

Is hypoglycemia expensive in China?

Kuixu Lan, PhD Candidate^{a,b,c}, Jian Wang, PhD^{d,e}, Stephen Nicholas, PhD^{f,g,h,i}, Qun Tang, BA^b, Alison Chang, BA^l, Junfang Xu, PhD^{k,*}

Abstract

Background: As a common medical emergency in individuals with diabetes, hypoglycemia events can impose significant demands on hospital resources. Based on diabetes patients with and without hypoglycemia, we assess the cost of hypoglycemic events on China's hospital system.

Method: Our study sample comprised 7110 diabetes episodes, including 1417 patients with hypoglycemia (297 patients with severe and 1120 with non-severe hypoglycemia) and 5693 diabetes patients without hypoglycemia. Data on patient social-demographics, length of hospital stay, and hospitalization costs were collected on each patient from Health Information System in Shandong province, China. The additional hospital costs caused by hypoglycemia were assessed by the cost difference between diabetes patients with and without hypoglycemia, including severe and non-severe hypoglycemia. China-wide hospital costs of hypoglycemia were estimated based on adjusted additional hospital costs, comprising inspection, treatment, drugs, materials, nursing, general medical costs, and other costs, caused by hypoglycemia, the prevalence of diabetes and hypoglycemia events, and the rates of hospitalization. Multiple sensitivity analyses were conducted to assess the impact of variations in the key input parameters on the primary estimates.

Results: Total hospital costs for patients with hypoglycemia (US\$3020.61) were significantly higher than that of patients without hypoglycemia (US\$1642.91). The average additional cost caused by hypoglycemia was US\$1377.70, with higher average costs of US\$1875.89 for severe hypoglycemia and lower average costs of US\$1244.76 for non-severe hypoglycemia. The additional hospital cost caused by severe and non-severe hypoglycemia patients was higher for the 60 to 75 year old group, married patients and patients accessing free medical services. Generally, hypoglycemic patients with Urban and Rural Resident Basic Medical Insurance incurred higher additional hospital costs than patients with Urban Employees Basic Medical Insurance. Based on these estimates, the total annual additional hospital costs arising from hypoglycemia events in China were estimated to be US\$67.52 million. Sensitivity analyses suggested that the costs of hypoglycemia events ranged up to US\$49.99 million to 67.52 million.

Conclusion: Hypoglycemic events imposed a substantial cost on China's hospital system, with certain subgroups of patients, such as older patients and those with free health insurance, using medical resources more intensively to treat hypoglycemia events. We recommend more effective planning of prevention and treatment regimes for hypoglycemia patients; further reform to China's health insurance schemes; and better hospital cost control for those accessing free hospital services.

Abbreviations: HIS = health information system, LOS = length of stay, URRBMI = Urban and Rural Resident Basic Medical Insurance.

Keywords: China, costs, hypoglycemia

Editor: Luis Mauricio Pinet Peralta.

This work was supported partly by the National Natural Science Foundation of China (Project no. 71702131) and Zhejiang University Education Foundation School of public health education fund health special fund.

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

^a School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan, ^b The Affiliated Hospital of Qingdao University, Qingdao, ^c NHC Key Laboratory of Health Economics and Policy Research, Shandong University, Jinan, ^d Dong Fureng Institute of Economic and Social Development, Beijing, ^e Center for Health Economics and Management at School of Economics and Management, Wuhan University, Wuhan, ^f School of Economics and School of Management, Tianjin Normal University, Tianjin, ^g Guangdong Institute for International Strategies, Guangdong University of Foreign Studies, Guangzhou, China, ^h TOP Education Institute 1 Central Avenue Australian Technology Park, Eveleigh, Sydney, ⁱ Newcastle Business School, University of Newcastle, University Drive, Newcastle, New South Wales, Australia, ^l Department of Anthropology, Princeton University, Princeton, USA, ^k Center for Health Policy Studies, School of Public Health, Zhejiang University School of Medicine, Hangzhou, China.

