, a sample size of n was obtained, where $N/n \geq K$ (To clarify, the extracted data were cross-sectional data set in each year (2013, 2014, 2015 and 2016), so we cannot capture the first visit of a patient with stroke. Each patient had his/her own ID number, we further checked our sample to make sure there was no patient

counted twice in the extracted data). We extracted the medical information including the date of birth, date of visit, health institute name, primary diagnosis (classified according to International Classification of Diseases, 10th edition (ICD-10)) and city of residence. A total of 382 906 patients with stroke were identified in the dataset between 2013 and 2016, based on the 10th revision of the International Statistical Classification of Diseases (ICD-10) codes (G45, I60, I61, I62, I63 and I64 as the diagnosis code).

Patient and public involvement

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

Measures

Comorbidity

The Elixhauser's translated ICD-10 coding algorithms were applied to define comorbidities in our study sample.¹⁶ Two variables were used to measure the condition of comorbidity: having comorbid conditions (yes or no) and the number of comorbid conditions (0, 1, 2 or ≥ 3). For further analysis on specific types of comorbidity, we identified the eight most prevalent types of comorbidities as binary variables: hypertension (uncomplicated and complicated), diabetes (uncomplicated and complicated), chronic pulmonary diseases (CPD), peripheral vascular diseases (PVD), cardiac arrhythmias (CA), other neurological diseases (OND), peptic ulcer diseases excluding bleeding (PUD) and rheumatoid arthritis/collagen vascular diseases (RA).

Health service utilisation and costs

Based on previous studies on similar topic^{12 17 18} and the availability of information in our dataset, we chose stroke-related health service costs and utilisation as the dependent variables in this study. The information on health service utilisation and costs were extracted based on the condition that stroke was claimed as the index disease, which indicated that the health service utilisation and cost of this outpatient visit or inpatient admission were stroke related. Health service utilisation included the number of annual (calendar year, which means that the annual resources use and cost were the totals of stroke-related service utilisation and cost in a whole calendar year (2013, 2014, 2015 or 2016)) outpatient visits (including pharmacies, primary care, secondary and tertiary hospitals), the number of annual inpatient admissions (including primary care, secondary and tertiary hospitals), the number of annual inpatient days and 31 days hospital readmission (defined as patient's admission to a hospital within 31 days after being discharged from an earlier hospital stay). Health service costs were measured by the annual outpatient expenditure, annual inpatient expenditure, the annual outpatient out-of-pocket (OOP) expenditure and the annual inpatient OOP expenditure in RMB. All the expenditures included spending

on pharmacy, diagnostic tests/medical consumables and medical service fees.

Control variables

Control variables included gender (male or female), age group (0–44, 45–54, 55–64, 65–74, 75–84, 85 years or older), type of insurance (UEBMI or URBMI), year (2013, 2014, 2015 or 2016) and stroke type, which was categorised as ischaemic (I63), haemorrhagic (I60, I61, I62), transient cerebral ischaemic attacks (TIA) (G45) and undetermined (I64) based on ICD-10 codes.

Statistical analysis

Descriptive analysis was used to analyse the characteristics of the study sample. While adjusting for the above-mentioned control variables, associations between health service utilisation (outpatient visits, inpatient admissions, inpatient days and 31 days readmission) and the presence of comorbidity, the number of comorbidities and the type of comorbidity were evaluated by negative binomial regression since over-dispersion is present. And generalised linear model (GLM) with a gamma distribution and a log link was used to assess the associations of annual total and OOP healthcare costs with the presence of comorbidities, the number of comorbidities and the specific type of comorbidities. Annual average health service utilisation and costs were estimated based on the multivariate analysis (negative binomial regression and GLM).

A *p* value of less than 0.05 was considered statistically significant. The software Stata V.14 for Mac (StataCorp) was used for the statistical analysis.

