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Burden of patients with visual impairment: a questionnaire survey in two tertiary hospitals in Beijing

Journal:	BMJ Open
Journal.	
Manuscript ID	bmjopen-2019-030561
Article Type:	Research
Date Submitted by the Author:	20-Mar-2019
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Keywords:	economic burden, catastrophic healthcare expenditure, quality of life, visual impairment



1 2	1	Burden of patients with visual impairment: a questionnaire survey in two
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26 27	15	
28 29	16	Keywords: economic burden, catastrophic healthcare expenditure, quality of life, visual
30	17	impairment
31 32	18	
33 34	19	
35 36	20	Word count: 2326
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Abstract **Objectives** To quantify the economic burden, prevalence of catastrophic healthcare expenditure (CHE) and the quality of life (QoL) of patients with visual impairment (VI) in China. Methods We conducted a questionnaire survey from March to May 2016 by structured face-to-face interviews of patients with VI. The economic burden was estimated by calculating participants' direct costs covered in 2015 and the definition of CHE was out of pocket costs exceeding 30% of annual household income. QoL was weighed by health utility value using time trade off valuation techniques. Results A total of 302 patients were included and 298 completed questionnaires were eligible for the study, yielding a response rate of 98.7%. Annual direct costs per patient caused by VI were US\$6988.6±10834.3 and 70.3% were direct medical costs. 32.2% households suffered from CHE, especially for less wealthy patients who were blind, living in rural areas and without medical insurance. The health utility value was rated at 0.65 on average and patients who were blind, aged 51-57, living alone and insured by commercial medical insurance had relatively poorer QoL. Conclusion Our study quantified the economic burden and QoL of patients with VI in China, indicating a substantial burden and poor life quality. Preferential medical insurance policies should be designed in relation to people with VI to further reduce the health inequalities, avoid the CHE and promote QoL.

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42 Article Summary
43 Strengths and limitations of this study
44 1. To our knowledge, this is the first study to quantify the prevalence of CHE and the QoL of
45 patients with VI in China.
46 2. The face-to-face interviews were conducted in tertiary general hospitals in Beijing, which
47 might result in potential sample selection bias.
48 2. The module of the later of

48 3. There could have been recall bias because the data were self-reported by the patients.

51 INTRODUCTION

With a rapidly aging population in mainland China, visual impairment (VI) is emerging as a public health concern ^[1]. According to the World Health Survey (2003), one in five adults reported some degree of far visual difficulty^[2]. In 2015, the number of people with moderate VI or worse was estimated to be 253 million globally ^[3]. More than 80% of the global total of VI occurs in developing countries ^[4], and 26.5% of the total of VI occurs in China ^[5]. The prevalence of VI in China is 0.94% yet, as for the people older than 50, the prevalence rises to 5.8%. In Tibet, one of the highest and harshest human habitations on earth, the prevalence is 13.2%^[6-8].

The main impact of VI is a diminished ability to perform daily activities ^[9], which often results in high health expenditures and the loss of independence ^[10]. The total financial cost of VI worldwide was estimated to be \$3 trillion in 2010 or \$4,030 per person who is visually impaired ^[11]. In addition to the economic burden, VI also has extensive social ramifications in terms of participation in society, employment and quality of life (QoL). The World Health Organization (WHO) estimated that 1% of the total global burden of disease measured as Disability-Adjusted Life Years (DALY) was attributable to VI increased by 47% from 12.9 million DALYs in 1990 to 18.8 million DALYs in 2010 [12-13].

The burden of VI has been well researched in countries such as the U.S., Australia, and some European countries ^[13-16]. However, little is known about the economic burden and QoL of patients with VI in China. Therefore, we aim to achieve an assessment to: quantify the economic burden; identify the prevelence of catastrophic healthcare expenditure (CHE); and describe the QoL of patients with VI in China.

74 METHODS

75 Questionnaire design

We conducted a questionnaire survey by structured face-to-face interviews of patients with VI. The study questionnaire included standardized items developed by reviewing related research as well as items developed by consulting ophthalmologists and pharmacists. The survey questionnaire included four parts: sociodemographic information, clinic-related information, economic burden and QoL.

81 Sociodemographic information

Age, gender, ethnicity, educational level, profession, marital status, living status, current
living place, medical insurance, personal income, household size and household income were
included.

85 Clinic-related information

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Healthcare service utilization, treatment history and visual condition were included. Visual condition was divided into three categories based on the WHO vision visual acuity (VA) categorization principles: moderate VI (6/60<VA<6/18), severe VI (3/60<VA<6/60) and blind (VA<3/60) [17].

Economic burden

Economic burden was estimated by calculating participants' direct costs covered in 2015, including direct medical costs and direct non-medical costs.

Quality of life

OoL was weighed by the "utility value" to evaluate patients' perception of their own health, using time trade-off (TTO) valuation technique ^[18]. TTO determined the length of lifetime the respondent would be willing to forego to live in perfect health ^[19], by asking "Assuming you will only live for 10 years, what is the maximum amount of that time, if any, you would be willing to trade for a return to permanent perfect vision (1.0) during the years that remain?"

The questionnaire was designed and optimized by ophthalmologists and clinical pharmacists. After conducting a pilot field research study in a tertiary hospital in Beijing, all of the experts agreed that the questionnaire was valid. The items and descriptions of survey questionnaire were shown in Appendix 1.

Recruitment and sampling

Participants were eligible for inclusion in the study if they were diagnosed with moderate VI or worse in both eyes (VA<6/18) and were physically and mentally able to participate in the survey and agreed to participate in the study. We excluded participants who were pregnant, had a concomitant malignant disease or an inability to complete the questionnaire.

Data collection and quality control

A questionnaire survey was conducted from March to May 2016 by structured face-to-face interviews of patients admitted in ophthalmic department in two tertiary hospitals in Beijing. All the investigators were trained for standard processes via a workshop. During the face-to-face interviews, the investigators read all the contents of the questionnaire to establish that patients with VI could hear and understand the questions. The interviews lasted approximately 0.5-1 hours to collect detailed information. Survey data were recorded on paper forms and translated using Epidata3.1.

Outcome measures

Catastrophic healthcare expenditure CHE was defined as out-of-pocket (OOP) for healthcare over a year that exceeded a certain proportion of a household's income. This threshold had been defined in many ways: one of the most common definitions was OOP costs exceeding 30% of annual household income ^[20]. Quality of life Answers to the time trade-off questions were converted to utility value. Z = (10 - N)/10Z was the health utility value; N was the number of years that the respondents were willing to trade for a return to permanent perfect vision. Utility values were anchored on a scale between 0 (the preference for death rather than living in the patient's current state of health) and 1(a perception of perfect health)^[18]. **Statistical analysis** Costs and income were assessed in Chinese Yuan (CNY) and converted into United States dollars (USD) uniformly based on exchange rates in June 1, 2016 (1 USD=6.5889 CNY) to make the results more comparable to other published studies. STATA 14.0 was applied to conduct the following statistical analysis: (a) descriptive analysis of the participants' demographic information, healthcare service utilization, expenditures, CHE prevalence and QoL; (b) bivariate chi-square test on the difference of CHE prevalence and QoL value between subgroups. The level of statistical significance was p < p0.05 (two-sided). **Ethics Statement** Ethics committee approval obtained from Peking University Institution Review Board (No. IRB00001052-16003). All participants were informed by an information sheet and have signed the declaration of consent to participate in the study. RESULTS **Description of demographic characteristics** A total of 302 patients were included and 298 completed questionnaires were eligible for this study, yielding a response rate of 98.7%. Patients' demographic data are shown in **Table** 1. The mean age in sample was 65.4 and there were slightly fewer males (47.7%). Most of the participants were married (85.2%), living with family (94.6%) and in urban areas (71.8%). 41.3% of the participants were covered by Urban Employee Basic Medical Insurance (UEBMI), 23.8% by New Cooperative Medical Scheme (NCMS), 14.1% by Government

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1	150	
2 3	156	Medical Insurance (GMI), and 13.4% by Urban Resident Basic Medical Insurance (URBMI).
4 5	157	Of the visual-related health conditions reported, 58.4% had moderate VI, 28.9% had severe
6	158	VI, and 12.8% were blind. 71.8% of the participants had been suffered from VI for more than
7 8	159	one year. The annual personnel income and household income of the participants were
9	160	US\$6,266.4±10,403.2 and US\$13,457.8±16,711.9, respectively.
10 11	161	
12 13	162	Healthcare service utilization
14	163	As shown in Table 1, the average number of healthcare service utilization due to VI within
15 16	164	1 year was 9.7 outpatient visits, ranging from 4.8 visits (cataract) to 16.7 visits (glaucoma).
17 18	165	Average number and length of inpatient hospital visits were 0.6 visit within 1 year and 2.7
19	166	days of hospital staying per visit.
20 21	167	
22 23	168	Direct costs
24	169	The total direct medical costs were US\$6,988.6±10,834.3 in 2015, including direct medical
25 26	170	costs of US\$4,909.8±8,981.7 (70.3%) and direct non-medical costs of US\$2,078.8±4,430.6
27 28	171	(29.7%).
29 30	172	As shown in Table 2 , of the direct medical costs, outpatient fees represented the largest
31	173	costs at US\$3,408.5 (69.4%), followed by inpatient costs at US\$1,369.5 (27.9%). Except
32 33	174	outpatient and inpatient costs, the participants also purchased drugs by themselves in retail
34 35	175	pharmacy (2.7%). Only 10.6% of the outpatient costs, 24.4% of the inpatient costs and 2.6%
36	176	of the self-purchased drug costs were covered by the medical insurance. Average total OOP
37 38	177	costs per patient were US\$4211.6 (85.8%).
39 40	178	Direct non-medical costs occurred mostly due to long-term home care at US\$1,216.6
41	179	(58.5%). Nutrition or assistive devices, food and accommodation, escort, transportation, and
42 43	180	home modifications costs accounted for 13.3%, 8.5%, 7.7%, 7.2% and 4.7% respectively.
44 45	181	The specific costs among different groups were shown in the Appendix 2 .
46 47	182	The specific costs among unreferit groups were shown in the Appendix 2.
48	182	Prevalence of CHE
49 50	185	Patients with VI paid in direct medical costs an average amount equal to 111.5% of their
51 52		
53	185	individual annual income and 51.9% of their household's annual income. As shown in Table
54 55	186	1, 32.2% households suffered from CHE caused by VI. The prevalence of CHE was generally
56	187	correlated with the severity of VI (moderate VI 28.2%, severe VI 31.4%, blind 52.6%; p<0.05).
57 58	188	Patients living in rural areas generally had greater risk of CHE compared with urban residents
59 60	189	(47.6%, 26.2%; p<0.001). Of all of the different types of medical insurances, the CHE
	190	prevalence of patients without medical insurance and insured by NCMS ostensibly

191 outweighed those insured by GMI and CMI (none 50.0%, NCMS 47.9%, GMI 16.7%, CMI

192 21.4%; p<0.01). In relation to the patients' economic status, the less wealthy patients (those
193 with the lowest or lower economic status) were much more likely to encounter CHE than
194 wealthier patients (p<0.01).

QoL

As shown in **Table 1**, the value of QoL was 0.65 on average and correlated with the severity of VI (moderate VI 0.69, severe VI 0.65, blind 0.49; p<0.01). Middle-aged patients (51-70) had the poorest life quality (0.58; p<0.001) and patients living alone had relatively poorer QoL than living with family (0.58, 0.68; p<0.01). Of all of the different types of medical insurances, the health utility values of patients insured by CMI were significantly lower than those insured by URBMI (0.49, 0.81; p<0.01).

DISCUSSION

This study quantified the economic burden and QoL of VI patients in China, indicating a substantial burden of VI, with considerable variation among the different age groups, rural or urban, type of medical insurance, visual condition and economic status.

We found annual direct cost per patient caused by VI in China was much lower than the US ^[13]. The direct medical costs occurred mostly due to outpatient visit, which was inconsistent with formal findings in the US. and Australia that direct medical costs occurred mostly due to hospitalization ^[13]. Previous studies demonstrated that even mild visual impairment had a significant and independent impact on vision-specific functioning ^[21] and diminished ability to perform activities of daily living alone, which led to long-term care for patients. Therefore, it was not surprising that the highest direct non-medical costs came from long-term home care (58.5%). A possible explanation for high nutrition or assistive devices costs (13.3%) in our study was that people in China were keen on buying nutrition or devices that usually advertised in the media ^[22], especially those visually impaired patients who rarely went out and had no other choices but to listen to TV for entertainment.

Our research showed that patients with VI had a relatively high financial burden in China, resulting in 32.2% households suffered from CHE. Patients with VI paid in direct costs an average amount equal to 111.5% of their individual annual income and 51.9% of their household's annual income, which indicated that the patients themselves are clearly unable to meet such substantial costs and the exorbitant burden was too costly for even the entire household to maintain. In particular, for households that have a lower economic status, the discrepancy between costs and income was greater, which made them more vulnerable facing Page 9 of 20

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the CHE. Furthermore, patients without medical insurance recording the highest CHE prevalence and the relative CHE prevalence also differed among different medical insurances, which may largely due to the different reimbursement rate of each insurance. Patients insured by NCMS, with the relatively lowest reimbursement rate ^[23,24], had substantially higher CHE prevalence than those with highest reimbursement rate (GMI and CMI). As patients living in rural areas have a relatively low income and were insured by NCMS^[25], they were ostensibly at greater risk of CHE.

Except for the economic burden, our study also suggested that VI had a substantial negative effect on health related QoL, and the life quality of patients with VI (0.65) in our study was worse than patients with cancer (0.92), mild stroke (0.9), gout (0.86), heart failure (0.78) and HIV/AIDS (0.70) ^[26]. This may largely due to the significant association between VI and mental stress such as anxiety ^[27], depression ^[10] and cognitive functions ^[28]. Among the study population, the utility value decreased dramatically with perceived total loss of vision. Previous studies have suggested that the utility values most highly correlated with the visual acuity in the better seeing eye, and as the vision in the better seeing eye decreased, the corresponding utility value decreased ^[29]. Besides, living with family could slightly enhance the life quality than living alone in our study, because family members were often called on to provide physical and emotional support ^[30]. However, unlike CHE, life quality of visual impaired patients was not associated with their wealth and patients with the highest reimbursement rate insurance (CMI) had the poorest life quality in our study. Thus, efforts are needed to promote the access to adequate and effective treatment for visual impaired patients to alleviate their diseases and recover their sight. Moreover, the government should evade the inconvenience with daily living of the visual impaired patients by consciously redesigning the built environment, public facilities and services.

We spent 3 months in two tertiary hospitals to interview 298 individuals. Due to the limitation of movement for patients with VI in China several limitations to this study should be noted. First, the face-to-face interviews were conducted in tertiary general hospitals in Beijing, which might result in a sample with higher education level, income, treatment costs, better health insurance, more serious disease than the average level of all the patients with VI in China. Second, there could have been recall bias because the data were self-reported by the patients.