* Correspondence: Junfang Xu, School of Public Health, Zhejiang University School of Medicine, Hangzhou 310058, China (e-mail: junfangxuhappy1987@163.com).

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How to cite this article: Lan K, Wang J, Nicholas S, Tang Q, Chang A, Xu J. Is hypoglycemia expensive in China?. *Medicine* 2021;100:5(e24067).

Received: 12 November 2019 / Received in final form: 6 March 2020 / Accepted: 4 December 2020

<http://dx.doi.org/10.1097/MD.0000000000024067>

1. Introduction

The global population of diabetes mellitus sufferers has risen from 108 million in 1980 to 422 million in 2016, with an estimated 1.6 million deaths directly caused by diabetes in 2016.^[1,2] Hypoglycemia, an acute complication of diabetes related to a very low level of blood sugar (glucose), presents unique challenges to the optimal management of diabetes.^[3–6] Hypoglycemia prevalence among diabetes sufferers is reported to range from 12% to 30%, especially depending on the patient's treatment regimen.^[7–9] Severe hypoglycemia is most common among type 1 diabetes patients with a long disease duration and among type 2 diabetes patients with a long insulin therapy duration.^[10] A recent Chinese study found that during a mean follow-up period of 5.88 years, 43.7% of 4874 type 2 diabetes patients had at least 1 hypoglycemic episode, while 432 patients, or 3.9% of the sample, experienced at least one severe hypoglycemic episode.^[11] Surprisingly, hypoglycemia is often neglected as a risk among diabetes patients, with potentially significant health consequences for individuals and the health service system.^[12] McCoy et al reported that the mortality in diabetes patients who self-reported severe hypoglycemia 5 years earlier was 3.4-fold higher than diabetics without hypoglycemia.^[4] Nocturnal hypoglycemia is usually asymptomatic and difficult to detect, but may cause “sleep death”.^[13–15] Furthermore, hypoglycemia often causes falls, accidents, reduced ability to drive and work, and diminished cardiovascular functioning over time, which suggest hypoglycemia is associated with significant reductions in the quality of life, including the psychological burden among diabetes patients caused by the fear of hypoglycemic events.^[16–18]

Hypoglycemia, especially severe hypoglycemia, imposes a considerable economic burden on the health care system where hospitalization requires substantial medical resources, including inspections, treatment, drugs, materials, nursing, general medical, and other costs.^[19–21] An analysis of multiple US databases revealed almost 100,000 emergency treatments each year for insulin-related hypoglycemia, and nearly one third of these hypoglycemic events resulted in hospitalization care.^[22] The reported hospital costs of a severe hypoglycemic event vary from US\$80 to US\$5000, depending on the medical resources required.^[4] For high income European countries, studies show that the average costs of hypoglycemia were €1300 to 3300 (US \$1480–3758), mainly due to hospital admissions.^[23] Given the significant hospitalization costs of hypoglycemia incurred by diabetes patients, it is important to accurately estimate the medical costs to the healthcare system in order to implement hypoglycemia preventive strategies and improve management-based health service programs. Surprisingly, there is only limited research on hospital costs caused by hypoglycemia in China. Using data from diabetes patients with and without hypoglycemia, this study estimates the real-world hospital costs of hypoglycemic events on China's health system.