RESULTS

Among 382 906 patients with stroke, 212 986 (55.6%) were male, 299 735 (78.3%) were covered by UEBMI and the mean age of the sample was 63.7 years. Approximately 64.9% of patients had ischaemic stroke, 27.3%, 7.7% and 0.1% had haemorrhagic stroke, undetermined type of stroke and TIA, respectively. The proportion of patients with none, one, two and three or more comorbidities was 59.0%, 23.2%, 9.4% and 8.5%, respectively. The most prevalent comorbid conditions were hypertension (22.9%), diabetes (18.7%), CPD (8.2%), PVD (3.8%), CA (2.7%), OND (2.5%), PUD excluding bleeding (1.9%) and RA/collagen vascular diseases (1.7%). Gender-specific results were also provided in [table 1](#).

Association between number of comorbidities and health service utilisation and cost among patients with stroke in urban China

[Figure 1](#) displays the comparison of health service utilisation and costs among patients with stroke by number of comorbidities, which was drawn based on the estimation from multivariate analyses (online supplemental appendix table 1). The annual outpatient total and OOP expenditure increased from 762.4 (95% CI 746.9,

777.8) and 306.7 (289.9, 323.5) among patients without any comorbidities to 1 156.4 (1 132.7, 1 180.2) and 516.4 (484.8, 548.0) RMB among patients with three or more comorbidities ([figure 1A,B](#)), respectively. Similarly, the annual inpatient total and OOP expenditure also increased with the number of comorbidities ([figure 1](#)). The estimated number of annual outpatient visits among patients with 0, 1, 2 and 3 or more comorbidities was 1.97, 2.30, 2.34 and 2.37 visits, respectively ([figure 1E](#)). The estimated number of annual inpatient admissions also increased with the number of comorbidities, with 1.18, 1.26, 1.34 and 1.43 admissions among patients with 0, 1, 2 and 3 or more comorbid conditions, respectively ([figure 1F](#)). The annual inpatient days and the probability of hospital readmission also increased with the number of comorbidities ([figure 1](#)). The result of generalised linear model showed statistical significance in all above-mentioned associations.

Association between main types of comorbidities and excess health service utilisation and cost among patients with stroke in urban China

[Figure 2](#) displays the association between each type of comorbidity and stroke-related health service utilisation and costs, which was drawn based on the results of multivariate analyses (online supplemental appendix table 2). In both annual outpatient total and OOP expenditure, diabetes and RA were associated with decreased cost, and other types of comorbidities were associated with increased cost ([figure 2AB](#)). And all types of comorbid conditions were significantly associated with increased annual inpatient expenditure ([figure 2C](#)), ranging from 13.1% ($=\exp^{0.12}-1$, $p<0.001$) in CPD to 62.1% ($=\exp^{0.48}-1$, $p<0.001$) in PVD. Except for CPD, PUD and RA, all other types of comorbid conditions were significantly associated with increased annual inpatient OOP expenditure ([figure 2D](#)). In annual outpatient service, except for patients with CA, among which the number of visits was significantly decreased by 0.94 ($=\exp^{-0.06}$, $p<0.001$) visits, other types of comorbidities were associated with increased number of visits, ranging from 1.04 ($=\exp^{0.04}$, $p<0.001$) in CPD to 1.20 ($=\exp^{0.18}$, $p<0.001$) visits in OND ([figure 2E](#)). In annual inpatient admissions, all types of comorbidities were associated with increased number of admissions ([figure 2F](#)). Some types of comorbidity, such as hypertension and diabetes, were associated with increased days of inpatient care and increased risk of hospital readmission ([figure 2G,H](#)).