CONCLUSION

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In general, our study quantified the economic burden and QoL of VI patients in China,

indicating that compared with people who were sighted, people with VI experienced greater

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5 6	263	difficulties with daily living, higher economic burden, greater chance of CHE and poorer
7	264	QoL. The findings in this study suggested that preferential medical insurance policies should
8 9	265	be designed of VI to further reduce the health inequalities, avoid the CHE and enhance the
10 11	266	QoL.
12 13	267	
14	268	Acknowledgements Our sincere appreciation to Professor Suodi Zhai and Chief Nurse Zheng
15 16	269	Liu from the sample hospitals who provided great support for this study. The authors
17 18	270	gratefully acknowledge all investigators participating in this study for their diligent work.
19 20	271	Contributors: Xiaodong Guan, Fanghui Lin and Luwen Shi conceptualised and designed the
21	272	study. Fanghui Lin and Mengyuan Fu conducted the questionnaire survey. Mengyuan Fu and
22 23	273	Dawei Zhu contributed to analysis of the data. Xiaodong Guan, Luwen Shi, Daniel Vuillermin
24 25	274	and Mengyuan Fu conducted the final analysis and drafted the initial manuscript. All authors
26 27	275	contributed to the critical revision of the paper and approved the final manuscript.
28	276	Funding This research received grant from Beijing Novartis Pharma Co., Ltd. The funders
29 30	277	had no role in study design, data collection and analysis, decision to publish, or preparation
31 32	278	of the manuscript.
33	279	Competing interests None declared.
34 35	280	Ethics approval Ethics committee approval obtained from Peking University Institution
36 37	281	Review Board (No. IRB00001052-16003). All participants were informed by an information
38 39	282	sheet and have signed the declaration of consent to participate in the study.
40	283	Provenance and peer review Not commissioned; externally peer reviewed.
41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	284	Data sharing statement No additional data are available.

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Characteristics	n (%)	Outpatient	Inpatient	Hospital stay per visit	Household income	CHE		QoL	θL	
Characteristics	П (70)	visit	visit	(days)	(USD)	Proportion (%)	Р	Mean	Р	
Total	298	9.7	0.6	2.7	13,457.8	32.2		0.65		
Age										
19-50 years old	39(13.1)	11.4	1.1	3.5	12,696.0	35.9	0.574	0.74	0.00	
51-70 years old	125(41.9)	10.8	0.6	2.6	13,452.4	34.4		0.58		
71-90 years old	134(45.0)	8.1	0.4	2.5	13,684.4	29.1		0.70		
Gender										
Male	142(47.7)	10.7	0.6	2.7	14,408.2	33.8	0.576	0.66	0.68	
Female	156(52.3)	8.8	0.5	2.7	12,592.6	30.8		0.65		
Ethnicity										
Han	278(93.3)	9.4	0.6	2.7	12,788.9	30.9	0.078	0.66	0.12	
Minority	20(6.7)	13.9	0.7	2.1	22,755.0	50.0		0.54		
Educational level										
Primary and below	71(23.8)	9.3	0.5	1.9	6,945.0	39.4	0.190	0.63	0.75	
Middle and high school	159(53.4)	9.9	0.6	2.7	13,853.7	32.1		0.66		
College and above	68(22.8)	9.6	0.7	3.3	19,332.0	25.0		0.66		
Occupation	~ /				,					
Management personnel	32(10.7)	12.1	0.8	12.0	15,623.8	20.7	0.107	0.73	0.86	
Professional personnel	81(27.2)	9.0	0.6	12.5	16,599.2	37.5		0.65		
General staff	89(29.9)	10.1	0.6	8.0	14,206.2	25.9		0.65		
Farmer	56(18.8)	6.9	0.4	5.6	4,707.6	30.3		0.65		
Other professions	11(3.7)	14.0	0.5	10.0	28,215.5	46.4		0.58		
Unemployed	29(9.7)	7.7	1.0	10.9	11,295.3	36.4		0.75		
Marital status					,					
Unmarried	44(14.8)	5.0	0.8	2.4	12,740.7	25.0	0.267	0.65	0.23	
Married	254(85.2)	10.5	0.5	2.7	13,582.0	33.5		0.65		
Living status	()				,					
Alone	16(5.4)	7.9	0.6	5.6	6,304.6	50.0	0.118	0.58	0.0	
With family	282(94.6)	9.8	0.6	2.5	13,863.6	31.2		0.68		
Current living place					,					
Urban	214(71.8)	9.7	0.6	2.7	15,792.0	26.2	0.000	0.67	0.45	
Rural	84(28.2)	9.6	0.6	2.6	7,511.1	47.6		0.62		
					,					

Table 1 Characteristic of study participants with visual impairment

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Chanastanistics	m (0/)	Outpatient	Inpatient	Hospital stay per visit	Household income	CHE		QoL	4
Characteristics	n (%)	visit	visit	(days)	(USD)	Proportion (%)	Р	Mean	Р
None	8(2.7)	18.1	1.4	26.2	18,299.2	50.0	0.008	0.64	0.003
NCMS	71(23.8)	9.8	0.6	11.3	15,099.4	47.9		0.63	
URBMI	40(13.4)	8.1	0.4	6.9	11,345.5	25.0		0.81	
UEBMI	123(41.3)	10.2	0.5	4.9	6,333.6	30.9		0.63	
GMI	42(14.1)	7.9	0.5	15.4	31,936.8	16.7		0.66	
CMI	14(4.7)	5.5	1.5	30.0	4,249.6	21.4		0.49	
Visual condition									
Moderate VI	174(58.4)	9.7	0.4	1.8	15,021.5	28.2	0.014	0.69	0.001
Severe VI	86(28.9)	9.6	0.7	3.5	12,308.5	31.4		0.65	
Blind	38(12.8)	10.0	1.2	4.7	8,898.5	52.6		0.49	
VI duration									
3-6 months	36(12.1)	4.6	0.4	1.3	12,948.3	27.8	0.804	0.58	0.066
6-12 months	48(16.1)	7.5	0.5	2.8	9,755.8	31.2		0.73	
More than 12 months	214(71.8)	11.1	0.6	2.9	14,373.8	33.2		0.65	
Ocular diseases condition									
Cataract	80(26.8)	4.8	0.3	4.3	10,898.1	17.5	0.018	0.76	0.000
Glaucoma	17(5.7)	16.7	1.2	19.7	17,850.1	41.2		0.64	
AMD	35(11.7)	12.1	0.3	7.6	12,185.9	51.4		0.72	
Retinal vascular disease	27(9.1)	8.9	0.9	9.4	14,326.4	37.0		0.67	
Other eye diseases	43(14.4)	7.9	0.6	7.7	11,445.6	30.2		0.58	
Congenital or traumatic	17(5.7)	15.9	0.7	4.6	11,677.6	35.3		0.63	
Complex diseases	759(26.5)	12.0	0.7	15.5	16,849.5	35.4		0.56	
Economic status †									
Lowest	59(19.8)	10.0	0.6	4.7	2,445.9	54.2	0.001	0.59	0.559
Lower	59(19.8)	7.7	0.8	12.0	6,464.2	33.9		0.66	
Middle	60(20.1)	8.3	0.5	9.8	10,890.3	26.7		0.68	
Higher	60(20.1)	14.2	0.5	5.5	15,481.5	21.7		0.73	
Highest	60(20.1)	8.4	0.6	15.6	32,134.7	25.0		0.62	

35 360 36 361 37 362 38 363 *New cooperative medical scheme in rural area (NCMS), urban employee basic medical insurance (UEBMI), urban resident basic medical insurance (URBMI), government medical insurance (GMI), and commercial medical insurance (CMI)

† Economic status was divided into five equal intervals based on household income per capita of the study participants. Lowest US\$[60.7,1274.9]; Lower US\$[1365.9, 2428.3]; Middle

US\$[2529.5,4097.8]; Higher US\$[4249.6, 6677.9]; Highest US\$[7183.8, 37942.6].

Table 2 Annual direct costs of visual impaired patients in China.

	1	1			
Characteristics	Mean (USD)	Median (USD)	Max (USD)	Min (USD)	Proportion (%)
Direct medical costs	()	()	()	()	70.3
Outpatient costs					69.4
Total	3,408.5	607.1	68,296.7	0.0	
Drug	2,352.7	215.5	54,637.3	0.0	
Out-of-pocket	3,048.5	324.8	68,296.7	0.0	
Inpatient costs					27.9
Total	1,369.5	0.0	31,871.8	0.0	
Drug	408.8	0.0	12,748.7	0.0	
Out-of-pocket	1,034.8	0.0	31,871.8	0.0	
Self-purchased drugs costs					2.7
Total	131.8	0.0	4,553.1	0.0	
Out-of-pocket	128.3	0.0	4,553.1	0.0	
Total direct medical costs	4,909.8	1,517.7	70,573.2	0.0	100.0
Direct non-medical costs					29.7
Long-term home care	1,216.6	0.0	28,836.4	0.0	58.5
Transportation	149.8	15.2	5,463.7	0.0	7.2
Food or accommodation	176.8	0.0	9,106.2	0.0	8.5
Escort	161.1	15.2	6,677.9	0.0	7.7
Nutrition or assistive devices	277.1	0.0	4,629.0	0.0	13.3
Home modifications	97.5	0.0	6,070.8	0.0	4.7
Total direct non-medical costs	2,078.8	440.1	33,237.7	0.0	100.0
Total direct costs	6,988.6	2,281.8	101,079.1	45.5	100.0

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367 Appendix 1 The items of the survey questionnaire.

Variable name	Description
Sociodemographic information	
age	[19,50], [51,70], [71,90]
gender	Male, Female
ethnicity	Han, Minority
educational level	Primary and below, Middle and high school, College and above
Occupation *	Management personnel, Professional personnel, General staff,
	Farmer, Other professions, Unemployed
marital status	Unmarried, Married
living status	Alone, With family
current living place	Urban, Rural
medical insurance †	GMI, UEBMI, URBMI, NCMS, CMI, None
personal income	Continuous
household size	Continuous
household income	Continuous
Clinic-related information	
Visual condition	moderate VI, severe VI, blind
VI duration ‡	3-6 months, 6-12 months, More than 12 months
Ocular diseases condition	Cataract, Glaucoma, AMD, Retinal vascular disease, Other eye
	diseases, Congenital or traumatic, Complex diseases
Outpatient visit	Continuous
Inpatient visit	Continuous
Hospital stay per visit	Continuous
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2		Economic burden	
3		Direct medical costs §	
4		Outpatient costs	Continuous
5		Outpatient drug costs	Continuous
6		Outpatient OOP costs	Continuous
7		Inpatient costs	Continuous
8		Inpatient drug costs	Continuous
9		Inpatient OOP costs	Continuous
10		Self-purchased drugs costs	Continuous
11		Self-purchased drugs COSts	Continuous
12 13		Direct non-medical costs	Continuous
14		Long-term home care costs	Continuous
15		-	Continuous
16		Transportation costs	
17		Food or accommodation costs	Continuous
18		Escort costs	Continuous
19		Nutrition or assistive devices costs	Continuous
20		Home modifications	Continuous
21	2.00	Quality of life	Continuous
22	368		unretired participants and former profession for the retired. Professional
23	369		nonnel, i.e. teachers, doctors, lawyers, engineer, etc.
24	370 371	· ·	edical scheme in rural area (NCMS), urban employee basic medical insurance
25	371		nce (URBMI) and government medical insurance (GMI). Commercial medical edical insurance purchased by respondents' employers or by themselves.
26	373		m the time which the participants became their current visual impaired level.
27	374		resources used for treating a particular illness, consisted of outpatient costs,
28	375		. Expenditures for medicine prescribed and purchased during outpatient and
29 30	376	· · · ·	outpatient and inpatient drug costs, respectively. The cost of self-purchased
30 31	377		nts bought in pharmacies (not in hospitals) for their ocular disease treatment
32	378	after the initial diagnosis.	
33	379	Cost of escort were meals, transport and acco	ommodation costs encountered by patients' escorts during all outpatient or
34	380	inpatient visits.	
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381 Appendix 2 Annual direct costs of different visual impaired patients in China.

	Dire	<u>ect medi</u> ca	l costs (USD)		Direct non-medical costs (USD)						
Characteristics	Outpatient	Inpatient	Self- purchased drugs	Total	Long- term home care	Transportation	Food or accommodation	Escort	Nutrition or assistive devices	Home modifications	Total	Total direct costs (USD
Total	3,408.5	1,369.5	131.8	4,909.8	1,216.6	149.8	176.7	161.1	277.1	97.5	2,078.8	6,988.
Age												
19-50 years old	2,009.3	3,572.4	211.5	5,793.2	1,269.1	248.1	407.7	249.6	77.8	43.2	2,295.5	8,088
51-70 years old	3,479.0	1,062.6	156.3	4,697.9	963.7	161.1	216.6	178.5	226.3	75.3	1,821.6	6,519
71-90 years old	3,749.9	1,014.6	85.8	4,850.3	1,437.2	110.6	72.4	119.1	382.4	134.0	2,255.7	7,106
Gender												
Male	3,321.3	1,860.7	98.6	5,280.6	1,069.2	130.7	132.7	179.2	300.4	118.4	1,930.6	7,211
Female	3,487.8	922.4	162.0	4,572.3	1,350.8	167.2	216.9	144.6	255.8	78.5	2,213.8	6,786
Ethnicity												
Han	3,404.2	1,325.0	130.2	4,859.4	1,039.7	135.5	166.1	167.0	250.6	86.5	1,845.5	6,704
Minority	3,468.1	1,988.2	154.7	5,611.0	3,675.2	348.7	324.7	78.2	645.0	250.4	5,322.3	10,93
Educational level												
Primary and below	2,924.6	991.6	85.3	4,001.6	2,331.9	173.9	138.3	96.1	146.7	51.3	2,938.2	6,939
Middle and high school	3,894.0	1,440.2	174.5	5,508.7	887.0	134.9	163.0	210.6	237.4	117.8	1,750.8	7,259
College and above	2,778.4	1,598.7	80.5	4,457.7	822.8	159.4	248.9	113.2	505.8	98.3	1,948.5	6,406
Occupation												
Management personnel	5,325.1	2,859.9	131.6	8,316.6	840.4	125.8	115.9	149.4	274.8	38.4	1,544.7	9,861
Professional personnel	3,924.7	1,129.7	137.3	5,191.6	1,035.5	182.0	281.2	207.9	503.9	111.5	2,322.1	7,51
General staff	2,751.8	1,414.9	97.5	4,264.1	1,592.0	156.1	136.3	97.0	211.6	109.5	2,302.4	6,56
Farmer	3,246.6	483.0	137.8	3,867.3	1,036.3	128.3	141.2	147.0	127.0	32.6	1,612.5	5,47
Other professions	2,467.8	2,635.3	146.8	5,249.9	2,731.9	172.9	242.8	226.6	531.3	275.9	4,181.6	9,43
Unemployed	2,536.8	1,487.3	204.9	4,229.1	758.8	100.0	119.8	242.1	40.4	144.4	1,405.7	5,634
Marital status												
Unmarried	869.9	1,715.0	172.2	2,757.1	1,922.0	78.0	59.7	71.5	120.7	79.4	2,331.4	5,088
Married	3,848.2	1,309.6	124.8	5,282.7	1,094.4	162.2	197.0	176.6	304.2	100.6	2,035.1	7,317
Living status												
Alone	1,546.6	1,218.0	138.6	2,903.2	1,015.9	82.9	39.2	126.8	158.1	95.8	1,518.7	4,422
With family	3,514.1	1,378.1	131.4	5,023.6	1,228.0	153.6	184.6	163.0	283.8	97.6	2,110.6	7,134
Current residence												
Urban	3,463.3	1,411.9	105.2	4,980.5	1,347.2	143.6	176.7	136.5	319.9	111.6	2,235.7	7,21
Rural	3,268.7	1,261.5	199.5	4,729.8	883.8	165.5	176.9	223.8	167.8	61.5	1,679.8	6 100