2. Methods

2.1. Data sources

Information on diabetes inpatients were collected from the hospital affiliated with Qingdao University, located in the east of Shandong province, between 1 January 2016 and 1 December 2018. Founded in 1898, the Qingdao University affiliated hospital provides medical services to Shandong province and

the surrounding provinces of Tianjin, Henan, Jiangsu, Anhui, and Hebei. This wide catchment area mitigates potential concern about the unrepresentativeness of using cost data from a single hospital located in 1 province to proxy national hypoglycemia costs. In addition, income per capita, health expenditures, and hospital costs were broadly comparable between Shandong province and China's national average data. The average income per capita in Shandong province was US\$5374 compared to the national average of US\$5893; health expenditure per capita was US\$276 versus the national average of US\$291; and the hospital costs per capita was US\$1080 versus the national average of US\$1125.^[24]

2.2. Data collection

Data were extracted from the Health Information System (HIS) at the Qingdao University affiliated hospital. The identification of diabetes was based on the ICD-10 codes of admission diagnoses recorded in the HIS. Hypoglycemia is defined by a blood glucose level less than 4.0 mmol/L for diabetes patients and severe hypoglycemia means blood glucose level less than 2.8 mmol/L that requires assistance by a third party to treat. Our sample comprised 7110 diabetes episodes, with 5693 inpatients without hypoglycemia and 1417 inpatients experiencing hypoglycemic events, comprising 297 patients with severe hypoglycemic events and 1120 patients with non-severe hypoglycemia. Only seven cases with incomplete HIS cost information were excluded from the sample. The following information was collected on each patient from the HIS: sex, age, marital status, occupation, health insurance types (the Urban Employee Basic Medical Insurance with a 60% to 70% reimbursement rate, Urban and Rural Resident Basic Medical Insurance (URRBMI) with a 40% to 50% reimbursement rate, free health services with a 100% reimbursement rate and no insurance with a 0% reimbursement rate), length of stay (LOS) in hospital, hospitalization date, and hospitalization costs (comprising inspection, treatment, drugs, materials, nursing, general medical costs, and other costs). Thus, hospitalization costs per patient per year in our study included all hospital related costs in 2016, 2017 and 2018 respectively. A major strength of the HIS is that it documents detailed, itemized and reliable cost data on all patient expenses incurred during hospitalization. All data were collected and recorded in accordance with the actual data on each patient.^[24,25]

2.3. Data analysis

The hospitalization costs per person per year (rather than the payment from health insurance company) related to hypoglycemia were measured by the cost difference between diabetes patients with and without hypoglycemic events. Therefore, the cost of hypoglycemia in our study means the costs of hypoglycemia among patients with diabetes. Non-hypoglycemic patients' costs provide a baseline, with additional costs added to the baseline for patients with hypoglycemic, non-severe hypoglycemic and severe hypoglycemic events. To estimate the national hospital costs of hypoglycemia, we multiplied the adjusted additional costs caused by hypoglycemia in our sample by the total number of patients with diabetes in China based on the 19.93% prevalence of hypoglycemia in our sample, comprising 4.08% prevalence of severe hypoglycemia and 15.85% non-severe hypoglycemia. A 1.5% rate of hospitalization

for diabetes patients was estimated by dividing the total number of diabetes hospitalizations by the total of diabetes patients based on data from China Health Statistics Yearbook 2018. The equation was: National hospital cost of hypoglycemia per year = adjusted additional hospital cost caused by hypoglycemia per year \times total number of diabetes \times prevalence of hypoglycemia \times hospitalization rate. Correspondingly, the national hospital cost of non-severe hypoglycemia per year = adjusted additional hospital cost caused by non-severe hypoglycemia per year \times total number of diabetes \times prevalence of non-severe hypoglycemia \times hospitalization rate. The national hospital cost of severe hypoglycemia per year = adjusted additional hospital cost caused by severe hypoglycemia per year \times total number of diabetes \times prevalence of severe hypoglycemia \times hospitalization rate.

Multiple sensitivity analyses were used to assess the impact of variations in the key input parameters on our primary cost estimates. Specifically, we estimated the total annual China-wide additional hospital costs caused by hypoglycemia by

- (1) using prevalence data of diabetes based on a systematic review of diabetes prevalence in China,^[26] which yielded a more conservative prevalence of diabetes compared to a survey of epidemiology and control of adult diabetes mellitus in China^[27];
- (2) assuming that 1.3%^[28] prevalence of severe hypoglycemia instead of 4.08%; and
- (3) using the median cost of hypoglycemia related hospital costs, instead of average additional costs.