DISCUSSION

This study, using claims data of urban medical insurance, is the first to provide the most recent situation on comorbidity and its association with health service utilisation and costs among patients with stroke in urban China. Our study estimated the prevalence and identified the main types of comorbidities, as well as its association with utilisation and costs of health service in Chinese patients with

Table 1 Characteristics of stroke patients in China urban medical insurance claims data 2013–2016

Characteristics	Total, N (%)	Male, N (%)	Female, N (%)
No of population	382 906	212 986	169 920
Insurance type			
UEBMI	299 735 (78.3)	174 780 (82.1)	124 955 (73.5)
URBMI	83 171 (21.7)	38 206 (17.9)	44 965 (26.5)
Year			
2013	60 928 (15.9)	34 853 (16.4)	26 075 (15.4)
2014	121 988 (31.9)	65 966 (31.0)	56 022 (33.0)
2015	94 563 (24.7)	53 548 (25.1)	41 015 (24.1)
2016	105 427 (27.5)	58 619 (27.5)	46 808 (27.6)
Agegroup			
0–44	38 239 (10.0)	20 383 (9.6)	17 856 (10.5)
45–54	55 897 (14.6)	31 572 (14.8)	24 325 (14.3)
55–64	92 307 (24.1)	52 605 (24.7)	39 702 (23.4)
65–74	97 073 (25.4)	53 835 (25.3)	43 238 (25.5)
75–84	80 452 (21.0)	44 625 (21.0)	35 827 (21.1)
85+	18 938 (5.0)	9966 (4.7)	8972 (5.3)
Stroke type			
Ischaemic	248 300 (64.9)	138 146 (64.9)	110 154 (64.8)
Haemorrhagic	104 541 (27.3)	58 225 (27.3)	46 316 (27.3)
Undetermined	29 571 (7.7)	16 340 (7.7)	13 231 (7.8)
TIA	494 (0.1)	275 (0.1)	219 (0.1)
No of comorbidities			
0	225 872 (59.0)	225 871 (59.0)	99 201 (58.4)
1	88 706 (23.2)	88 707 (23.2)	39 422 (23.2)
2	35 931 (9.4)	35 931 (9.4)	15 882 (9.4)
3+	32 397 (8.5)	32 397 (8.5)	15 415 (9.1)
Comorbid conditions			
Hypertension	87 758 (22.9)	48 072 (22.6)	39 686 (23.4)
Diabetes	71 621 (18.7)	38 478 (18.1)	33 143 (19.5)
Chronic pulmonary disease	31 433 (8.2)	16 766 (7.9)	14 667 (8.6)
Peripheral vascular disease	14 544 (3.8)	7853 (3.7)	6691 (3.9)
Cardiac arrhythmias	10 285 (2.7)	5240 (2.5)	5045 (3.0)
Other neurological disease	9641 (2.5)	5636 (2.7)	4005 (2.4)
Peptic ulcer disease	7133 (1.9)	3731 (1.8)	3402 (2.0)
Rheumatoid arthritis	6476 (1.7)	3232 (1.5)	3244 (1.9)

TIA, transient ischaemic attacks; UEBMI, Urban Employees' Basic Medical Insurance; URBMI, Urban Residents' Basic Medical Insurance.

stroke. Overall, more than 40% of patients have a comorbidity. Healthcare utilisation, and both total and OOP costs in outpatient and inpatient service were significantly higher among patients with a comorbidity than those without any comorbidities. And these costs and service use increased with the number of chronic conditions. We also found variations of outpatient and inpatient service utilisation and costs between individuals with different types of comorbid conditions.

The prevalence of comorbidities among patients with stroke in urban China (41.0%) was relatively lower than that in most developed countries. Prior studies showed that the prevalence of comorbidity varied widely between different regions, ranging from 44% in Denmark¹⁷ to 99% in Ontario, Canada.¹⁸ Different prevalence of comorbidity across studies might be caused by the heterogeneity of data sources, including the difference in selection, detection and classification.¹⁹ Besides, the medical insurance