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	Dir	ect medica	l costs (USD)			Direct non-medic	al costs ((USD)		—— T			
Characteristics	Outpatient	Inpatient	Self- purchased drugs	Total	Long- term home care	Transportation	Food or accommodation	Escort	Nutrition or assistive devices	Home modifications	Total	Total direct 'otal costs (USD)		
Medical insurance														
None	298.9	4,249.6	202.1	4,750.5	4,078.8	192.6	147.0	180.2	154.5	151.8	4,905.0	9,655		
NCMS	3,488.4	1,208.2	209.3	4,905.9	881.5	156.2	173.2	233.0	96.9	42.8	1,583.8	6,489		
URBMI	3,258.8	359.3	65.0	3,683.1	1,061.2	71.0	23.5	86.2	103.0	25.0	1,370.0	5,053		
UEBMI	3,351.3	1,658.9	123.1	5,133.3	1,251.4	181.4	225.9	115.2	326.5	112.1	2,212.4	7,345		
GMI	3,924.8	1,368.5	92.1	5,385.3	1,585,7	128.4	183.4	252.0	500.4	195.1	2,845.0	8,230		
CMI	4,160.8	888.9	85.7	5,135.4	311.7	104.2	197.8	130.1	653.7	130.1	1,527.6	6,66		
Visual condition														
Moderate VI	3,120.7	853.8	118.6	4,093.1	916.4	142.4	138.5	125.9	222.0	65.3	1,610.4	5,70		
Severe VI	4,479.9	1,694.5	147.5	6,321.8	1,793.8	158.7	226.7	128.2	293.3	137.0	2,737.6	9,05		
Blind	2,301.6	2,995.5	156.8	5,453.9	1,284.8	163.9	238.9	396.6	492.7	155.8	2,732.6	8,18		
VI duration														
3-6 months	1,574.8	503.8	225.0	2,303.6	1,643.7	103.1	89.4	110.6	308.8	123.5	2,379.2	4,68		
6-12 months	2,182.5	1,070.6	70.9	3,324.0	429.4	152.8	282.8	104.2	104.5	85.4	1,159.1	4,48		
More than 12 months	3,992.0	1,582.2	129.8	5,703.9	1,321.3	157.0	167.6	182.4	310.4	95.9	2,234.6	7,93		
Ocular diseases condition														
Cataract	1,236.9	583.9	27.5	1,848.3	790.1	55.1	67.7	48.4	63.2	19.4	1,043.7	2,89		
Glaucoma	4,909.7	2,297.1	208.0	7,414.8	380.0	78.6	100.9	102.7	118.7	35.7	816.6	8,23		
AMD	8,162.3	524.7	134.8	8,821.8	346.9	189.3	172.0	174.6	480.9	0.0	1,363.7	10,18		
Retinal vascular disease	4,151.1	2,270.9	249.9	6,671.9	930.5	139.1	84.9	141.1	237.9	194.2	1,727.8	8,39		
Other eye diseases	1,392.9	2,191.8	185.5	3,770.2	2,309.9	331.9	486.5	149.8	175.0	28.6	3,461.8	7,23		
Congenital or traumatic	2,324.4	2,750.6	166.8	5,241.7	444.2	192.2	232.7	337.4	70.1	197.3	1,473.9	6,71		
Complex diseases	4,255.0	1,286.8	142.7	5,684.5	1,882.8	149.8	156.4	256.8	550.9	216.2	3,212.9	8,89		
Economic status														
Lowest	3,662.3	1,342.8	177.1	5,182.2	1,523.5	254.6	315.7	294.5	173.4	36.0	2,597.8	7,78		
Lower	1,996.4	1,738.2	95.0	3,829.6	479.0	174.2	295.0	158.1	200.8	54.9	1,362.1	5,19		
Middle	2,614.7	1,345.7	142.5	4,102.9	1,196.1	94.0	37.3	77.9	220.6	76.1	1,702.0	5,80		
Higher	4,761.2	934.9	114.9	5,811.0	800.9	84.0	49.2	108.5	250.0	5.0	1,297.7	7,10		
Highest	3,988.4	1,491.6	129.7	5,609.8	2076.3	144.4	190.8	168.6	537.5	313.7	3,431.3	9,04		

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	Item No	Recommendation	Pag No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1
		(<i>b</i>) 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	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
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	5
Participants	6	(<i>a</i>) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment	6
		methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for confounding	6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	
		(<i>d</i>) If applicable, describe analytical methods taking account of sampling strategy	
		(<u>e</u>) Describe any sensitivity analyses	
Results			
Participants	13*	(a) 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	6
		(b) Give reasons for non-participation at each stage	6
D	4.4.4	(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	7-8
Main results	16	(<i>a</i>) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear	

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	(b) Report category boundaries when continuous variables were	13-
	categorized	14
	(c) If relevant, consider translating estimates of relative risk into absolute	
	risk for a meaningful time period	
17	Report other analyses done-eg analyses of subgroups and interactions,	15-
	and sensitivity analyses	16
		_
18	Summarise key results with reference to study objectives	8
19	Discuss limitations of the study, taking into account sources of potential	9
	bias or imprecision. Discuss both direction and magnitude of any potential	
	bias	
20	Give a cautious overall interpretation of results considering objectives,	8-9
	limitations, multiplicity of analyses, results from similar studies, and other	
	relevant evidence	
21	Discuss the generalisability (external validity) of the study results	
22	Give the source of funding and the role of the funders for the present study	10
	and, if applicable, for the original study on which the present article is	
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	18 19 20 21	categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses 18 Summarise key results with reference to study objectives 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence 21 Discuss the generalisability (external validity) of the study results 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

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Burden of visual impairment associated with eye diseases: an exploratory survey of 298 Chinese patients

Journal:	BMJ Open
Manuscript ID	bmjopen-2019-030561.R1
Article Type:	Original research
Date Submitted by the Author:	10-Jul-2019
Complete List of Authors:	Guan, Xiaodong; Peking University, Department of Pharmacy Administration and Clinical Pharmacy Fu, Mengyuan; Peking University, Department of Pharmacy Administration and Clinical Pharmacy Lin, Fanghui; Peking University, International Research Center for Medicinal Administration Zhu, Dawei; Chinese Academy of Medical Sciences and Peking Union Medical College, Center for Health Policy and Management, Institute of Medical Information & Library Vuillermin, Daniel; Peking University, School of Health Humanities Shi, Luwen; School of Pharmceutial Sciences, Peking University, Depertment of Pharmacy Adiministration and Clinical Pharmacy
Primary Subject Heading :	Health economics
Secondary Subject Heading:	Public health, Ophthalmology
Keywords:	economic burden, catastrophic healthcare expenditure, quality of life, visual impairment

SCHOLARONE[™] Manuscripts

1 2	1	Burden of visual impairment associated with eye diseases: an exploratory
3 4	2	survey of 298 Chinese patients
5 6	3	
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26 27	15	
28 29	16	Keywords: economic burden, catastrophic healthcare expenditure, quality of life, visual
30	17	impairment
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33 34	19	
35	20	Word count: 3,175
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22 Abstract23 Objectives To exp

Objectives To explore the economic burden, prevalence of catastrophic healthcare
expenditure (CHE) and the quality of life (QoL) of Chinese patients with visual impairment
(VI) associated with eye diseases.

Design A questionnaire survey from March to May 2016 by structured face-to-face interviews
 of patients with VI.

Participants 302 patients who were diagnosed with moderate VI or worse in both eyes
(VA<6/18) were included and 298 patients (98.7%) completed the survey questionnaires were
eligible for the study.

Outcome measures The economic burden was estimated by calculating participants' direct 32 costs covered in 2015 and the definition of CHE was out-of-pocket costs exceeding 30% of 33 annual household income. QoL was weighed by health utility value using time-trade-off 34 valuation techniques.

Results Annual average direct costs per patient caused by VI were US\$6988.6±10834.3 and 70.3% were direct medical costs of which only 26.9% were reimbursable by medical insurance. 32.2% of households suffered from CHE, in particular, less wealthy patients with VI living in rural areas and without medical insurance. The health utility value was rated at 0.65 on average and VI patients aged 51-57, living alone and insured by commercial medical insurance had relatively less QoL.

41 Conclusion Our study explored the economic burden and QoL of visual impairment
42 associated with patients with eye diseases in China, indicating a substantial economic burden
43 and poor quality of life. Preferential medical insurance policies should be designed in relation
44 to people with VI to further reduce the health inequalities, avoid CHE and promote QoL.

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Article Summary

Strengths and limitations of this study

Chinese patients with VI associated with eye diseases.

which might result in potential sample selection bias.

1 2

1. To our knowledge, this is the first study to explore the prevalence of CHE and QoL of

2. The face-to-face interviews were conducted in two tertiary general hospitals in Beijing,

3. There could have been recall bias because the data were self-reported by the patients.

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54 INTRODUCTION

With a large rapidly-aging population in mainland China, visual impairment (VI) is emerging as a significant public health concern ^[1]. According to the World Health Survey (2003), one in five adults reported some degree of far visual difficulty ^[2]. In 2015, the number of people with moderate VI or worse was estimated to be 253 million globally ^[3]. More than 80% of the global total of VI occurs in developing countries ^[4], and 26.5% of the total of VI occurs in China^[5]. The prevalence of VI in China is 0.94% yet, for the people older than 50, this figure rises to 5.8%. In Tibet, one of the highest and harshest human habitations on earth, the prevalence is 13.2% ^[6-8].

The main impact of VI is a diminished ability to perform daily activities, which often results in high health expenditures and the loss of independence ^[9]. The total financial cost of VI worldwide was estimated to be \$3 trillion in 2010 or \$4,030 per person who is visually impaired ^[10]. In addition to the economic burden, VI also has extensive social ramifications in terms of participation in society, employment and quality of life (QoL). The World Health Organization (WHO) estimated that 1% of the total global burden of disease measured as Disability-Adjusted Life Years (DALY) attributable to VI increased by 47% from 12.9 million DALYs in 1990 to 18.8 million DALYs in 2010 [11, 12].

The burden of VI has been well researched in countries such as the United States, Australia and some European countries^[12-14]. However, little is known about the economic burden and QoL of patients with VI associated with eye diseases in China. Therefore, we undertook an explanatory survey to: quantify the economic burden; identify the prevalence of catastrophic healthcare expenditure (CHE); and describe the QoL of Chinese patients with VI associated with ocular diseases. The results will provide primary information for policy-makers when allocating limited public insurance financial resources in mainland China.

79 METHODS

80 Questionnaire design

81 We conducted a questionnaire survey by structured face-to-face interviews of patients with 82 VI. The study questionnaire included standardized items developed by reviewing related 83 research as well as items developed by consulting ophthalmologists and pharmacists. The 84 survey questionnaire included four parts: 1. sociodemographic information; 2. clinic-related 85 information; 3. economic burden; 4. Quality of life.

86 Sociodemographic information

87 Age, gender, ethnicity, educational level, occupation, marital status, living status, current 88 living place, medical insurance, personal income, household size and household income were

1 2	89	included.					
3	90	Clinic-related information					
4 5	91	Healthcare service utilization, treatment history and level of visual impairment were					
6 7	92	included. The level of VI was divided into three categories based on the WHO visual acuity					
8 9	93	(VA) categorization principles: 1. moderate VI (6/60 <va<6 18);="" 2.="" severe="" td="" vi<=""></va<6>					
10	94	(3/60 < VA < 6/60); 3. Total blindness $(VA < 3/60)$ ^[15] . Causes of VI were noted using standard					
11 12	95	WHO methodology for surveys on VI ^[16] .					
13 14	96	Economic burden					
15 16	97	Economic burden was estimated by calculating participants' direct costs related to the					
17	98	diagnosis, treatment and follow up care of eye diseases leading to VI and the expenses related					
18 19	99	to the vision loss/inability to see in the year 2015. Direct costs included direct medical costs,					
20 21	100	which were further divided into insurance covered and out-of-pocket parts, and direct non-					
22 23	100	medical costs.					
24	101	Quality of life					
25 26	102	The time trade-off (TTO) valuation technique is a commonly used QoL measurement,					
27 28	104	which is understood by the majority of patients and shows good reproducibility ^[17] . In our					
29 30	105	study, TTO determined the length of lifetime the respondent would be willing to forego to					
31	106	live in perfect health by asking, "Assuming you will only live for 10 years, what is the					
32 33	107	maximum amount of that time, if any, you would be willing to trade for a return to permanent					
34 35	108	perfect vision (1.0) during the years that remain?" ^[18]					
36 37	109	The questionnaire was designed and optimized by ophthalmologists and clinical					
38	110	pharmacists in Beijing, China. After conducting a pilot field research study in a tertiary					
39 40	111	hospital in Beijing, all of the experts agreed that the questionnaire was valid. The items and					
41 42	112	descriptions of survey questionnaire were shown in Appendix 1.					
43 44	113						
45	114	Recruitment and sampling					
46 47	115	Two tertiary hospitals in Beijing were recruited based on the volume of ocular outpatient					
48 49 50 51 52 53 54 55 56	116	visits using convenience sampling methods. Participants were eligible for inclusion in the					
	117	study if they were diagnosed with moderate VI or worse in both eyes (VA<6/18) and were					
	118	physically and mentally able to participate in the survey and agreed to participate in the study.					
	119	We excluded participants who were pregnant, had a concomitant malignant disease or an					
	120	inability to complete the questionnaire. Given the time required for each face-to-face					
57	121	interview and the volume of VI patient visits in the both sample hospitals per day, we aimed					
58 59 60	122	to collect data from approximately 300 patients.					
	123						

Data collection and quality control

A questionnaire survey was conducted from March to May 2016 by structured face-to-face interviews of outpatients admitted in ophthalmic department in Peking University Third Hospital and Beijing Hospital. These two hospitals accept most ocular outpatient visits in Beijing. All of the investigators were trained for standard processes via a workshop before implementation of the survey to minimize performance bias. In order to control ascertainment bias, the investigators read all the contents of the questionnaire during the face-to-face interviews to establish that patients with VI could hear and understand the questions. The interviews lasted approximately 0.5-1 hours to collect detailed information. The researchers emphasized to participants that only vision-related costs were to be included after reading through every question in the economic burden section to ensure accurate recording of economic burden. Survey data were recorded on paper forms and translated using Epidata3.1. All patients were de-identified into a unique project sequence number during data analysis to ensure anonymity and control analysis bias.

Outcome measures

0 Catastrophic healthcare expenditure

141 CHE was defined as out-of-pocket (OOP) for healthcare over a year that exceeded a certain
142 proportion of a household's income. This threshold had been defined in many ways. One of
143 the most common definitions was OOP costs exceeding 30% of annual household income^[19].

144 Quality of life

145 Answers to the time trade-off questions were converted to utility value.

Z=(10-N)/10

147 Z was the health utility value; N was the number of years that the respondents were willing
148 to trade for a return to permanent perfect vision. Utility values were anchored on a scale
149 between 0 (the preference for death rather than living in the patient's current state of health)
150 and 1 (a perception of perfect health)^[17].

- 10 151
- ⁰ 152 Statistical analysis

52153Costs and income were assessed in Chinese Yuan (CNY) and converted into United States5354154dollars (USD) uniformly based on exchange rates on June 1, 2016 (1 USD=6.5889 CNY) to55155make the results more comparable to other published studies.

57 156 STATA 14.0 was applied to conduct the following statistical analysis: 1. descriptive
 58 157 analysis of the participants' demographic information, healthcare service utilization,
 60 158 insurance reimbursement rate, expenditures, CHE prevalence and QoL; 2. bivariate chi-square

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159 test on the difference of CHE prevalence and QoL value between subgroups. The level of 160 statistical significance was p < 0.05 (two-sided).

Ethics Statement

Ethics committee approval obtained from Peking University Institution Review Board (No. IRB00001052-16003). All participants were informed by an information sheet and have signed the declaration of consent to participate in the study.

Patient and public involvement

168 There were no patients and public involved in the development of the research 169 questionnaire, the outcome measures, the design, recruitment and implementation of the study. 170 The results will be disseminated through scientific journals.