Frequency, percentage, mean and standard deviations were used to describe the demographic information, LOS, and hospitalization costs. The hospital cost in the analysis was the average hospital costs per person, which means that if a patient made multiple inpatient visits in one year, the hospital costs was the total costs of all visits during the period. Generalized linear regression was conducted to assess the factors that influence the hospital costs among diabetes patients. Given the highly skewed distribution of hospital costs, a log₁₀ transformation of total

hospital cost was used as the dependent variable. The independent variables included experiencing hypoglycemia (or not), sex, age, marital status, health insurance, and hospital LOS. Moreover, all the costs were adjusted to eliminate the impact of inflation or deflation based on consumer price index. Mann–Whitney and Kruskal–Wallis test were used to examine whether there was differences in hospital costs among patients. $P < .05$ was considered the significant difference. All statistical analyses were performed using SPSS17.0.

2.4. Ethical review

This study used the health service utilization data collected from HIS database, does not include any private personal information and human data or tissue that require ethical approval and consent.

3. Results

In our sample, 19.93% (1417/7110) of diabetes inpatients had hypoglycemic events. The number of patients with severe and non-severe hypoglycemia was 297 and 1120 respectively. Compared to non-hypoglycemia patients, hypoglycemia patients displayed no significant differences in sex, age, marital status, and health insurance ($P > .05$), but it showed a statistically difference in LOS ($P < .05$). As shown in Table 1, among the diabetes patients with hypoglycemia, 52.36% were male; 51.10% were older than 60 years; 9.03% were single; and only 8.19% did not have health insurance. Among the diabetes patients without hypoglycemia, 47.80% were male; 42.75% were older than 60 years; 6.52% were single people and 11.47% had no health insurance. However, hypoglycemic patients had significantly longer hospital stays than patients without hypoglycemia (11.88 \pm 7.90 days versus 8.65 \pm 4.87 days).

Based on the HIS data recording all hospitalization costs, Supplementary Figure (<http://links.lww.com/MD/F498>) presents the hospital costs of diabetes patients with and without

Table 1
The characteristics of diabetes patients with and without hypoglycemia.

Items	Severe hypoglycemia		Non-severe hypoglycemia		Total hypoglycemia		Without hypoglycemia	
	Number	%	Number	%	Number	%	Number	%
Sex								
Male	151	50.8	591	52.8	742	52.36	2721	47.80
Female	146	49.2	529	47.2	675	47.64	2972	52.20
Age								
18–30	57	19.2	87	7.8	144	10.16	474	8.33
31–44	31	10.4	100	8.9	131	9.24	860	15.11
45–59	76	25.6	342	30.5	418	29.50	1945	34.16
60–74	108	36.4	444	39.6	552	38.96	1881	33.04
≥ 75	25	8.4	147	13.1	172	12.14	553	9.71
Marital status								
Married	246	82.8	1043	93.1	1289	90.97	5322	93.48
Single	51	17.2	77	6.9	128	9.03	371	6.52
Health insurance								
No	32	10.8	84	7.5	116	8.19	653	11.47
URBMI*	93	31.3	308	27.5	401	28.30	1309	22.99
UEBMI*	146	49.2	631	56.3	777	54.83	3274	57.51
Free medical service	26	8.8	97	8.7	123	8.68	457	8.03
Length of stay (d) ^a	12.36 \pm 7.95		11.75 \pm 7.88		11.88 \pm 7.90		8.65 \pm 4.87	

* UEBMI = Basic Medical Insurance for Urban Employees, URBMI = Basic Medical Insurance for Urban Resident.

^a With significant differences.