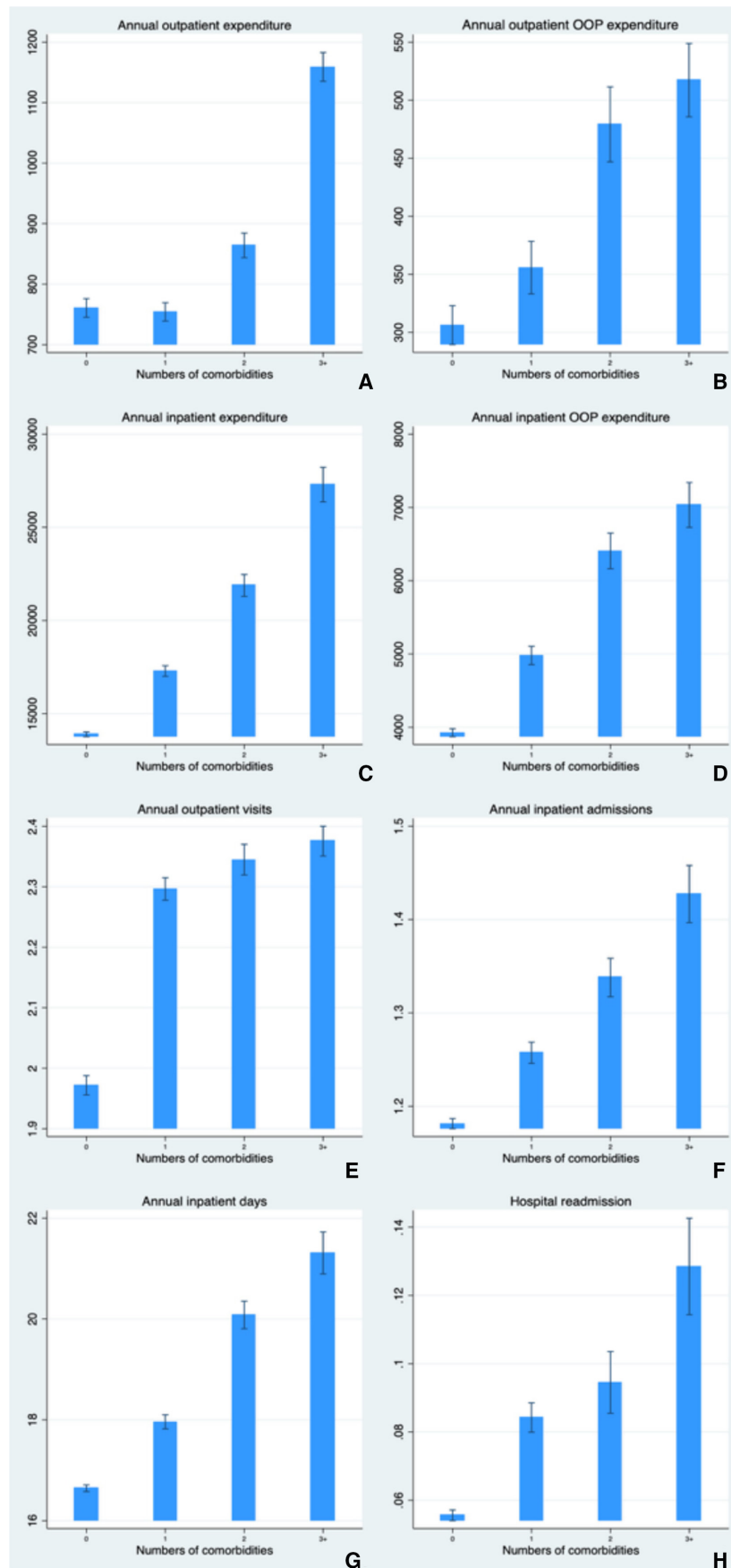


Figure 1 (A–H) Showed the predicted annual outpatient expenditure, annual outpatient OOP expenditure, annual inpatient expenditure, annual inpatient OOP expenditure, annual outpatient visits, annual inpatient admissions, annual inpatient days and hospital readmission by number of comorbidities among patients with stroke in urban China. OOP, out of pocket.