RESULTS

173 Description of demographic characteristics

A total of 302 patients were included and 298 completed questionnaires were eligible for this study, yielding a response rate of 98.7%. Patients' demographic data are shown in Table 1. The mean age in sample was 65.4 and there were slightly fewer males (47.7%). Most of the participants were married (85.2%), living with family (94.6%) and in urban areas (71.8%). 41.3% of the participants were covered by Urban Employee Basic Medical Insurance (UEBMI), 23.8% by New Cooperative Medical Scheme (NCMS), 14.1% by Government Medical Insurance (GMI), and 13.4% by Urban Resident Basic Medical Insurance (URBMI). Of the visual-related health conditions reported, 58.4% had moderate VI, 28.9% had severe VI, and 12.8% were blind. 71.8% of the participants had been suffered from VI for more than one year. 26.8%, 11.7% and 9.1% of the participants' VI were caused by cataract, AMD and vascular retinopathy separately, while 26.5% by multiple ocular diseases. The annual personnel income and household income of the participants were US\$6,266.4±10,403.2 and US\$13,457.8±16,711.9, respectively.

50 187

188 Healthcare service utilization

As shown in **Table 1**, the average number of healthcare service utilization due to VI within 1 year was 9.7 outpatient visits, ranging from 4.8 visits (cataract) to 16.7 visits (glaucoma). Average number and length of inpatient hospital visits were 0.6 visit within 1 year and 2.7 days of hospital staying per visit.

Direct costs

The total direct medical costs were US\$6,988.6±10,834.3 in 2015, including direct medical costs of US\$4,909.8±8,981.7 (70.3%) and direct non-medical costs of US\$2,078.8±4,430.6 (29.7%).

As shown in Table 2, of the direct medical costs, outpatient fees represented the largest costs at US\$3,408.5 (69.4%), followed by inpatient costs at US\$1,369.5 (27.9%). Except outpatient and inpatient costs, the participants also purchased drugs by themselves in retail pharmacies (2.7%). Only 10.6% of the outpatient costs, 24.4% of the inpatient costs and 2.6% of the self-purchased drug costs were covered by the medical insurance. Average total OOP costs per patient were US\$4211.6 (85.8%).

Direct non-medical costs occurred mostly due to long-term home care at US\$1,216.6 (58.5%). Nutrition or assistive devices, food and accommodation, escort, transportation, and home modifications costs accounted for 13.3%, 8.5%, 7.7%, 7.2% and 4.7% respectively.

The specific costs among different groups were shown in the Appendix 2.

Insurance reimbursement rate

As shown in Table 3, 28.1%, 9,5%, 2,7% and 26.9% of the outpatient, inpatient, self-purchased drugs and total direct medical costs caused by VI were reimbursable. However, the reimbursement rate decreased with the severity of VI (moderate VI 28.1%, severe VI 27.0%, blind 21.4%) and increased with patient's economic status (lowest 15.0%, lower 25.4%, middle 28.7%, higher 31.7% and highest 39.3%). Rural patients received a lower reimbursement rate (13.9%) as most of their medical insurance scheme was NCMS which has much lower reimbursement rate than other insurance schemes. The reimbursement rate of different diseases ranged from AMD (23.9%) and glaucoma (24.8%) to cataract (26.7%) and multiple ocular diseases (32.1%).

Prevalence of CHE

Patients with VI paid in direct medical costs an average amount equal to 111.5% of their individual annual income and 51.9% of their household's annual income. As shown in Table **3**, 32.2% households suffered from CHE caused by VI. The prevalence of CHE was generally correlated with the severity of VI (moderate VI 28.2%, severe VI 31.4%, blind 52.6%; p<0.05). Patients living in rural areas generally had greater risk of CHE compared with urban residents (47.6%, 26.2%; p<0.001). Of all of the different types of medical insurances, the CHE prevalence of patients without medical insurance and insured by NCMS ostensibly outweighed those insured by GMI and CMI (none 50.0%, NCMS 47.9%, GMI 16.7%, CMI

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- - QoL

As shown in **Table 3**, the value of QoL was 0.65 on average and correlated with the severity of VI (moderate VI 0.69, severe VI 0.65, blind 0.49; p<0.01). Middle-aged patients (51-70) had the poorest life quality (0.58; p<0.001) and patients living alone had relatively poorer QoL than living with family (0.58, 0.68; p<0.01). Of all of the different types of medical insurances, the health utility values of patients insured by CMI were significantly lower than those insured by URBMI (0.49, 0.81; p < 0.01). Patients with multiple ocular diseases (0.56) had relatively poorer QoL than those with cataract (0.76) and AMD (0.72, p<0.001).

DISCUSSION

This study provided primary information for the economic burden and QoL of Chinese patients with VI associated with ocular diseases, indicating a substantial burden of VI, with considerable variation among the different level of VI, type of medical insurance and economic status.

In our study, annual direct medical costs per VI patient associated with ocular disease were US\$4,093.1 for moderate VI, US\$6,321.8 for severe VI and US\$5,453,9 for blindness, which were much lower than several previous studies in the US, which reported mean annual direct medical expenses per patient to be US\$12,175-14,029 for moderate VI, US\$13,154-16,321 for severe VI and US\$14,882-24,180 for blindness^[12]. This was understandable as the gross domestic product per capita of China was much lower than the United States in 2015 (China (US\$8,033.4), US (US\$56,803.5))^[20]. Direct medical costs occurred mostly due to outpatient visits, which was inconsistent with formal findings in the United States and Australia that direct medical costs occurred mostly due to hospitalization^[12]. As for different diseases, AMD and glaucoma reported highest average annual direct medical costs in our study (US\$8,821.8, US\$7,414.8), which were higher than studies of AMD in Thailand (US\$3,604), ^[21] and glaucoma in Germany (€814-€1195), UK (€457-1065), France (€313-€1002) and Italy (€153-€791). ^[14, 22] Previous studies demonstrated that even mild visual impairment had a significant and independent impact on vision-specific functioning ^[23] and diminished ability to perform activities of daily living alone, which led to long-term care for patients. Therefore, it was not surprising that the highest direct non-medical costs came from long-term home care (58.5%).

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A possible explanation for high nutrition or assistive devices costs (13.3%) in our study was that people in China were keen on buying nutrition or devices that usually advertised in the media,^[24] especially those visually impaired patients who rarely went out and had no other choices but to listen to TV for entertainment.

Our research showed that Chinese patients with VI had a relatively-high financial burden, resulting in 32.2% households suffered from CHE. Patients with VI paid in direct costs an average amount equal to 111.5% of their individual annual income and 51.9% of their household's annual income, which indicated that the patients themselves are clearly unable to meet such substantial costs and the exorbitant burden was too costly for even the entire household to maintain. In particular, for households that have a lower economic status, the discrepancy between costs and income was greater, which made them more vulnerable facing the CHE. Medical insurance plays a vital role in preventing patients from CHE by assisting to cover patients' medical expenses. However, our results showed that the average insurance reimbursement rate of Chinese VI patients was low (26.9%), and varied greatly between different insurance schemes. Patients without medical insurance recorded the highest CHE prevalence and patients insured by NCMS, with the relatively lowest reimbursement rate ^[25], had substantially higher CHE prevalence than those with the highest reimbursement rate (GMI and CMI). Patients living in rural areas, who usually had a relatively low economic status and were insured by NCMS^[26] were ostensibly at greater risk of CHE. This was the result of the "urban-rural dual structure" of medical insurance system in China, ^[27] which showed a significant difference in coverage reimbursement scope, payment level, funding level, etc.^[28] Besides, our study found that higher severity level of VI caused higher direct costs, but received a lower reimbursement rate, which resulted in dramatically increased risk of CHE with the severity of VI. Furthermore, patients with AMD and glaucoma with a relatively low reimbursement rate had a heavier economic burden and were more likely to incur catastrophic spending. This result may largely due to the high price of AMD treatment therapy, ^[29] which also explain the highest fraction of outpatient costs of AMD patients and limited drug covered by medical insurance. This situation was alleviated after the national pricing negotiations on two innovative but expensive medicines (Razumab and Conbercept) in 2017, which eventually reached an average price discount of 18.74% by the pharmaceutical companies and 70% public medical insurance reimbursement rate by Chinese government. ^[30] Recommended management of glaucoma which requires regular attendance of follow-up clinic visits^[31] may explain the highest number of outpatient visit, inpatient visit, the longest stay per inpatient visit as well as the high costs.

In addition to the economic burden posed by VI, our study also suggested that VI had a

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substantial negative effect on health-related OoL. Moreover, the life quality of patients with VI (0.65) in our study was worse than patients with cancer (0.92), mild stroke (0.9), gout (0.86), heart failure (0.78) and HIV/AIDS (0.70)^[32]. This may largely due to the significant association between VI and mental stress such as anxiety, ^[33] depression ^[9] and cognitive functions. ^[34] Among the study population, the utility value decreased dramatically with perceived total loss of vision, which was consistent with a study in rural Africa ^[35]. Previous studies have suggested that the utility values most highly correlated with the visual acuity in the better seeing eye, and as the vision in the better seeing eye decreased, the corresponding utility value decreased. ^[36] Patients with cataract reported the highest TTO utility value (0.76) than those with other diseases especially multi ocular diseases (0.56). One of the reasons for this is that cataract can be effectively treated by surgery, which is a disability-preventing and highly cost-effective intervention, ^[37] and patients' TTO utility value could improve significantly after cataract surgery.^[38] Besides, living with family could slightly enhance the life quality rather than living alone because family members were often called on to provide physical and emotional support.^[39] However, unlike CHE, the life quality of visual impaired patients was not associated with their wealth and patients with one of the highest reimbursement rate insurance (CMI) had the poorest life quality in our study. Thus, efforts are needed to promote the access to adequate and effective treatment for visual impaired patients to alleviate their diseases and recover their sight. Moreover, the government should evade the inconvenience with daily living of the visual impaired patients by consciously redesigning the built environment, public facilities and services.

We spent 3 months in two tertiary hospitals to interview 298 individuals. Due to the limitation of movement for patients with VI in China several limitations to this study should be noted. First, the face-to-face interviews were conducted in tertiary general hospitals in Beijing, which might result in a sample with higher education levels, income, treatment costs, better health insurance, more serious disease than the average level of all the patients with VI in China. Second, there could have been recall bias because the data were self-reported by the patients.

50 327

52 328 CONCLUSION

Our study provided primary information for the economic burden and QoL of visual impairment associated with eve diseases of patients in China, indicating that compared with people who were sighted, people with VI experienced greater difficulties with daily living, higher economic burden, greater chance of CHE and poorer QoL. The findings in this study

suggested that preferential medical insurance policies should be designed of VI to further reduce the health inequalities, avoid the CHE and enhance the QoL.

Acknowledgements Our sincere appreciation to Professor Suodi Zhai and Chief Nurse Zheng Liu from the sample hospitals who provided great support for this study. The authors gratefully acknowledge all investigators participating in this study for their diligent work.

Contributors: Xiaodong Guan, Fanghui Lin and Luwen Shi conceptualised and designed the study. Fanghui Lin and Mengyuan Fu conducted the questionnaire survey. Mengyuan Fu and Dawei Zhu contributed to analysis of the data. Xiaodong Guan, Luwen Shi, Daniel Vuillermin and Mengyuan Fu conducted the final analysis and drafted the initial manuscript. All authors contributed to the critical revision of the paper and approved the final manuscript.

Funding This research received a grant from Beijing Novartis Pharma Co., Ltd. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests None declared.

Ethics approval Ethics committee approval obtained from Peking University Institution Review Board (No. IRB00001052-16003). All participants were informed by an information sheet and have signed the declaration of consent to participate in the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Data of this study can be available upon reasonable request from

prof. Luwen Shi, shiluwen211@163.com. In order to ensure full anonymity, confidentiality and data protection for the participants, the full survey data cannot be made accessible to the public.

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Characteristics	n (%)	Outpatien t visit	Inpatient visit	Hospital stay per visit (days)	Household income (USD)
Total	298	9.7	0.6	2.7	13,457.8
Age					
19-50 years old	39 (13.1)	11.4	1.1	3.5	12,696.0
51-70 years old	125 (41.9)	10.8	0.6	2.6	13,452.4
71-90 years old	134 (45.0)	8.1	0.4	2.5	13,684.4
Gender					
Male	142 (47.7)	10.7	0.6	2.7	14,408.2
Female	156 (52.3)	8.8	0.5	2.7	12,592.6
Ethnicity					
Han	278 (93.3)	9.4	0.6	2.7	12,788.9
Minority	20 (6.7)	13.9	0.7	2.1	22,755.0
Educational level					
Primary and below	71 (23.8)	9.3	0.5	1.9	6,945.0
Middle and high school	159 (53.4)	9.9	0.6	2.7	13,853.7
College and above	68 (22.8)	9.6	0.7	3.3	19,332.0
Occupation *					
Management personnel	32 (10.7)	12.1	0.8	2.3	15,623.8
Professional personnel	81 (27.2)	9.0	0.6	2.5	16,599.2
General staff	89 (29.9)	10.1	0.6	2.2	14,206.2
Farmer	56 (18.8)	6.9	0.4	2.0	4,707.6
Other professions	11 (3.7)	14.0	0.5	2.9	28,215.5
Unemployed	29 (9.7)	7.7	1.0	3.1	11,295.3
Marital status					
Unmarried	44 (14.8)	5.0	0.8	2.4	12,740.7

Characteristics	n (%)	Outpatien t visit	Inpatient visit	Hospital stay per visit (days)	Household income (USD)
Married	254 (85.2)	10.5	0.5	2.7	13,582.0
Living status					
Alone	16 (5.4)	7.9	0.6	5.6	6,304.6
With family	282 (94.6)	9.8	0.6	2.5	13,863.6
Current living place					
Urban	214 (71.8)	9.7	0.6	2.7	15,792.0
Rural	84 (28.2)	9.6	0.6	2.6	7,511.1
Medical insurance †					
None	8 (2.7)	18.1	1.4	3	18,299.2
NCMS	71 (23.8)	9.8	0.6	2.3	15,099.4
URBMI	40 (13.4)	8.1	0.4	1.8	11,345.5
UEBMI	123 (41.3)	10.2	0.5	3.6	6,333.6
GMI	42 (14.1)	7.9	0.5	1.8	31,936.8
CMI	14 (4.7)	5.5	1.5	1.4	4,249.6
level of VI					
Moderate VI	174 (58.4)	9.7	0.4	1.8	15,021.5
Severe VI	86 (28.9)	9.6	0.7	3.5	12,308.5
Blind	38 (12.8)	10.0	1.2	4.7	8,898.5
Duration of VI ‡					
3-6 months	36 (12.1)	4.6	0.4	1.3	12,948.3
6-12 months	48 (16.1)	7.5	0.5	2.8	9,755.8
More than 12 months	214 (71.8)	11.1	0.6	2.9	14,373.8
Cause of VI					
Cataract	80 (26.8)	4.8	0.3	1.5	10,898.1
AMD	35 (11.7)	12.1	0.3	1.4	12,185.9
Vascular retinopathy	27 (9.1)	8.9	0.9	2.1	14,326.4

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Characteristics	n (%)	Outpatien t visit	Inpatient visit	Hospital stay per visit (days)	Household income (USD)
Glaucoma	17 (5.7)	16.7	1.2	6.2	17,850.1
Other eye diseases	60 (20.1)	10.1	0.6	2.6	11,511.3
Multiple ocular diseases	79 (26.5)	12.0	0.7	3.8	16,849.5
Economic status §					
Lowest	59 (19.8)	10.0	0.6	2.3	2,445.9
Lower	59 (19.8)	7.7	0.8	3.9	6,464.2
Middle	60 (20.1)	8.3	0.5	3.3	10,890.3
Higher	60 (20.1)	14.2	0.5	1.4	15,481.5
Highest	60 (20.1)	8.4	0.6	2.4	32,134.7

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 Yoccupation included current profession of unretired participants and former profession for the retired. Professional personnel were professional and technical personnel, i.e. teachers, doctors, lawyers, engineer among others.