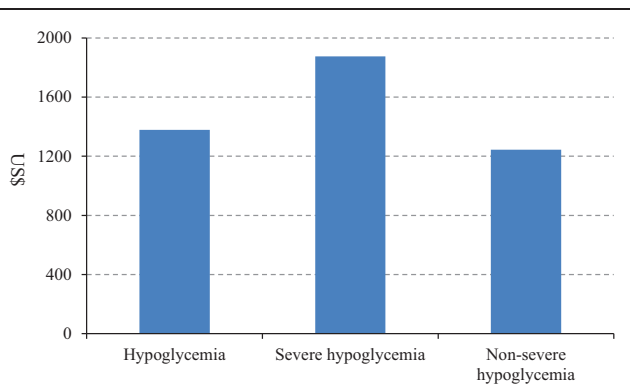


Figure 1. The additional hospital costs caused by hypoglycemia.

hypoglycemia. For patients with hypoglycemia, total hospital costs (US\$3020.61) and all cost components were significantly higher than that of patients without hypoglycemia (US\$1642.91). Figure 1 shows the average additional hospital cost caused by hypoglycemia was US\$1377.70, with the additional hospital costs of severe hypoglycemia US\$1875.89 and non-severe hypoglycemia US\$1244.76.

The total hospitalization costs by gender, age, and health insurance in Supplementary Table 1 (<http://links.lww.com/MD/F499>) were higher among patients with hypoglycemia than patients without hypoglycemia, and generally higher costs among severe hypoglycemia than that of non-severe hypoglycemia. The total hospital costs for hypoglycemia males (US\$3263.71) was higher than for females (US\$2752.11), and much higher than for non-hypoglycemic patients, both male (US\$1637.89) and female (US\$1647.54). The total hospital costs associated with severe hypoglycemia male (US\$3538.78) and female (US\$3498.13) patients were higher than for non-severe hypoglycemia male (US\$3193.20) and female (US\$2544.24) patients.

Figure 2 and supplementary Table 2 (<http://links.lww.com/MD/F500>) displays the components of the additional hospitalization costs caused by hypoglycemia, non-severe hypoglycemia and severe hypoglycemia by patient sex, age, and type of health insurance. The hospital costs components of severe hypoglycemia were much higher than the counterparts of non-severe hypoglycemia by sex, age, and health insurance. The additional hospital costs of hypoglycemia including severe and non-severe hypoglycemia were mainly due to drug costs (33.4%), followed by material costs (21.6%), treatment (21.4%), and inspection (14.7%) costs. The components of additional costs caused by hypoglycemia, especially severe hypoglycemia, were highest for the 60 to 75 year old group. The additional costs of severe hypoglycemia for patients with free medical services were the highest.

Regression results for the factors influencing hospitalization costs among diabetes patients are presented in Table 2, in which hypoglycemia patients have significantly higher hospitalization costs than non-hypoglycemia patients ($P < .05$). Male patients had significantly higher hospital costs than female patients ($P < .05$); older patients and patients with longer LOS had higher costs than younger and shorter LOS patients ($P < .05$); and patients who could use the medical resources for free had higher hospital cost than insured and uninsured patients ($P < .05$).

Table 3 estimated the baseline total additional hospital costs caused by hypoglycemia in China were US\$67.52 million,

comprising US\$53.70 million for non-severe hypoglycemia and US\$13.82 million for severe hypoglycemia. Sensitivity analyses suggests that variations in diabetes prevalence, hypoglycemia prevalence and hospital costs did not significantly influence our cost estimates. The total annual additional hospital costs ranged from 49.99 million to 67.52 million. The impact of the alternative scenarios was modest, and our baseline estimates relatively insensitive to alternative assumptions.