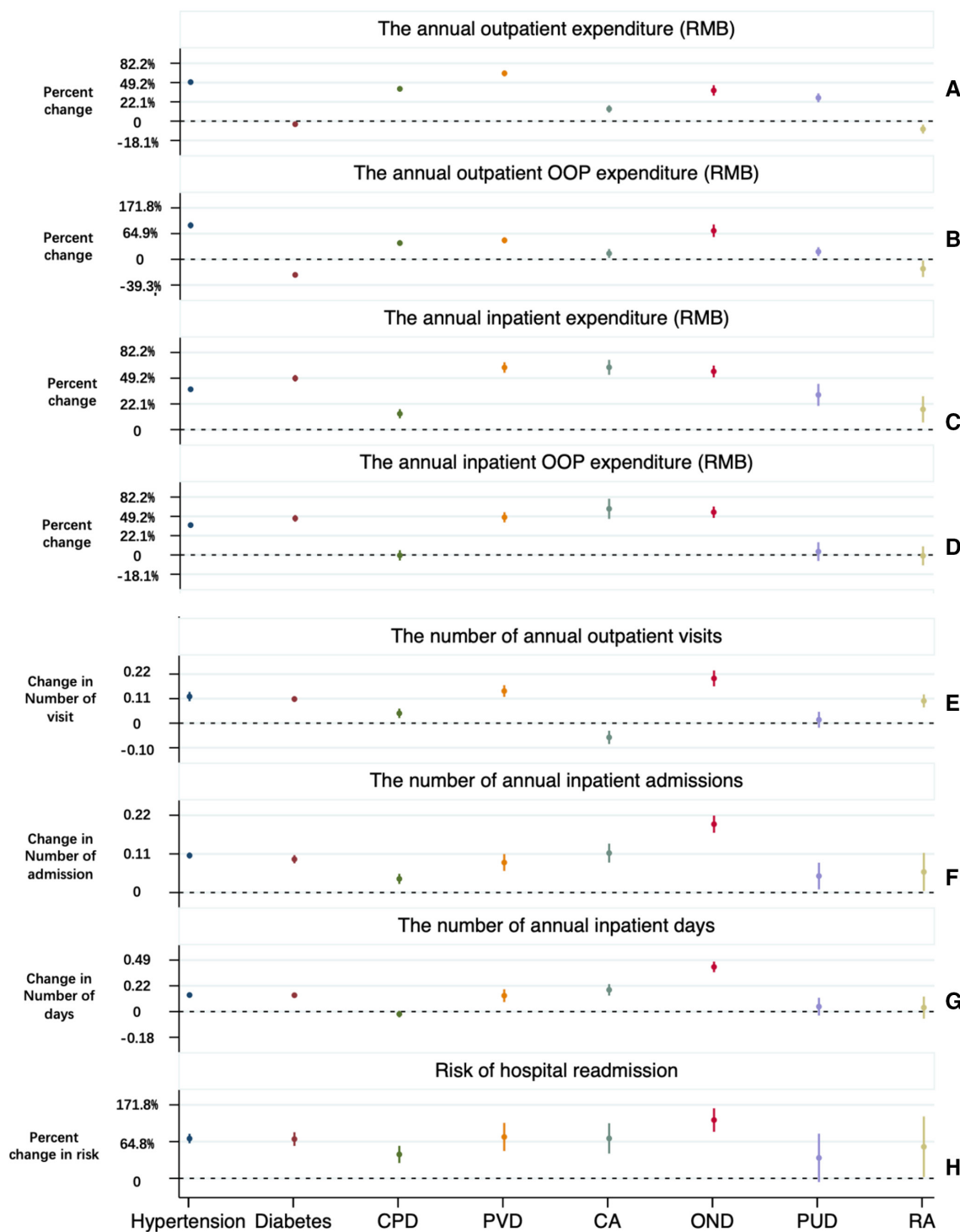


Figure 2 (A–H) Showed the adjusted association between eight main types of comorbidities and health service utilisation and cost (annual outpatient expenditure, annual outpatient OOP expenditure, annual inpatient expenditure, annual inpatient OOP expenditure, annual outpatient visits, annual inpatient admissions, annual inpatient days and hospital readmission) among patients with stroke in urban China. CA, cardiac arrhythmias; CPD, chronic pulmonary diseases; OND, neurological diseases; OOP, out of pocket; PUD, peptic ulcer disease; PVD, peripheral vascular disease; RA, rheumatoid arthritis.