[†] Public insurance included new cooperative medical scheme in rural area (NCMS), urban employee basic medical insurance (UEBMI), urban resident basic medical insurance (URBMI) and Government medical insurance (GMI). NCMS was insurance for rural residents, UEBMI was for urban employees of urban enterprises, and URBMI was for those who were not employed or flexible employees and children with urban household registration, students of urban schools, and rural migrants who worked in cities. GMI, also called publicly-funded free medical care, was insurance for some of the civil servants and personnel at public institutions. Commercial medical insurance (CMI) was supplements of public medical insurance, purchased by respondents' employers or by themselves from insurance company.

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Table 2 Annual direct costs of Chinese patients with visual impairment associated with

⁴² 473 ocular diseases.

Characteristics	Mean (USD)	Median (USD)	Max (USD)	Min (USD)	Proportion (%)
Direct medical costs *					70.3
Outpatient costs					69.4
Total	3,408.5	607.1	68,296.7	0.0	
Drug	2,352.7	215.5	54,637.3	0.0	
Out-of-pocket	3,048.5	324.8	68,296.7	0.0	
Inpatient costs					27.9
Total	1,369.5	0.0	31,871.8	0.0	
Drug	408.8	0.0	12,748.7	0.0	

Out-of-pocket	1,034.8	0.0	31,871.8	0.0	
Self-purchased drugs costs					2.7
Total	131.8	0.0	4,553.1	0.0	
Out-of-pocket	128.3	0.0	4,553.1	0.0	
Total direct medical costs	4,909.8	1,517.7	70,573.2	0.0	100.0
Direct non-medical costs					29.7
Long-term home care	1,216.6	0.0	28,836.4	0.0	58.5
Transportation	149.8	15.2	5,463.7	0.0	7.2
Food or accommodation	176.8	0.0	9,106.2	0.0	8.5
Escort †	161.1	15.2	6,677.9	0.0	7.7
Nutrition or assistive devices	277.1	0.0	4,629.0	0.0	13.3
Home modifications	97.5	0.0	6,070.8	0.0	4.7
Total direct non-medical costs	2,078.8	440.1	33,237.7	0.0	100.0
Total direct costs	6,988.6	2,281.8	101,079. 1	45.5	100.0

* Direct medical costs measured the cost of resources used for treating a particular illness and consisted of outpatient costs, inpatient costs and self-purchased drugs costs. Outpatient costs were vision-related medical costs during outpatient visits, including registration fee, medical service fee, treatment fee, examination fee, drug expenses, medical supply expenses, etc. Inpatient costs were vision-related medical costs during hospitalization, including medical service fee, treatment fee, examination fee, surgery fee, drug expenses, medical supply expenses, etc. Expenditures of medicine prescribed and purchased during outpatient and inpatient visits in hospitals were included in outpatient and inpatient drug costs, respectively. The cost of self-purchased drugs was the expense of the drugs that patients bought in pharmacies (not in hospitals) for their ocular disease treatment after the initial diagnosis.

482 † Cost of escort were meals, transport and accommodation costs encountered by patients' escorts during all outpatient or
 483 inpatient visits.

Table 3 Reimbursement rate, proportion of CHE and QoL by related characteristics.

	Reim	bursemen	t rate (%	() *	СНЕ	QoL
Characteristics	Outpatien t	Inpatie nt	SPD	Total	Proport ion (%)	Mea n p
Total	28.1	9.5	2.7	26.9	32.2	0.65
Level of VI						
Moderate VI	29.9	6.4	2.9	28.1	28.2 0.014	4 0.69 0.001
Severe VI	26.9	14.8	2.9	27.0	31.4	0.65
Blind	22.2	11.7	1.4	21.4	52.6	0.49
Cause of VI						
Cataract	29.5	4.3	2.3	26.7	17.5 0.010	0 0.76 0.000
AMD	26.9	7.6	0.6	23.9	51.4	0.72

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	Reim	bursemen	t rate (%	() *	СН	E	Q	oL
Characteristics	Outpatien t	Inpatie nt	SPD	Total	Proport ion (%)	р	Mea n	р
Vascular retinopathy	24.8	9.4	1.7	25.2	37.0		0.67	
Glaucoma	32.4	19.7	0.0	24.8	41.2		0.64	
Other eye diseases	22.2	6.8	5.1	23.5	31.7		0.59	
Multiple ocular diseases	31.7	15.5	3.2	32.1	35.4		0.56	
Current living place								
Urban	30.9	15.0	5.9	33.5	26.2	0.000	0.67	0.4
Rural	27.9	9.2	2.5	26.5	47.6		0.62	
Medical insurance								
None	0.0	0.0	0.0	0.0	50.0	0.008	0.64	0.0
NCMS	14.2	4.9	2.3	13.9	47.9		0.63	
URBMI	24.2	6.9	4.3	21.6	25.0		0.81	
UEBMI	35.7	11.3	2.1	33.5	30.9		0.63	
GMI	38.5	14.5	2.6	38.0	16.7		0.66	
CMI	26.8	15.4	7.1	31.4	21.4		0.49	
Economic status								
Lowest	15.0	4.7	3.1	14.7	54.2	0.001	0.59	0.5
Lower	25.4	12.2	2.5	23.3	33.9		0.66	
Middle	28.7	8.3	2.9	31.3	26.7		0.68	
Higher	31.7	7.0	0.0	27.2	21.7		0.73	
Highest	39.3	15.4	4.9	38.0	25.0		0.62	

* Medical insurance reimbursement rate in our study was the percent of the whole year costs that is covered by insurance.
 * Abbreviations: SPD, self-purchased drugs costs; CHE, catastrophic healthcare expenditure; QoL, quality of life; NCMS

⁴⁸⁷ † Abbreviations: SPD, self-purchased drugs costs; CHE, catastrophic healthcare expenditure; QoL, quality of life; NCMS, new cooperative medical scheme; UEBMI, urban employee basic medical insurance; URBMI, urban resident basic medical insurance; GMI, government medical insurance; CMI, commercial medical insurance.

Supplementary File

Burden of visual impairment associated with eye diseases: an exploratory survey of 298 Chinese patients

Appendix 1 The items of the survey questionnaire.

Variable name	Description
Sociodemographic information	
age	[19,50], [51,70], [71,90]
gender	Male, Female
ethnicity	Han, Minority
educational level	Primary and below, Middle and high school, College and above
Occupation *	Management personnel, Professional personnel, General staff, Farmer, Other professions, Unemployed
marital status	Unmarried, Married
living status	Alone, With family
current living place	Urban, Rural
medical insurance †	None, NCMS, URBMI, UEBMI, GMI, CMI,
personal income	Continuous
household size	Continuous
household income	Continuous
linic-related information	
level of visual impairment	moderate VI, severe VI, blind
Duration of visual impairment ‡	3-6 months, 6-12 months, More than 12 months
Cause of visual impairment	Cataract, AMD, Vascular retinopathy, Glaucoma, Other eye diseases, Multiple ocular diseases
Outpatient visit	Continuous
Inpatient visit	Continuous
Hospital stay per visit	Continuous
conomic burden	
Direct medical costs §	
Outpatient costs	Continuous
Outpatient drug costs	Continuous
Outpatient out-of-pocket costs	Continuous
Inpatient costs	Continuous
Inpatient drug costs	Continuous
Inpatient out-of-pocket costs	Continuous
Self-purchased drugs costs	Continuous
Self-purchased drugs out-of-pocket co	ostsContinuous
Direct non-medical costs	
Long-term home care costs	Continuous
Transportation costs	Continuous
Food or accommodation costs	Continuous
Escort costs	Continuous
Nutrition or assistive devices costs	Continuous
Home modifications	Continuous
Quality of life	Continuous

* Occupation included current profession of unretired participants and former profession for the retired. Professional personnel were professional and technical personnel, i.e. teachers, doctors, lawyers, engineer, etc.

† Public insurance included new cooperative medical scheme in rural area (NCMS), urban employee basic medical insurance (UEBMI), urban resident basic medical insurance (URBMI) and government medical insurance (GMI). Commercial medical insurance (CMI) was supplements of public medical insurance purchased by respondents' employers or by themselves.

[‡] Duration of VI was defined by the period from the time which the participants became their current visual impaired level. § Direct medical costs measured the cost of resources used for treating a particular illness, consisted of outpatient costs, inpatient costs and self-purchased drugs costs. Expenditures for medicine prescribed and purchased during outpatient and inpatient visits in hospitals were included in outpatient and inpatient drug costs, respectively. The cost of self-purchased drugs was the expense of the drugs that patients bought in pharmacies (not in hospitals) for their ocular disease treatment after the initial diagnosis.

|| Cost of escort were meals, transport and accommodation costs encountered by patients' escorts during all outpatient or inpatient visits.

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Supplementary File

Burden of visual impairment associated with eye diseases: an exploratory survey of 298 Chinese patients

Appendix 2 Annual direct costs of different visual impaired patients in China.

	Dir	ect medica	l costs (USD)	Direct non-medical costs (USD)							Tota
Characteristics	Outpatient	Inpatient	Self- purchased drugs	Total	Long- term home care	Transportation	Food or accommodation	Escort	Nutrition or assistive devices	Home modifications	Total	direc costs (USD
Fotal	3,408.5	1,369.5	131.8	4,909.8	1,216.6	149.8	176.7	161.1	277.1	97.5	2,078.8	6,988.
Age												
19-50 years old	2,009.3	3,572.4	211.5	5,793.2	1,269.1	248.1	407.7	249.6	77.8	43.2	2,295.5	8,088
51-70 years old	3,479.0	1,062.6	156.3	4,697.9	963.7	161.1	216.6	178.5	226.3	75.3	1,821.6	6,519
71-90 years old	3,749.9	1,014.6	85.8	4,850.3	1,437.2	110.6	72.4	119.1	382.4	134.0	2,255.7	7,106
Gender												
Male	3,321.3	1,860.7	98.6	5,280.6	1,069.2	130.7	132.7	179.2	300.4	118.4	1,930.6	7,211
Female	3,487.8	922.4	162.0	4,572.3	1,350.8	167.2	216.9	144.6	255.8	78.5	2,213.8	6,786
Ethnicity												
Han	3,404.2	1,325.0	130.2	4,859.4	1,039.7	135.5	166.1	167.0	250.6	86.5	1,845.5	6,704
Minority	3,468.1	1,988.2	154.7	5,611.0	3,675.2	348.7	324.7	78.2	645.0	250.4	5,322.3	10,93
Educational level												
Primary and below	2,924.6	991.6	85.3	4,001.6	2,331.9	173.9	138.3	96.1	146.7	51.3	2,938.2	6,939
Middle and high school	3,894.0	1,440.2	174.5	5,508.7	887.0	134.9	163.0	210.6	237.4	117.8	1,750.8	7,259
College and above	2,778.4	1,598.7	80.5	4,457.7	822.8	159.4	248.9	113.2	505.8	98.3	1,948.5	6,406
Occupation												
Management personnel	5,325.1	2,859.9	131.6	8,316.6	840.4	125.8	115.9	149.4	274.8	38.4	1,544.7	9,861
Professional personnel	3,924.7	1,129.7	137.3	5,191.6	1,035.5	182.0	281.2	207.9	503.9	111.5	2,322.1	7,513
General staff	2,751.8	1,414.9	97.5	4,264.1	1,592.0	156.1	136.3	97.0	211.6	109.5	2,302.4	6,566
Farmer	3,246.6	483.0	137.8	3,867.3	1,036.3	128.3	141.2	147.0	127.0	32.6	1,612.5	5,479
Other professions	2,467.8	2,635.3	146.8	5,249.9	2,731.9	172.9	242.8	226.6	531.3	275.9	4,181.6	9,431
Unemployed	2,536.8	1,487.3	204.9	4,229.1	758.8	100.0	119.8	242.1	40.4	144.4	1,405.7	,
Marital status	,	<i>,</i>		,							·	,
Unmarried	869.9	1,715.0	172.2	2,757.1	1,922.0	78.0	59.7	71.5	120.7	79.4	2,331.4	5.088
Married	3,848.2	1,309.6	124.8	5,282.7	1,094.4	162.2	197.0	176.6	304.2	100.6	2,035.1	7,317
Living status	- ,	,		,	,						,	. ,
Alone	1,546.6	1,218.0	138.6	2,903.2	1,015.9	82.9	39.2	126.8	158.1	95.8	1,518.7	4,42
With family	3,514.1	1,378.1	131.4	5,023.6	1,228.0	153.6	184.6	163.0	283.8	97.6	2,110.6	

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	Dir	ect medica	l costs (USD)	_		Direct non-medic	al costs ((USD)			Toto
Characteristics	Outpatient	Inpatient	Self- purchased drugs	Total	Long- term home care	Transportation	Food or accommodation	Escort	Nutrition or assistive devices	Home modifications	Total	Tota direc costs (USD
Current residence												
Urban	3,463.3	1,411.9	105.2	4,980.5	1,347.2	143.6	176.7	136.5	319.9	111.6	2,235.7	7,216
Rural	3,268.7	1,261.5	199.5	4,729.8	883.8	165.5	176.9	223.8	167.8	61.5	1,679.8	6,409
Medical insurance												
None	298.9	4,249.6	202.1	4,750.5	4,078.8	192.6	147.0	180.2	154.5	151.8	4,905.0	9,655
NCMS	3,488.4	1,208.2	209.3	4,905.9	881.5	156.2	173.2	233.0	96.9	42.8	1,583.8	6,489
URBMI	3,258.8	359.3	65.0	3,683.1	1,061.2	71.0	23.5	86.2	103.0	25.0	1,370.0	5,053
UEBMI	3,351.3	1,658.9	123.1	5,133.3	1,251.4	181.4	225.9	115.2	326.5	112.1	2,212.4	7,345
GMI	3,924.8	1,368.5	92.1	5,385.3	1,585,7	128.4	183.4	252.0	500.4	195.1	2,845.0	8,230
CMI	4,160.8	888.9	85.7	5,135.4	311.7	104.2	197.8	130.1	653.7	130.1	1,527.6	6,663
level of VI												
Moderate VI	3,120.7	853.8	118.6	4,093.1	916.4	142.4	138.5	125.9	222.0	65.3	1,610.4	5,70
Severe VI	4,479.9	1,694.5	147.5	6,321.8	1,793.8	158.7	226.7	128.2	293.3	137.0	2,737.6	9,05
Blind	2,301.6	2,995.5	156.8	5,453.9	1,284.8	163.9	238.9	396.6	492.7	155.8	2,732.6	8,180
duration of VI												
3-6 months	1,574.8	503.8	225.0	2,303.6	1,643.7	103.1	89.4	110.6	308.8	123.5	2,379.2	4,682
6-12 months	2,182.5	1,070.6	70.9	3,324.0	429.4	152.8	282.8	104.2	104.5	85.4	1,159.1	4,483
More than 12 months	3,992.0	1,582.2	129.8	5,703.9	1,321.3	157.0	167.6	182.4	310.4	95.9	2,234.6	,
Cause of VI	,			,	,							,
Cataract	1,236.9	583.9	27.5	1,848.3	790.1	55.1	67.7	48.4	63.2	19.4	1,043.7	2,892
AMD	8,162.3	524.7	134.8	8,821.8	346.9	189.3	172.0	174.6	480.9	0.0	1,363.7	
Vascular retinopathy	4,151.1	2,270.9	249.9	6,671.9	930.5	139.1	84.9	141.1	237.9	194.2	1,727.8	8,39
Glaucoma	4,909.7	2,297.1	208.0	7,414.8	380.0	78.6	100.9	102.7	118.7	35.7	816.6	8,23
Other eye diseases	1,656.8	2,350.2	180.2	4,187.1	1,781.2	278.0	414.6	203.0	145.3	76.4	2,898.5	7,08
Multiple ocular diseases	4,255.0	1,286.8	142.7	5,684.5	1,882.8	149.8	156.4	256.8	550.9	216.2	3,212.9	8,89
Economic status	.,	-,		-,	-,						-,	-,
Lowest	3,662.3	1,342.8	177.1	5,182.2	1,523.5	254.6	315.7	294.5	173.4	36.0	2,597.8	7.78
Lower	1,996.4	1,738.2	95.0	3,829.6	479.0	174.2	295.0	158.1	200.8	54.9	1,362.1	5,19
Middle	2,614.7	1,345.7	142.5	4,102.9	1,196.1	94.0	37.3	77.9	220.6	76.1	1,702.0	,
Higher	4,761.2	934.9	114.9	5,811.0	800.9	84.0	49.2	108.5	250.0	5.0	1,297.7	7,108
Highest	3,988.4	1,491.6	129.7	5,609.8	2076.3	144.4	190.8	168.6	537.5	313.7	3,431.3	9,04

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* Abbreviations: NCMS, new cooperative medical scheme; UEBMI, urban employee basic medical insurance; URBMI, urban resident basic medical insurance; GMI, government medical insuran

CMI, commercial medical insurance.