4. Discussion

We found that the prevalence of non-severe hypoglycemia (15.85%) was higher than that of severe hypoglycemia (4.08%), but the prevalence of hypoglycemia, especially non-severe hypoglycemia, was lower than some other studies.^[29] This was mainly due to the samples in our study were inpatients that receiving professional care serviced by physicians and nurses in hospital settings. We did not include diabetes patients who treated hypoglycemia successfully at home by themselves. Based on our estimates, the hospitalization costs of diabetes patients with hypoglycemia (US\$3020.61) was 83.86% greater than patients without hypoglycemia (US\$1642.91). This was related to patients with hypoglycemic events were more likely to visit a hospital and have long LOS as well as more costs ($P < .05$). This result is consistent with previous studies.^[30,31] For example, in a U.S. study, patients with hypoglycemic events had a 71% increase in diabetes-related medical costs during a 1 year period compared to patients without hypoglycemia.^[30] Other studies also show that hypoglycemic episodes among patients with diabetes more than doubled the length of hospital stays and increased hospital costs by almost a quarter.^[31] Consistent with other research, hospitalization costs in our study were higher among patients with severe hypoglycemia (US\$3518.80) than non-severe hypoglycemia patients (US\$2887.67), which reflected the more intensive use of inspections, drugs, materials, and nursing resources among patients with severe hypoglycemic events (see Fig. 2).

Hypoglycemia costs varied across different healthcare systems because of the impact of severity, the LOS and number of patients, the diverse quality of service and extent of care. For example, we estimated that the total annual hospital cost caused by severe hypoglycemia was US\$13.82 million, averaging US\$1875.9 per episode. For the US, the economic costs of hypoglycemia were estimated to be US\$900 million each year and the direct costs for severe hypoglycemia requiring assistance from doctors to be US\$1161 for each episode.^[32] In Italy, the average cost of hypoglycemia was €1911 (US\$2175) and the yearly total cost of severe hypoglycemia were estimated to be €23 (US\$26.1) million, which was mainly caused by hospital admissions.^[33] The hospitalization costs caused by hypoglycemia were calculated at €3023-3298 (US\$3440-3753) in Germany, but only €1400 (US\$1593) in Spain.^[34,35]

Of course, these hospitalization costs underestimate the full costs for hypoglycemia patients. Indirect costs, including economic losses caused by the reduction in work days and health-related quality of life for diabetes patients and their families, and other direct non-medical costs, such as transportation costs, were not included in these studies. Moreover, most hypoglycemia patients incurred costs related to being treated at home without incurring hospitalization expenses, which were also not included in these studies.^[32,34-36]

As shown in Figure 2, the hospital cost differences between hypoglycemia and non-hypoglycemia patients were mainly due