information system in China has yet to be improved,²⁰ some clinicians may fail to fully record related disease information and thus the inaccuracy and incompleteness of patients' information could result in low comorbidity prevalence. The most commonly identified comorbidities were consistent with both international studies¹⁸ and

localised research¹³ in China. This could be explained by the fact that comorbidities like hypertension, diabetes, CPD, PVD, CA and neurological disease are closely related to stroke.^{21–25}

We demonstrated that the use and costs of stroke-related outpatient and inpatient service increased with

the number of comorbidities among patients with stroke in China. It has been suggested that the odds of functional recovery decreased as the number of comorbidities increase among patients with stroke,²⁶ and patients with multiple chronic conditions were more likely to spend a larger amount of health spending in a short term due to a relatively poorer prognosis including stroke recurrence, which was also pointed out by the association between the number of comorbidities and the risk of 31 days readmission in our study. This result suggests that the presence and the number of comorbidities should be considered by clinicians when formulating treatment plans, to improve prognosis and reduce the excess healthcare costs and service utilisation.

The presence of most types of comorbidities was associated with increased cost and utilisation of both outpatient and inpatient service. Our results showed that the annual stroke-related outpatient and inpatient expenditure among patients with hypertension, diabetes, CPD, were 13.1% to 64.2% more costly compared with that among their counterparts without these comorbidities, which have been shown to increase the severity and complexity of stroke by previous studies.^{12 26 27} However, we found that some types of comorbidity, such as diabetes, RA/collagen vascular diseases and CA, were associated with decreased costs and use of outpatient services among patients with stroke. It has been pointed out that pioglitazone and methotrexate, which were the widely used medication for type 2 diabetes and arthritis, were associated with a reduced risk of recurrent fatal and nonfatal stroke by previous studies.^{28 29} Such pharmacological treatment effects of comorbidities may indirectly reduce the medication expenditure for the prevention of recurrent stroke in outpatient services. On the other side, as a frequent and fatal complication of stroke, CA may harm individuals by haemodynamic instability and cause sudden cardiac death during the acute phase of stroke.²⁵ The decreased number of outpatient visits may be explained by the shortened survival in this population. Nevertheless, given a limited explanation for this issue, further in-depth investigation, such as analysis of the interaction between specific comorbidity and different types of pharmacological treatment is required to explore the causation.

Implications

This study provided a comprehensive assessment of the association between comorbidity and health service utilisation and costs in urban population in China. From the perspective of disease management, together with the estimation of specific comorbidities, our results provided further evidence on the impact of comorbidity on the treatment and performance of patients with stroke. Therefore, our results offered information for insurance providers and medical professionals to develop enhanced risk assessment protocols and tailored therapeutic interventions, as well as integrated care pathways for patients with stroke. Furthermore, our findings quantified the extra burden of comorbidity on major types of health

service utilisation and costs, which allows governments to estimate the medical budget, optimise resource allocation and enhance modelling of the potential return on prevention investment.

Limitation

Several limitations of this study should be noted. First, due to a lack of related information in the data source, we were unable to estimate the excess costs of comorbidity and potential associations according to stroke severity. Second, the diagnostic validity of comorbidity might be influenced by the heterogeneity of physician documentation and code assignment accuracy from different sites. Third, due to a lack of survival information in our dataset, we cannot identify patients lived less than 1 year, and these patients were also included in the analysis, which may result in potential bias to our result. Fourth, extrapolation from our findings to the comorbid situation of patients with stroke in China should be cautious because the claims database we used was restricted to the urban population. Lastly, the lack of information on the time of occurrence of comorbidity and the cross-sectional data excludes the possibility to determine the sequence of comorbidities and stroke events for further analysis. Despite of the above limitation, the main strength of this study is using the predominant urban basic insurance claims data, which universally covered urban residents in China,¹⁵ to identify comorbidities. The health insurance record is generally regarded as a relatively complete and valid source of information on the patient's health status³⁰ and thus provides an opportunity for us to examine comorbidity and its association with the use and costs of health services among patients with stroke in urban China.