	Item No	Recommendation	Pag No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) 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	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
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	5
Participants	6	(<i>a</i>) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/	8*	For each variable of interest, give sources of data and details of methods	6
measurement		of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	6-7
		(c) Explain how missing data were addressed	/
		(<i>d</i>) If applicable, describe analytical methods taking account of sampling strategy	/
		(<u>e</u>) Describe any sensitivity analyses	/
Results			
Participants	13*	(a) 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	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	/
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	/
Outcome data	15*	Report numbers of outcome events or summary measures	7-9
Main results	16	(<i>a</i>) 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	/

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		(b) Report category boundaries when continuous variables were	15-
		categorized	17
		(c) If relevant, consider translating estimates of relative risk into absolute	/
		risk for a meaningful time period	
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions,	18-
		and sensitivity analyses	19
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential	11
		bias or imprecision. Discuss both direction and magnitude of any potential	
		bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	9-11
		limitations, multiplicity of analyses, results from similar studies, and other	
		relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	/
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study	12
		and, if applicable, for the original study on which the present article is	
		based	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Burden of visual impairment associated with eye diseases: an exploratory survey of 298 Chinese patients

Journal:	BMJ Open
Manuscript ID	bmjopen-2019-030561.R2
Article Type:	Original research
Date Submitted by the Author:	19-Aug-2019
Complete List of Authors:	Guan, Xiaodong; Peking University, Department of Pharmacy Administration and Clinical Pharmacy Fu, Mengyuan; Peking University, Department of Pharmacy Administration and Clinical Pharmacy Lin, Fanghui; Peking University, International Research Center for Medicinal Administration Zhu, Dawei; Chinese Academy of Medical Sciences and Peking Union Medical College, Center for Health Policy and Management, Institute of Medical Information & Library Vuillermin, Daniel; Peking University, School of Health Humanities Shi, Luwen; School of Pharmceutial Sciences, Peking University, Depertment of Pharmacy Adiministration and Clinical Pharmacy
Primary Subject Heading :	Health economics
Secondary Subject Heading:	Public health, Ophthalmology
Keywords:	economic burden, catastrophic healthcare expenditure, quality of life, visual impairment

SCHOLARONE[™] Manuscripts

1 2	1	Burden of visual impairment associated with eye diseases: an exploratory
3 4	2	survey of 298 Chinese patients
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7 8	4	Xiaodong Guan, ^{1,2} Mengyuan Fu, ¹ Fanghui Lin, ² Dawei Zhu, ^{2,3} Daniel Vuillermin, ⁴ and Luwen
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26 27	15	
28 29	16	Keywords: economic burden, catastrophic healthcare expenditure, quality of life, visual
30	17	impairment
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22 Abstract23 Objectives To exp

Objectives To explore the economic burden, prevalence of catastrophic healthcare
 expenditure (CHE) and the quality of life (QoL) of Chinese patients with visual impairment
 (VI) associated with eye diseases.

Design A questionnaire survey from March to May 2016 by structured face-to-face interviews
 of patients with VI.

Participants 302 patients who were diagnosed with moderate VI or worse in both eyes
(VA<6/18) were included and 298 patients (98.7%) completed the survey questionnaires were
eligible for the study.

Outcome measures The economic burden was estimated by calculating participants' direct 32 costs covered in 2015 and the definition of CHE was out-of-pocket costs exceeding 30% of 33 annual household income. QoL was weighed by health utility value using time-trade-off 34 valuation techniques.

Results Annual average direct costs per patient caused by VI were US\$6988.6±10834.3 and 70.3% were direct medical costs of which only 26.9% were reimbursable by medical insurance. 32.2% of households suffered from CHE, in particular, less wealthy patients with VI living in rural areas and without medical insurance. The health utility value was rated at 0.65 on average and VI patients aged 51-57, living alone and insured by commercial medical insurance had relatively less QoL.

41 Conclusion Our study explored the economic burden and QoL of visual impairment
42 associated with patients with eye diseases in China, indicating a substantial economic burden
43 and poor quality of life. Preferential medical insurance policies should be designed in relation
44 to people with VI to further reduce the health inequalities, avoid CHE and promote QoL.

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Article Summary

Strengths and limitations of this study

Chinese patients with VI associated with eye diseases.

which might result in potential sample selection bias.

1 2

1. To our knowledge, this is the first study to explore the prevalence of CHE and QoL of

2. The face-to-face interviews were conducted in two tertiary general hospitals in Beijing,

3. There could have been recall bias because the data were self-reported by the patients.

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54 INTRODUCTION

With a large rapidly-aging population in mainland China, visual impairment (VI) is emerging as a significant public health concern ^[1]. According to the World Health Survey (2003), one in five adults reported some degree of far visual difficulty ^[2]. In 2015, the number of people with moderate VI or worse was estimated to be 253 million globally ^[3]. More than 80% of the global total of VI occurs in developing countries ^[4], and 26.5% of the total of VI occurs in China^[5]. The prevalence of VI in China is 0.94% yet, for the people older than 50, this figure rises to 5.8%. In Tibet, one of the highest and harshest human habitations on earth, the prevalence is 13.2% ^[6-8].

The main impact of VI is a diminished ability to perform daily activities, which often results in high health expenditures and the loss of independence ^[9]. The total financial cost of VI worldwide was estimated to be \$3 trillion in 2010 or \$4,030 per person who is visually impaired ^[10]. In addition to the economic burden, VI also has extensive social ramifications in terms of participation in society, employment and quality of life (QoL). The World Health Organization (WHO) estimated that 1% of the total global burden of disease measured as Disability-Adjusted Life Years (DALY) attributable to VI increased by 47% from 12.9 million DALYs in 1990 to 18.8 million DALYs in 2010 [11, 12].

The burden of VI has been well researched in countries such as the United States, Australia and some European countries^[12-14]. However, little is known about the economic burden and QoL of patients with VI associated with eye diseases in China. Therefore, we undertook an explanatory survey to: quantify the economic burden; identify the prevalence of catastrophic healthcare expenditure (CHE); and describe the QoL of Chinese patients with VI associated with ocular diseases. The results will provide primary information for policy-makers when allocating limited public insurance financial resources in mainland China.

79 METHODS

80 Questionnaire design

81 We conducted a questionnaire survey by structured face-to-face interviews of patients with 82 VI. The study questionnaire included standardized items developed by reviewing related 83 research as well as items developed by consulting ophthalmologists and pharmacists. The 84 survey questionnaire included four parts: 1. sociodemographic information; 2. clinic-related 85 information; 3. economic burden; 4. Quality of life.

86 Sociodemographic information

87 Age, gender, ethnicity, educational level, occupation, marital status, living status, current 88 living place, medical insurance, personal income, household size and household income were

1 2	89	included.
3	90	Clinic-related information
4 5	91	Healthcare service utilization, treatment history and level of visual impairment were
6 7	92	included. The level of VI was divided into three categories based on the WHO visual acuity
8 9	93	(VA) categorization principles: 1. moderate VI (6/60 <va<6 18);="" 2.="" severe="" td="" vi<=""></va<6>
10	94	(3/60 < VA < 6/60); 3. Total blindness $(VA < 3/60)$ ^[15] . Causes of VI were noted using standard
11 12	95	WHO methodology for surveys on VI ^[16] .
13 14	96	Economic burden
15 16	97	Economic burden was estimated by calculating participants' direct costs related to the
17	98	diagnosis, treatment and follow up care of eye diseases leading to VI and the expenses related
18 19	99	to the vision loss/inability to see in the year 2015. Direct costs included direct medical costs,
20 21	100	which were further divided into insurance covered and out-of-pocket parts, and direct non-
22 23	100	medical costs.
24	101	Quality of life
25 26	102	The time trade-off (TTO) valuation technique is a commonly used QoL measurement,
27 28	104	which is understood by the majority of patients and shows good reproducibility ^[17] . In our
29 30	105	study, TTO determined the length of lifetime the respondent would be willing to forego to
31	106	live in perfect health by asking, "Assuming you will only live for 10 years, what is the
32 33	107	maximum amount of that time, if any, you would be willing to trade for a return to permanent
34 35	108	perfect vision (1.0) during the years that remain?" ^[18]
36 37	109	The questionnaire was designed and optimized by ophthalmologists and clinical
38	110	pharmacists in Beijing, China. After conducting a pilot field research study in a tertiary
39 40	111	hospital in Beijing, all of the experts agreed that the questionnaire was valid. The items and
41 42	112	descriptions of survey questionnaire were shown in Appendix 1.
43 44	113	
45	114	Recruitment and sampling
46 47	115	Two tertiary hospitals in Beijing were recruited based on the volume of ocular outpatient
48 49	116	visits using convenience sampling methods. Participants were eligible for inclusion in the
50	117	study if they were diagnosed with moderate VI or worse in both eyes (VA<6/18) and were
51 52	118	physically and mentally able to participate in the survey and agreed to participate in the study.
53 54	119	We excluded participants who were pregnant, had a concomitant malignant disease or an
55 56	120	inability to complete the questionnaire. Given the time required for each face-to-face
57	121	interview and the volume of VI patient visits in the both sample hospitals per day, we aimed
58 59	122	to collect data from approximately 300 patients.
60	123	

Data collection and quality control

A questionnaire survey was conducted from March to May 2016 by structured face-to-face interviews of outpatients admitted in ophthalmic department in Peking University Third Hospital and Beijing Hospital. These two hospitals accept most ocular outpatient visits in Beijing. All of the investigators were trained for standard processes via a workshop before implementation of the survey to minimize performance bias. In order to control ascertainment bias, the investigators read all the contents of the questionnaire during the face-to-face interviews to establish that patients with VI could hear and understand the questions. The interviews lasted approximately 0.5-1 hours to collect detailed information. The researchers emphasized to participants that only vision-related costs were to be included after reading through every question in the economic burden section to ensure accurate recording of economic burden. Survey data were recorded on paper forms and translated using Epidata3.1. All patients were de-identified into a unique project sequence number during data analysis to ensure anonymity and control analysis bias.

Outcome measures

0 Catastrophic healthcare expenditure

141 CHE was defined as out-of-pocket (OOP) for healthcare over a year that exceeded a certain
142 proportion of a household's income. This threshold had been defined in many ways. One of
143 the most common definitions was OOP costs exceeding 30% of annual household income^[19].

144 Quality of life

145 Answers to the time trade-off questions were converted to utility value.

Z=(10-N)/10

147 Z was the health utility value; N was the number of years that the respondents were willing
148 to trade for a return to permanent perfect vision. Utility values were anchored on a scale
149 between 0 (the preference for death rather than living in the patient's current state of health)
150 and 1 (a perception of perfect health)^[17].

- 10 151
- ⁰ 152 Statistical analysis

52153Costs and income were assessed in Chinese Yuan (CNY) and converted into United States5354154dollars (USD) uniformly based on exchange rates on June 1, 2016 (1 USD=6.5889 CNY) to55155make the results more comparable to other published studies.

57 156 STATA 14.0 was applied to conduct the following statistical analysis: 1. descriptive
 58 157 analysis of the participants' demographic information, healthcare service utilization,
 60 158 insurance reimbursement rate, expenditures, CHE prevalence and QoL; 2. bivariate chi-square

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159 test on the difference of CHE prevalence and QoL value between subgroups. The level of 160 statistical significance was p < 0.05 (two-sided).

Ethics Statement

Ethics committee approval obtained from Peking University Institution Review Board (No. IRB00001052-16003). All participants were informed by an information sheet and have signed the declaration of consent to participate in the study.

Patient and public involvement

168 There were no patients and public involved in the development of the research 169 questionnaire, the outcome measures, the design, recruitment and implementation of the study. 170 The results will be disseminated through scientific journals.

RESULTS

173 Description of demographic characteristics

A total of 302 patients were included and 298 completed questionnaires were eligible for this study, yielding a response rate of 98.7%. Patients' demographic data are shown in **Table** 1. The mean age in sample was 65.4 and there were slightly fewer males (47.7%). Most of the participants were married (85.2%), living with family (94.6%) and in urban areas (71.8%). 41.3% of the participants were covered by Urban Employee Basic Medical Insurance (UEBMI), 23.8% by New Cooperative Medical Scheme (NCMS), 14.1% by Government Medical Insurance (GMI), and 13.4% by Urban Resident Basic Medical Insurance (URBMI). Of the visual-related health conditions reported, 58.4% had moderate VI, 28.9% had severe VI, and 12.8% were blind. 71.8% of the participants had been suffered from VI for more than one year. 26.8%, 11.7% and 9.1% of the participants' VI were caused by cataract, AMD and vascular retinopathy separately, while 26.5% by multiple ocular diseases. The annual personnel income and household income of the participants were US\$6,266.4±10,403.2 and US\$13,457.8±16,711.9, respectively.

50 187

188 Healthcare service utilization

As shown in **Table 1**, the average number of healthcare service utilization due to VI within 1 year was 9.7 outpatient visits, ranging from 4.8 visits (cataract) to 16.7 visits (glaucoma). Average number and length of inpatient hospital visits were 0.6 visit within 1 year and 2.7 days of hospital staying per visit.

Direct costs

The total direct medical costs were US\$6,988.6±10,834.3 in 2015, including direct medical costs of US\$4,909.8±8,981.7 (70.3%) and direct non-medical costs of US\$2,078.8±4,430.6 (29.7%).

As shown in Table 2, of the direct medical costs, outpatient fees represented the largest costs at US\$3,408.5 (69.4%), followed by inpatient costs at US\$1,369.5 (27.9%). Except outpatient and inpatient costs, the participants also purchased drugs by themselves in retail pharmacies (2.7%). Only 10.6% of the outpatient costs, 24.4% of the inpatient costs and 2.6% of the self-purchased drug costs were covered by the medical insurance. Average total OOP costs per patient were US\$4211.6 (85.8%).

Direct non-medical costs occurred mostly due to long-term home care at US\$1,216.6 (58.5%). Nutrition or assistive devices, food and accommodation, escort, transportation, and home modifications costs accounted for 13.3%, 8.5%, 7.7%, 7.2% and 4.7% respectively.

The specific costs among different groups were shown in the Appendix 2.