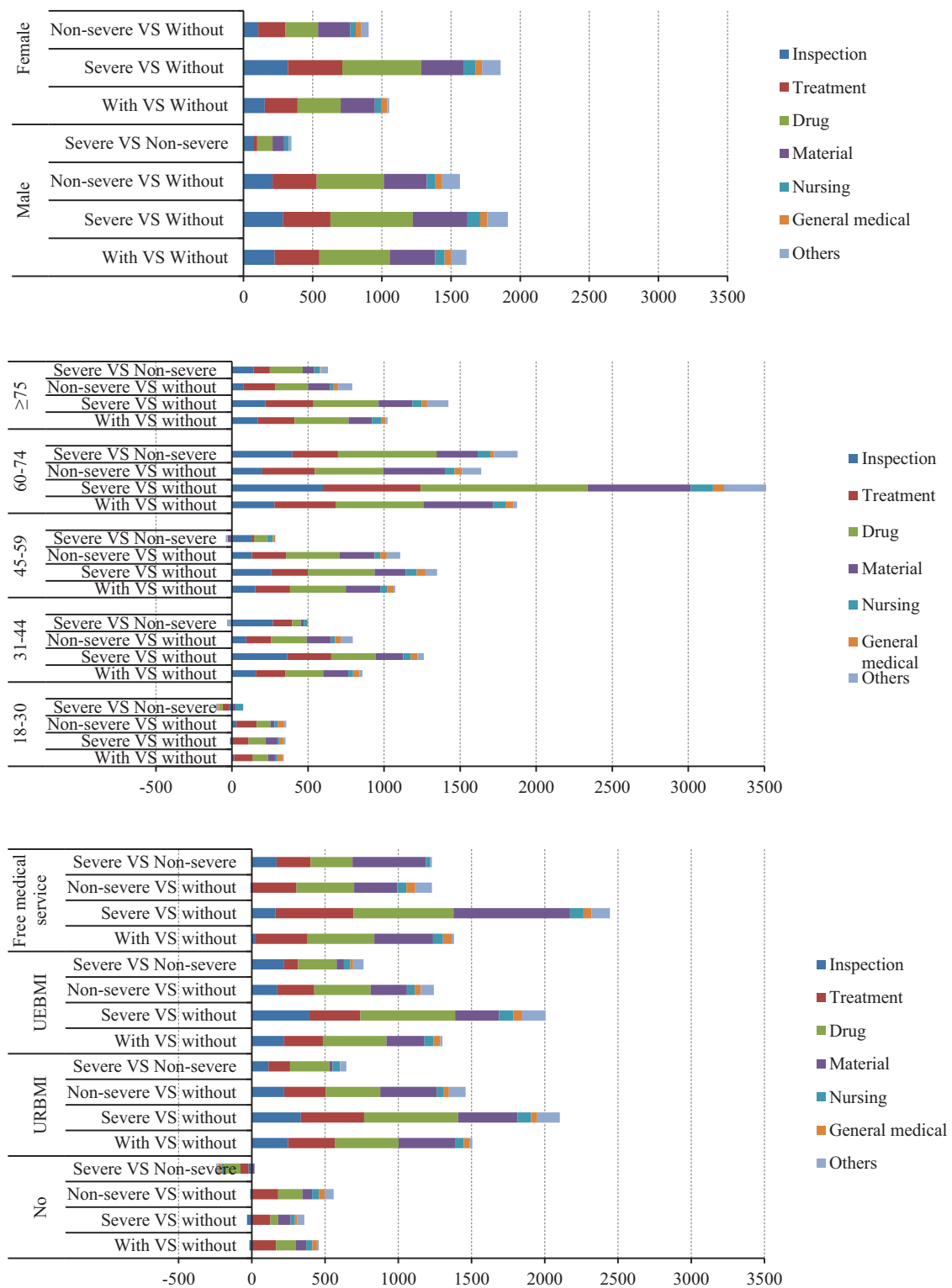


Figure 2. Additional hospital costs of hypoglycemia, non-severe and severe patients by sex, age, and health insurance (US\$).

to the utilization of medicine and material resources in hospital. This can be partly explained by the additional treatment therapies of hypoglycemic events in hospitals – for example, sugar-containing foods or intravenous injection of glucose. Moreover, the cost difference between severe, non-severe patients was the

highest for the 60 to 75 years old group. The reason is related to the fact that 60 to 75 year old people are more likely to have type 2 diabetes, thus they are most likely to be treated with insulin, which is associated with an increased risk of hypoglycemia compared to other therapies. Hypoglycemia patients insured with

Table 2
The influencing factors of hospital costs among diabetes patients^a.

Variables	B	95%CI		P
With hypoglycemia	.073	.060	.086	.000
Sex				
Male	.016	.005	.026	.003
Age				
<30	-.199	-.231	-.168	.000
30–45	-.143	-.165	-.122	.000
45–60	-.070	-.088	-.051	.000
60–75	-.026	-.044	-.008	.005
Marital status				
Married	.019	-.011	.050	.214
Health insurance				
No	-.087	-.111	-.064	.000
URRBMI	-.037	-.057	-.016	.000
UIBMI	-.002	-.021	.017	.860
LOS	.033	.032	.034	.000

LOS = length of stay, UIBMI = Basic Medical Insurance for Urban Employees, URBMI = Basic Medical Insurance for Urban Resident.

^a The reference group was non-hypoglycemic, females, aged 75 or above, single and receiving free medical services respectively.