CONCLUSION

Comorbidity among patients with stroke was associated with increased healthcare utilisation and cost. It poses an extra substantial healthcare burden in China. Research is warranted to further characterise the interaction between stroke and comorbidities, such as the investigation on the effect of pharmacological and treatment interactions on healthcare cost among patients with stroke. Our study provided information for relevant authorities to identify individuals with greater needs of health service by assessing comorbidity profiles for stroke care resources targeting. Insights from this study may also contribute to the design of integrated programmes to enhance the efficiency of healthcare, and to manage cost in the meantime.

Contributors RD initiated the study, analysed data and wrote the original manuscript. DZ provided advices on research design, data analysis and manuscript writing. XS and MY provided advices on manuscript writing and obtained the data. PH originated the study, obtained the funding, supervised all aspects of its implementation and contributed to writing the article. All authors contributed to and have approved the final manuscript.

Funding This study was funded by Peking University's Start-up Fund (BMU2018YJ004)

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Since the claims data we used were anonymised database and had no impact on patients' health and care, the informed consent was exempted. This study was approved by the Ethics Committee of Beijing University of Chinese medicine (No.2019BZHLL0201).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Data may be obtained from a third party and are not publicly available. The data were provided by China Health Insurance Research Association. These are third party data. Authors in this study have the right to use this dataset, but not the right to share and distribute. A deidentified minimal dataset of the quantitative data is available on request to researchers who meet the criteria for confidential information, by sending a request to phe@pku.edu.cn.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Ruoxi Ding <http://orcid.org/0000-0001-7504-0355>