Insurance reimbursement rate

As shown in Table 3, 28.1%, 9,5%, 2,7% and 26.9% of the outpatient, inpatient, self-purchased drugs and total direct medical costs caused by VI were reimbursable. However, the reimbursement rate decreased with the severity of VI (moderate VI 28.1%, severe VI 27.0%, blind 21.4%) and increased with patient's economic status (lowest 15.0%, lower 25.4%, middle 28.7%, higher 31.7% and highest 39.3%). Rural patients received a lower reimbursement rate (13.9%) as most of their medical insurance scheme was NCMS which has much lower reimbursement rate than other insurance schemes. The reimbursement rate of different diseases ranged from AMD (23.9%) and glaucoma (24.8%) to cataract (26.7%) and multiple ocular diseases (32.1%).

Prevalence of CHE

Patients with VI paid in direct medical costs an average amount equal to 111.5% of their individual annual income and 51.9% of their household's annual income. As shown in Table **3**, 32.2% households suffered from CHE caused by VI. The prevalence of CHE was generally correlated with the severity of VI (moderate VI 28.2%, severe VI 31.4%, blind 52.6%; p<0.05). Patients living in rural areas generally had greater risk of CHE compared with urban residents (47.6%, 26.2%; p<0.001). Of all of the different types of medical insurances, the CHE prevalence of patients without medical insurance and insured by NCMS ostensibly outweighed those insured by GMI and CMI (none 50.0%, NCMS 47.9%, GMI 16.7%, CMI

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- - QoL

As shown in **Table 3**, the value of QoL was 0.65 on average and correlated with the severity of VI (moderate VI 0.69, severe VI 0.65, blind 0.49; p<0.01). Middle-aged patients (51-70) had the poorest life quality (0.58; p<0.001) and patients living alone had relatively poorer QoL than living with family (0.58, 0.68; p<0.01). Of all of the different types of medical insurances, the health utility values of patients insured by CMI were significantly lower than those insured by URBMI (0.49, 0.81; p < 0.01). Patients with multiple ocular diseases (0.56) had relatively poorer QoL than those with cataract (0.76) and AMD (0.72, p<0.001).

DISCUSSION

This study provided primary information for the economic burden and QoL of Chinese patients with VI associated with ocular diseases, indicating a substantial burden of VI, with considerable variation among the different level of VI, type of medical insurance and economic status.

In our study, annual direct medical costs per VI patient associated with ocular disease were US\$4,093.1 for moderate VI, US\$6,321.8 for severe VI and US\$5,453,9 for blindness, which were much lower than several previous studies in the US, which reported mean annual direct medical expenses per patient to be US\$12,175-14,029 for moderate VI, US\$13,154-16,321 for severe VI and US\$14,882-24,180 for blindness^[12]. This was understandable as the gross domestic product per capita of China was much lower than the United States in 2015 (China (US\$8,033.4), US (US\$56,803.5))^[20]. Direct medical costs occurred mostly due to outpatient visits, which was inconsistent with formal findings in the United States and Australia that direct medical costs occurred mostly due to hospitalization^[12]. As for different diseases, AMD and glaucoma reported highest average annual direct medical costs in our study (US\$8,821.8, US\$7,414.8), which were higher than studies of AMD in Thailand (US\$3,604), ^[21] and glaucoma in Germany (€814-€1195), UK (€457-1065), France (€313-€1002) and Italy (€153-€791). ^[14, 22] Previous studies demonstrated that even mild visual impairment had a significant and independent impact on vision-specific functioning ^[23] and diminished ability to perform activities of daily living alone, which led to long-term care for patients. Therefore, it was not surprising that the highest direct non-medical costs came from long-term home care (58.5%).

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A possible explanation for high nutrition or assistive devices costs (13.3%) in our study was that people in China were keen on buying nutrition or devices that usually advertised in the media,^[24] especially those visually impaired patients who rarely went out and had no other choices but to listen to TV for entertainment.

Our research showed that Chinese patients with VI had a relatively-high financial burden, resulting in 32.2% households suffered from CHE. Patients with VI paid in direct costs an average amount equal to 111.5% of their individual annual income and 51.9% of their household's annual income, which indicated that the patients themselves are clearly unable to meet such substantial costs and the exorbitant burden was too costly for even the entire household to maintain. In particular, for households that have a lower economic status, the discrepancy between costs and income was greater, which made them more vulnerable facing the CHE. Medical insurance plays a vital role in preventing patients from CHE by assisting to cover patients' medical expenses. However, our results showed that the average insurance reimbursement rate of Chinese VI patients was low (26.9%), and varied greatly between different insurance schemes. Patients without medical insurance recorded the highest CHE prevalence and patients insured by NCMS, with the relatively lowest reimbursement rate ^[25], had substantially higher CHE prevalence than those with the highest reimbursement rate (GMI and CMI). Patients living in rural areas, who usually had a relatively low economic status and were insured by NCMS^[26] were ostensibly at greater risk of CHE. This was the result of the "urban-rural dual structure" of medical insurance system in China, ^[27] which showed a significant difference in coverage reimbursement scope, payment level, funding level, etc.^[28] Besides, our study found that higher severity level of VI caused higher direct costs, but received a lower reimbursement rate, which resulted in dramatically increased risk of CHE with the severity of VI. Furthermore, patients with AMD and glaucoma with a relatively low reimbursement rate had a heavier economic burden and were more likely to incur catastrophic spending. This result may largely due to the high price of AMD treatment therapy, ^[29] which also explain the highest fraction of outpatient costs of AMD patients and limited drug covered by medical insurance. This situation was alleviated after the national pricing negotiations on two innovative but expensive medicines (Razumab and Conbercept) in 2017, which eventually reached an average price discount of 18.74% by the pharmaceutical companies and 70% public medical insurance reimbursement rate by Chinese government. ^[30] Recommended management of glaucoma which requires regular attendance of follow-up clinic visits^[31] may explain the highest number of outpatient visit, inpatient visit, the longest stay per inpatient visit as well as the high costs.

In addition to the economic burden posed by VI, our study also suggested that VI had a

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substantial negative effect on health-related OoL. Moreover, the life quality of patients with VI (0.65) in our study was worse than patients with cancer (0.92), mild stroke (0.9), gout (0.86), heart failure (0.78) and HIV/AIDS (0.70)^[32]. This may largely due to the significant association between VI and mental stress such as anxiety, ^[33] depression ^[9] and cognitive functions. ^[34] Among the study population, the utility value decreased dramatically with perceived total loss of vision, which was consistent with a study in rural Africa ^[35]. Previous studies have suggested that the utility values most highly correlated with the visual acuity in the better seeing eye, and as the vision in the better seeing eye decreased, the corresponding utility value decreased. ^[36] Patients with cataract reported the highest TTO utility value (0.76) than those with other diseases especially multi ocular diseases (0.56). One of the reasons for this is that cataract can be effectively treated by surgery, which is a disability-preventing and highly cost-effective intervention, ^[37] and patients' TTO utility value could improve significantly after cataract surgery.^[38] Besides, living with family could slightly enhance the life quality rather than living alone because family members were often called on to provide physical and emotional support.^[39] However, unlike CHE, the life quality of visual impaired patients was not associated with their wealth and patients with one of the highest reimbursement rate insurance (CMI) had the poorest life quality in our study. Thus, efforts are needed to promote the access to adequate and effective treatment for visual impaired patients to alleviate their diseases and recover their sight. Moreover, the government should evade the inconvenience with daily living of the visual impaired patients by consciously redesigning the built environment, public facilities and services.

We spent 3 months in two tertiary hospitals to interview 298 individuals. Due to the limitation of movement for patients with VI in China several limitations to this study should be noted. First, the study population is not fully representative of all the patients with VI in mainland China. Second, the face-to-face interviews were conducted in tertiary general hospitals in Beijing, which might result in a sample with higher education levels, income, treatment costs, better health insurance, more serious disease than the average level of all the patients with VI in China. Third, there could have been recall bias because the data were self-reported by the patients.

CONCLUSION

Our study provided primary information for the economic burden and QoL of visual impairment associated with eye diseases of patients in China, indicating that compared with people who were sighted, people with VI experienced greater difficulties with daily living, higher economic burden, greater chance of CHE and poorer QoL. The findings in this study suggested that preferential medical insurance policies should be designed of VI to further

reduce the health inequalities, avoid the CHE and enhance the QoL.

Acknowledgements Our sincere appreciation to Professor Suodi Zhai and Chief Nurse Zheng Liu from the sample hospitals who provided great support for this study. The authors gratefully acknowledge all investigators participating in this study for their diligent work.

Contributors: Xiaodong Guan, Fanghui Lin and Luwen Shi conceptualised and designed the study. Fanghui Lin and Mengyuan Fu conducted the questionnaire survey. Mengyuan Fu and Dawei Zhu contributed to analysis of the data. Xiaodong Guan, Luwen Shi, Daniel Vuillermin and Mengyuan Fu conducted the final analysis and drafted the initial manuscript. All authors contributed to the critical revision of the paper and approved the final manuscript.

Funding This research received a grant from Beijing Novartis Pharma Co., Ltd. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests None declared.

Ethics approval Ethics committee approval obtained from Peking University Institution Review Board (No. IRB00001052-16003). All participants were informed by an information sheet and have signed the declaration of consent to participate in the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Data of this study can be available upon reasonable request from

prof. Luwen Shi, shiluwen211@163.com. In order to ensure full anonymity, confidentiality and data protection for the participants, the full survey data cannot be made accessible to the public.

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Characteristics	n (%)	Outpatien t visit	Inpatient visit	Hospital stay per visit (days)	Household income (USD)
Total	298	9.7	0.6	2.7	13,457.8
Age					
19-50 years old	39 (13.1)	11.4	1.1	3.5	12,696.0
51-70 years old	125 (41.9)	10.8	0.6	2.6	13,452.4
71-90 years old	134 (45.0)	8.1	0.4	2.5	13,684.4
Gender					
Male	142 (47.7)	10.7	0.6	2.7	14,408.2
Female	156 (52.3)	8.8	0.5	2.7	12,592.6
Ethnicity					
Han	278 (93.3)	9.4	0.6	2.7	12,788.9
Minority	20 (6.7)	13.9	0.7	2.1	22,755.0
Educational level					
Primary and below	71 (23.8)	9.3	0.5	1.9	6,945.0
Middle and high school	159 (53.4)	9.9	0.6	2.7	13,853.7
College and above	68 (22.8)	9.6	0.7	3.3	19,332.0
Occupation *					
Management personnel	32 (10.7)	12.1	0.8	2.3	15,623.8
Professional personnel	81 (27.2)	9.0	0.6	2.5	16,599.2
General staff	89 (29.9)	10.1	0.6	2.2	14,206.2
Farmer	56 (18.8)	6.9	0.4	2.0	4,707.6
Other professions	11 (3.7)	14.0	0.5	2.9	28,215.5
Unemployed	29 (9.7)	7.7	1.0	3.1	11,295.3
Marital status					
Unmarried	44 (14.8)	5.0	0.8	2.4	12,740.7

Characteristics	n (%)	Outpatien t visit	Inpatient visit	Hospital stay per visit (days)	Household income (USD)
Married	254 (85.2)	10.5	0.5	2.7	13,582.0
Living status					
Alone	16 (5.4)	7.9	0.6	5.6	6,304.6
With family	282 (94.6)	9.8	0.6	2.5	13,863.6
Current living place					
Urban	214 (71.8)	9.7	0.6	2.7	15,792.0
Rural	84 (28.2)	9.6	0.6	2.6	7,511.1
Medical insurance †					
None	8 (2.7)	18.1	1.4	3	18,299.2
NCMS	71 (23.8)	9.8	0.6	2.3	15,099.4
URBMI	40 (13.4)	8.1	0.4	1.8	11,345.5
UEBMI	123 (41.3)	10.2	0.5	3.6	6,333.6
GMI	42 (14.1)	7.9	0.5	1.8	31,936.8
CMI	14 (4.7)	5.5	1.5	1.4	4,249.6
level of VI					
Moderate VI	174 (58.4)	9.7	0.4	1.8	15,021.5
Severe VI	86 (28.9)	9.6	0.7	3.5	12,308.5
Blind	38 (12.8)	10.0	1.2	4.7	8,898.5
Duration of VI ‡					
3-6 months	36 (12.1)	4.6	0.4	1.3	12,948.3
6-12 months	48 (16.1)	7.5	0.5	2.8	9,755.8
More than 12 months	214 (71.8)	11.1	0.6	2.9	14,373.8
Cause of VI					
Cataract	80 (26.8)	4.8	0.3	1.5	10,898.1
AMD	35 (11.7)	12.1	0.3	1.4	12,185.9
Vascular retinopathy	27 (9.1)	8.9	0.9	2.1	14,326.4

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Characteristics	n (%)	Outpatien t visit	Inpatient visit	Hospital stay per visit (days)	Household income (USD)
Glaucoma	17 (5.7)	16.7	1.2	6.2	17,850.1
Other eye diseases	60 (20.1)	10.1	0.6	2.6	11,511.3
Multiple ocular diseases	79 (26.5)	12.0	0.7	3.8	16,849.5
Economic status §					
Lowest	59 (19.8)	10.0	0.6	2.3	2,445.9
Lower	59 (19.8)	7.7	0.8	3.9	6,464.2
Middle	60 (20.1)	8.3	0.5	3.3	10,890.3
Higher	60 (20.1)	14.2	0.5	1.4	15,481.5
Highest	60 (20.1)	8.4	0.6	2.4	32,134.7

* Occupation included current profession of unretired participants and former profession for the retired. Professional personnel were professional and technical personnel, i.e. teachers, doctors, lawyers, engineer among others.

† Public insurance included new cooperative medical scheme in rural area (NCMS), urban employee basic medical insurance (UEBMI), urban resident basic medical insurance (URBMI) and Government medical insurance (GMI). NCMS was insurance for rural residents, UEBMI was for urban employees of urban enterprises, and URBMI was for those who were not employed or flexible employees and children with urban household registration, students of urban schools, and rural migrants who worked in cities. GMI, also called publicly-funded free medical care, was insurance for some of the civil servants and personnel at public institutions. Commercial medical insurance (CMI) was supplements of public medical insurance, purchased by respondents' employers or by themselves from insurance company.

[‡] Duration of VI was defined by the period from the time which the participants became their current visual impaired level. § Economic status was divided into five equal intervals based on household income per capita of the study participants. Lowest US\$[60.7,1274.9]; Lower US\$[1365.9, 2428.3]; Middle US\$[2529.5,4097.8]; Higher US\$[4249.6, 6677.9]; Highest US\$[7183.8, 37942.6].

Table 2 Annual direct costs of Chinese patients with visual impairment associated with

ocular diseases.

Characteristics	Mean (USD)	Median (USD)	Max (USD)	Min (USD)	Proportion (%)	
Direct medical costs *					70.3	
Outpatient costs					69.4	
Total	3,408.5	607.1	68,296.7	0.0		
Drug	2,352.7	215.5	54,637.3	0.0		
Out-of-pocket	3,048.5	324.8	68,296.7	0.0		
Inpatient costs					27.9	
Total	1,369.5	0.0	31,871.8	0.0		
Drug	408.8	0.0	12,748.7	0.0		

		0.0			
Out-of-pocket	1,034.8	0.0	31,871.8	0.0	
Self-purchased drugs costs					2.7
Total	131.8	0.0	4,553.1	0.0	
Out-of-pocket	128.3	0.0	4,553.1	0.0	
Total direct medical costs	4,909.8	1,517.7	70,573.2	0.0	100.0
Direct non-medical costs					29.7
Long-term home care	1,216.6	0.0	28,836.4	0.0	58.5
Transportation	149.8	15.2	5,463.7	0.0	7.2
Food or accommodation	176.8	0.0	9,106.2	0.0	8.5
Escort †	161.1	15.2	6,677.9	0.0	7.7
Nutrition or assistive devices	277.1	0.0	4,629.0	0.0	13.3
Home modifications	97.5	0.0	6,070.8	0.0	4.7
Total direct non-medical costs	2,078.8	440.1	33,237.7	0.0	100.0
Total direct costs	6,988.6	2,281.8	101,079. 1	45.5	100.0

475 * Direct medical costs measured the cost of resources used for treating a particular illness and consisted of outpatient costs, 476 inpatient costs and self-purchased drugs costs. Outpatient costs were vision-related medical costs during outpatient visits, 477 including registration fee, medical service fee, treatment fee, examination fee, drug expenses, medical supply expenses, etc. 478 Inpatient costs were vision-related medical costs during hospitalization, including medical service fee, treatment fee, 479 examination fee, surgery fee, drug expenses, medical supply expenses, etc. Expenditures of medicine prescribed and 480 purchased during outpatient and inpatient visits in hospitals were included in outpatient and inpatient drug costs, respectively. 481 The cost of self-purchased drugs was the expense of the drugs that patients bought in pharmacies (not in hospitals) for their ocular disease treatment after the initial diagnosis.