URRBMI patients incurred higher additional hospital costs than Urban Employee Basic Medical Insurance patients generally, and had a lower rebate, imposing higher out-of-pocket expenses on URRBMI patients, and their families. There is scope for further reform of China's health insurance schemes to ensure that hospitalization costs, reimbursement rates and out-of-pocket expenses should not vary across schemes for different categories of residents. However, compared to the other health insurance schemes, the additional costs of severe hypoglycemia were significantly greater for patients with free medical services. Not surprisingly, patients with free medical services, which means health insurance paid 100% of medical costs, without any out-of-pocket expenses, incurred more medical resources with higher hospital costs probably due to some combination of over-servicing by medical staff or demands by patients for excessive medical services. Better hospital cost control for patients with free medical care is required. Patients with no insurance incurred the lowest hospital costs, which might reflect under-servicing of uninsured patients, who were likely to be poor and reside in rural areas. An information and education campaign for uninsured residents should provide advice on the benefits of health insurance, especially for diabetes and hypoglycemic patients.

Since hypoglycemia constitutes a substantial burden to healthcare systems, prevention strategies that could reduce the health care burden would be important to be investigated. For example, educating diabetes patients, their relatives and physicians is fundamental to reducing the number of severe

Table 3
Estimated additional hospitalization costs caused by hypoglycemia in China (US\$, Million).

Items	Baseline	Sensitivity analysis		
		Diabetes prevalence	Hypoglycemia prevalence	Median cost
Hypoglycemia	67.52	63.44	67.52	49.99
Non-severe	53.70	50.45	63.12	39.76
Severe	13.82	12.98	4.40	10.23

hypoglycemia episodes.^[37] Improved self-monitoring of blood glucose is important for diabetes patients, especially insulin treated patients, to prevent and cure hypoglycemia. Physicians should review the signs and symptoms of hypoglycemia regularly with diabetes patients, particularly when their therapies are associated with a high risk of hypoglycemic events. Also, the availability of alternative treatment options, such as Insulin Degludec, which has been shown to significantly reduce the risk of hypoglycemia compared with Glargine Insulin, should be considered.^[21] Studies have also shown that comprehensively assessing comorbidities reduces the risk of hypoglycemia, and that simplified or carefully selected treatment regimens in older patients are important for managing hypoglycemia.^[38]

5. Limitations

Our study has a number of limitations. First, we used patient administrative data to analyse the hospital costs caused by hypoglycemia. Therefore, hypoglycemia patients who were successfully treated in pre-hospital settings were not incorporated in the analysis. Future studies should address the burden of non-hospital costs on the health-related quality of life for diabetes patient when estimating hypoglycemia costs. Second, we used data from 1 hospital in Shandong Province, and samples should be drawn from other provinces in future studies, even though the key hospital cost indicators are comparative between Shandong province and the whole country. Moreover, patients who have hypoglycemia may likely to have other health conditions, which could also influence the hospital costs. However, because of the limitation of HIS database, other health conditions for diabetes patients were not available.

6. Conclusion

Our results highlighted that the costs caused by hypoglycaemic events in a hospital setting impose a significant cost burden on China's healthcare system. The 60 to 75 years old age group tend to more intensively use hospital medical resources to treat hypoglycaemia, while the 18 to 30 year old group, single patients and those without insurance had the lower hospital costs. Given the significant costs imposed on the health system by hypoglycaemia patients, effective care programs on the prevention or efficient treatment of hypoglycaemia among diabetes patients is required and further reform to China's health insurance schemes, especially for unemployed rural and urban residents, is a priority.

Acknowledgments

The authors would like to thank the hospital for their support of the data.

Author contributions

Conceptualization: Jian Wang, Stephen Nicholas, Junfang Xu.

Investigation: Qun Tang.

Writing – original draft: Kuixu Lan.

Writing – review & editing: Stephen Nicholas, Alison Chang.

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