Xuefeng Shi <http://orcid.org/0000-0001-7056-2912>

REFERENCES

- Johnson, C.O., GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the global burden of disease study 2016. *Lancet Neurol* 2019;18:439–58.
- Naghavi M, Abajobir AA, Abbafati C, et al. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the global burden of disease study 2016. *The Lancet* 2017;390:1151–210.
- China, I.O.o.M.o.H.o. Report on the third national survey of death causes. *China Cancer* 2008;17:2.
- Chen Z. The mortality and death cause of national sample areas. In: *The third national survey on the cause of death.*, 2008: 1, 14–15.
- Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. *Lancet Neurol* 2009;8:345–54.
- Zhou M, Wang H, Zeng X, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990–2017: a systematic analysis for the global burden of disease study 2017. *The Lancet* 2019;394:1145–58.
- PRC, M.o.H. 2010 annual Chinese healthcare statistics. Beijing: China Union Medical University Publication, 2010.
- Denti L, Artoni A, Casella M, et al. Validity of the modified Charlson comorbidity index as predictor of short-term outcome in older stroke patients. *J Stroke Cerebrovasc Dis* 2015;24:330–6.
- Falsetti L, Viticchi G, Tarquinio N, et al. Charlson comorbidity index as a predictor of in-hospital death in acute ischemic stroke among very old patients: a single-cohort perspective study. *Neurol Sci* 2016;37:1443–8.
- Calderón-Larrañaga A, Poblador-Plou B, González-Rubio F, et al. Multimorbidity, polypharmacy, referrals, and adverse drug events: are we doing things well? *Br J Gen Pract* 2012;62:e821–6.
- Cortaredona S, Ventelou B. The extra cost of comorbidity: multiple illnesses and the economic burden of non-communicable diseases. *BMC Med* 2017;15:216.
- Zhao Y, Condon J, Lawton P, et al. Lifetime direct costs of stroke for Indigenous patients adjusted for comorbidities. *Neurology* 2016;87:458–65.
- Si Y, Xiao X, Xiang S, et al. Mortality-specific comorbidity among inpatients with ischemic stroke in West China. *Acta Neurol Scand* 2019;140:100–6.
- Zhu H, Hill MD. Stroke: the Elixhauser index for comorbidity adjustment of in-hospital case fatality. *Neurology* 2008;71:283–7.
- Zhao C, Wang C, Shen C, et al. China's achievements and challenges in improving health insurance coverage. *Drug Discov Ther* 2018;12:1–6.
- Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43:1130–9.
- Schmidt M, Jacobsen JB, Johnsen SP, et al. Eighteen-year trends in stroke mortality and the prognostic influence of comorbidity. *Neurology* 2014;82:340–50.
- Gruneir A, Griffith LE, Fisher K, et al. Increasing comorbidity and health services utilization in older adults with prior stroke. *Neurology* 2016;87:2091–8.
- Janssen-Heijnen ML, Schipper RM, Razenberg PP, et al. Prevalence of co-morbidity in lung cancer patients and its relationship with treatment: a population-based study. *Lung Cancer* 1998;21:105–13.
- PR Newswire Association LLC. China medical information system industry report 2011, 2011. Biomedical market Newsletter. Available: U6 - ctx_ver=Z39.88-2004&ctx_enc=info%3Aofi%2Fenc%3AUTF-8&fr_id=info%3Aofid%2Fsummon.serialssolutions.com&rft_val_fmt=info%3Aofi%2Ffmt%3Akev%3Amtx%3Ajournal&rft.genre=article&rft.atitle=China+Medical+Information+System+Industry+Report%2C+2011&rft.jtitle=PR+Newswire&rft.date=2011-11-02&rft.pub=PR+Newswire+Association+LLC&rft.externalDBID=IBG&rft.externalDocID=A271659962¶mdict=en-US U7 - Newspaper Article
- Boehme AK, Esenwa C, Elkind MS, et al. Genetics, and prevention. *Circulation research* 2017;120:472–95.
- Peters SAE, Huxley RR, Woodward M. Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775,385 individuals and 12,539 strokes. *Lancet* 2014;383:1973–80.
- Sahathevan R, Brodtmann A, Donnan GA. Dementia, stroke, and vascular risk factors; a review. *Int J Stroke* 2012;7:61–73.
- Schwab P, Dhamane AD, Hopson SD, et al. Impact of comorbid conditions in COPD patients on health care resource utilization and costs in a predominantly Medicare population. *Int J Chron Obstruct Pulmon Dis* 2017;12:735–44.
- Kallmünzer B, Breuer L, Kahl N, et al. Serious cardiac arrhythmias after stroke: incidence, time course, and predictors--a systematic, prospective analysis. *Stroke* 2012;43:2892–7.
- Liu M, Domen K, Chino N. Comorbidity measures for stroke outcome research: a preliminary study. *Arch Phys Med Rehabil* 1997;78:166–72.
- Jia Q, Zhao X, Wang C, et al. Diabetes and poor outcomes within 6 months after acute ischemic stroke: the China national stroke Registry. *Stroke* 2011;42:2758–62.
- Wilcox R, Bousser M-G, Betteridge DJ, et al. Effects of pioglitazone in patients with type 2 diabetes with or without previous stroke: results from proactive (prospective pioglitazone clinical trial in macrovascular events 04). *Stroke* 2007;38:865–73.
- BioMed Central/Arthritis Research & Therapy. Arthritis medications reduce risk of heart attacks and strokes, study suggests, 2008. Science Daily. Available: www.sciencedaily.com/releases/2008/03/080306075231.htm [Accessed 7 March 2008].
- Janssen-Heijnen ML, et al. *Age and Co-Morbidity in Cancer Patients: A Population-Based Approach*. In: Balducci L, Extermann M, eds. *Biological basis of geriatric oncology*. Boston, MA: Springer US, 2005: 89–107.