483 † Cost of escort were meals, transport and accommodation costs encountered by patients' escorts during all outpatient or inpatient visits.

Table 3 Reimbursement rate, proportion of CHE and QoL by related characteristics.

	Reim	bursemen	t rate (%	ó)*	СНЕ		oL
Characteristics	Outpatien t	Inpatie nt	SPD	Total	Proport ion (%)	n Mea	р
Total	28.1	9.5	2.7	26.9	32.2	0.65	
Level of VI							
Moderate VI	29.9	6.4	2.9	28.1	28.2 0.0	0.69	0.001
Severe VI	26.9	14.8	2.9	27.0	31.4	0.65	
Blind	22.2	11.7	1.4	21.4	52.6	0.49	
Cause of VI							
Cataract	29.5	4.3	2.3	26.7	17.5 0.0	010 0.76	0.000
AMD	26.9	7.6	0.6	23.9	51.4	0.72	

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	Reim	bursemen	t rate (%	(0)*	СН	E	QoL	
Characteristics	Outpatien t	Inpatie nt	SPD	Total	Proport ion (%)	р	Mea n	р
Vascular retinopathy	24.8	9.4	1.7	25.2	37.0		0.67	
Glaucoma	32.4	19.7	0.0	24.8	41.2		0.64	
Other eye diseases	22.2	6.8	5.1	23.5	31.7		0.59	
Multiple ocular disease	es 31.7	15.5	3.2	32.1	35.4		0.56	
Current living place								
Urban	30.9	15.0	5.9	33.5	26.2	0.000	0.67	0.4
Rural	27.9	9.2	2.5	26.5	47.6		0.62	
Medical insurance								
None	0.0	0.0	0.0	0.0	50.0	0.008	0.64	0.0
NCMS	14.2	4.9	2.3	13.9	47.9		0.63	
URBMI	24.2	6.9	4.3	21.6	25.0		0.81	
UEBMI	35.7	11.3	2.1	33.5	30.9		0.63	
GMI	38.5	14.5	2.6	38.0	16.7		0.66	
CMI	26.8	15.4	7.1	31.4	21.4		0.49	
Economic status								
Lowest	15.0	4.7	3.1	14.7	54.2	0.001	0.59	0.5
Lower	25.4	12.2	2.5	23.3	33.9		0.66	
Middle	28.7	8.3	2.9	31.3	26.7		0.68	
Higher	31.7	7.0	0.0	27.2	21.7		0.73	
Highest	39.3	15.4	4.9	38.0	25.0		0.62	

* Medical insurance reimbursement rate in our study was the percent of the whole year costs that is covered by insurance.

† Abbreviations: SPD, self-purchased drugs costs; CHE, catastrophic healthcare expenditure; QoL, quality of life; NCMS, new cooperative medical scheme; UEBMI, urban employee basic medical insurance; URBMI, urban resident basic medical insurance; GMI, government medical insurance; CMI, commercial medical insurance.

Supplementary File

Burden of visual impairment associated with eye diseases: an exploratory survey of 298 Chinese patients

Appendix 1 The items of the survey questionnaire.

Variable name	Description
Sociodemographic information	
age	[19,50], [51,70], [71,90]
gender	Male, Female
ethnicity	Han, Minority
educational level	Primary and below, Middle and high school, College and above
Occupation *	Management personnel, Professional personnel, General staff, Farmer, Other professions, Unemployed
marital status	Unmarried, Married
living status	Alone, With family
current living place	Urban, Rural
medical insurance †	None, NCMS, URBMI, UEBMI, GMI, CMI,
personal income	Continuous
household size	Continuous
household income	Continuous
linic-related information	
level of visual impairment	moderate VI, severe VI, blind
Duration of visual impairment ‡	3-6 months, 6-12 months, More than 12 months
Cause of visual impairment	Cataract, AMD, Vascular retinopathy, Glaucoma, Other eye diseases, Multiple ocular diseases
Outpatient visit	Continuous
Inpatient visit	Continuous
Hospital stay per visit	Continuous
conomic burden	
Direct medical costs §	
Outpatient costs	Continuous
Outpatient drug costs	Continuous
Outpatient out-of-pocket costs	Continuous
Inpatient costs	Continuous
Inpatient drug costs	Continuous
Inpatient out-of-pocket costs	Continuous
Self-purchased drugs costs	Continuous
Self-purchased drugs out-of-pocket co	ostsContinuous
Direct non-medical costs	
Long-term home care costs	Continuous
Transportation costs	Continuous
Food or accommodation costs	Continuous
Escort costs	Continuous
Nutrition or assistive devices costs	Continuous
Home modifications	Continuous
Quality of life	Continuous

* Occupation included current profession of unretired participants and former profession for the retired. Professional personnel were professional and technical personnel, i.e. teachers, doctors, lawyers, engineer, etc.

† Public insurance included new cooperative medical scheme in rural area (NCMS), urban employee basic medical insurance (UEBMI), urban resident basic medical insurance (URBMI) and government medical insurance (GMI). Commercial medical insurance (CMI) was supplements of public medical insurance purchased by respondents' employers or by themselves.

[‡] Duration of VI was defined by the period from the time which the participants became their current visual impaired level. § Direct medical costs measured the cost of resources used for treating a particular illness, consisted of outpatient costs, inpatient costs and self-purchased drugs costs. Expenditures for medicine prescribed and purchased during outpatient and inpatient visits in hospitals were included in outpatient and inpatient drug costs, respectively. The cost of self-purchased drugs was the expense of the drugs that patients bought in pharmacies (not in hospitals) for their ocular disease treatment after the initial diagnosis.

|| Cost of escort were meals, transport and accommodation costs encountered by patients' escorts during all outpatient or inpatient visits.

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Supplementary File

Burden of visual impairment associated with eye diseases: an exploratory survey of 298 Chinese patients

Appendix 2 Annual direct costs of different visual impaired patients in China.

	Dir	ect medica	l costs (USD)	Direct non-medical costs (USD)							Tota
Characteristics	Outpatient	Inpatient	Self- purchased drugs	Total	Long- term home care	Transportation	Food or accommodation	Escort	Nutrition or assistive devices	Home modifications	Total	direc costs (USD
Fotal	3,408.5	1,369.5	131.8	4,909.8	1,216.6	149.8	176.7	161.1	277.1	97.5	2,078.8	6,988
Age												
19-50 years old	2,009.3	3,572.4	211.5	5,793.2	1,269.1	248.1	407.7	249.6	77.8	43.2	2,295.5	8,088
51-70 years old	3,479.0	1,062.6	156.3	4,697.9	963.7	161.1	216.6	178.5	226.3	75.3	1,821.6	6,519
71-90 years old	3,749.9	1,014.6	85.8	4,850.3	1,437.2	110.6	72.4	119.1	382.4	134.0	2,255.7	7,106
Gender												
Male	3,321.3	1,860.7	98.6	5,280.6	1,069.2	130.7	132.7	179.2	300.4	118.4	1,930.6	7,21
Female	3,487.8	922.4	162.0	4,572.3	1,350.8	167.2	216.9	144.6	255.8	78.5	2,213.8	6,786
Ethnicity												
Han	3,404.2	1,325.0	130.2	4,859.4	1,039.7	135.5	166.1	167.0	250.6	86.5	· ·	,
Minority	3,468.1	1,988.2	154.7	5,611.0	3,675.2	348.7	324.7	78.2	645.0	250.4	5,322.3	10,93
Educational level												
Primary and below	2,924.6	991.6	85.3	4,001.6	2,331.9	173.9	138.3	96.1	146.7	51.3	2,938.2	6,93
Middle and high school	3,894.0	1,440.2	174.5	5,508.7	887.0	134.9	163.0	210.6	237.4	117.8	1,750.8	7,25
College and above	2,778.4	1,598.7	80.5	4,457.7	822.8	159.4	248.9	113.2	505.8	98.3	1,948.5	6,40
Decupation												
Management personnel	5,325.1	2,859.9	131.6	8,316.6	840.4	125.8	115.9	149.4	274.8	38.4	1,544.7	9,86
Professional personnel	3,924.7	1,129.7	137.3	5,191.6	1,035.5	182.0	281.2	207.9	503.9	111.5	2,322.1	7,51
General staff	2,751.8	1,414.9	97.5	4,264.1	1,592.0	156.1	136.3	97.0	211.6	109.5	2,302.4	6,56
Farmer	3,246.6	483.0	137.8	3,867.3	1,036.3	128.3	141.2	147.0	127.0	32.6	1,612.5	5,47
Other professions	2,467.8	2,635.3	146.8	5,249.9	2,731.9	172.9	242.8	226.6	531.3	275.9	4,181.6	9,43
Unemployed	2,536.8	1,487.3	204.9	4,229.1	758.8	100.0	119.8	242.1	40.4	144.4	1,405.7	5,63
Marital status												
Unmarried	869.9	1,715.0	172.2	2,757.1	1,922.0	78.0	59.7	71.5	120.7	79.4	2,331.4	5,08
Married	3,848.2	1,309.6	124.8	5,282.7	1,094.4	162.2	197.0	176.6	304.2	100.6	2,035.1	7,31
Living status												
Alone	1,546.6	1,218.0	138.6	2,903.2	1,015.9	82.9	39.2	126.8	158.1	95.8	1,518.7	4,42
With family	3,514.1	1,378.1	131.4	5,023.6	1,228.0	153.6	184.6	163.0	283.8	97.6	2,110.6	7,13

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	Dir	ect medica	l costs (USD)	Direct non-medical costs (USD)							Toto
Characteristics	Outpatient	Inpatient	Self- purchased drugs	Total	Long- term home care	Transportation	Food or accommodation	Escort	Nutrition or assistive devices	Home modifications	Total	Tota direc costs (USD
Current residence												
Urban	3,463.3	1,411.9	105.2	4,980.5	1,347.2	143.6	176.7	136.5	319.9	111.6	2,235.7	7,216
Rural	3,268.7	1,261.5	199.5	4,729.8	883.8	165.5	176.9	223.8	167.8	61.5	1,679.8	6,409
Medical insurance												
None	298.9	4,249.6	202.1	4,750.5	4,078.8	192.6	147.0	180.2	154.5	151.8	4,905.0	9,655
NCMS	3,488.4	1,208.2	209.3	4,905.9	881.5	156.2	173.2	233.0	96.9	42.8	1,583.8	6,489
URBMI	3,258.8	359.3	65.0	3,683.1	1,061.2	71.0	23.5	86.2	103.0	25.0	1,370.0	5,053
UEBMI	3,351.3	1,658.9	123.1	5,133.3	1,251.4	181.4	225.9	115.2	326.5	112.1	2,212.4	7,345
GMI	3,924.8	1,368.5	92.1	5,385.3	1,585,7	128.4	183.4	252.0	500.4	195.1	2,845.0	8,230
CMI	4,160.8	888.9	85.7	5,135.4	311.7	104.2	197.8	130.1	653.7	130.1	1,527.6	6,663
level of VI												
Moderate VI	3,120.7	853.8	118.6	4,093.1	916.4	142.4	138.5	125.9	222.0	65.3	1,610.4	5,70
Severe VI	4,479.9	1,694.5	147.5	6,321.8	1,793.8	158.7	226.7	128.2	293.3	137.0	2,737.6	9,05
Blind	2,301.6	2,995.5	156.8	5,453.9	1,284.8	163.9	238.9	396.6	492.7	155.8	2,732.6	8,180
duration of VI												
3-6 months	1,574.8	503.8	225.0	2,303.6	1,643.7	103.1	89.4	110.6	308.8	123.5	2,379.2	4,682
6-12 months	2,182.5	1,070.6	70.9	3,324.0	429.4	152.8	282.8	104.2	104.5	85.4	1,159.1	4,483
More than 12 months	3,992.0	1,582.2	129.8	5,703.9	1,321.3	157.0	167.6	182.4	310.4	95.9	2,234.6	,
Cause of VI	,			,	,							,
Cataract	1,236.9	583.9	27.5	1,848.3	790.1	55.1	67.7	48.4	63.2	19.4	1,043.7	2,892
AMD	8,162.3	524.7	134.8	8,821.8	346.9	189.3	172.0	174.6	480.9	0.0	1,363.7	
Vascular retinopathy	4,151.1	2,270.9	249.9	6,671.9	930.5	139.1	84.9	141.1	237.9	194.2	1,727.8	8,39
Glaucoma	4,909.7	2,297.1	208.0	7,414.8	380.0	78.6	100.9	102.7	118.7	35.7	816.6	8,23
Other eye diseases	1,656.8	2,350.2	180.2	4,187.1	1,781.2	278.0	414.6	203.0	145.3	76.4	2,898.5	7,08
Multiple ocular diseases	4,255.0	1,286.8	142.7	5,684.5	1,882.8	149.8	156.4	256.8	550.9	216.2	3,212.9	8,89
Economic status	.,	-,		-,	-,						-,	-,
Lowest	3,662.3	1,342.8	177.1	5,182.2	1,523.5	254.6	315.7	294.5	173.4	36.0	2,597.8	7.78
Lower	1,996.4	1,738.2	95.0	3,829.6	479.0	174.2	295.0	158.1	200.8	54.9	1,362.1	5,19
Middle	2,614.7	1,345.7	142.5	4,102.9	1,196.1	94.0	37.3	77.9	220.6	76.1	1,702.0	,
Higher	4,761.2	934.9	114.9	5,811.0	800.9	84.0	49.2	108.5	250.0	5.0	1,297.7	7,108
Highest	3,988.4	1,491.6	129.7	5,609.8	2076.3	144.4	190.8	168.6	537.5	313.7	3,431.3	9,04

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* Abbreviations: NCMS, new cooperative medical scheme; UEBMI, urban employee basic medical insurance; URBMI, urban resident basic medical insurance; GMI, government medical insuran

CMI, commercial medical insurance.

	Item No	Recommendation	Pag No
Title and abstract	1	(<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) 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	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
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	5
Participants	6	(<i>a</i>) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/	8*	For each variable of interest, give sources of data and details of methods	6
measurement		of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(<i>a</i>) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	6-7
		(c) Explain how missing data were addressed	/
		(<i>d</i>) If applicable, describe analytical methods taking account of sampling strategy	/
		(<u>e</u>) Describe any sensitivity analyses	/
Results			
Participants	13*	(a) 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	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	/
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	/
Outcome data	15*	Report numbers of outcome events or summary measures	7-9
Main results	16	(<i>a</i>) 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	/

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		(b) Report category boundaries when continuous variables were	15-
		categorized	17
		(c) If relevant, consider translating estimates of relative risk into absolute	/
		risk for a meaningful time period	
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions,	18-
		and sensitivity analyses	19
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential	11
		bias or imprecision. Discuss both direction and magnitude of any potential	
		bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	9-11
		limitations, multiplicity of analyses, results from similar studies, and other	
		relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	/
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study	12
		and, if applicable, for the original study on which the present article is	
		based 🚫	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.