

Prospective Study

Economic burden of irritable bowel syndrome in China

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Abstract**AIM**

To estimate annual direct and indirect costs for patients diagnosed with irritable bowel syndrome (IBS) and subtypes.

METHODS

Patients completed a standardized questionnaire concerning usage of healthcare resources, travel costs, meals, and productivity loss of patients when seeking treatment for IBS. Total annual costs per patient were calculated as the sum of direct (including medical and nonmedical) and indirect costs. Total annual costs per patient among various IBS subtypes were compared. Analysis of variance and bootstrapped independent sample *t*-tests were performed to determine differences between groups after controlling for IBS subtypes.

RESULTS

A total of 105 IBS patients (64.80% female), mean age of 57.12 years \pm 10.31 years, mean disease duration of 4.31 years \pm 5.40 years, were included. Total annual costs per patient were estimated as CNY18262.84 (USD2933.08). Inpatient and outpatient healthcare use were major cost drivers, accounting for 46.41% and 23.36% of total annual costs, respectively. Productivity loss accounted for 25.32% of total annual costs. The proportions of direct and indirect costs were similar

to published studies in other countries. Nationally, the total costs of managing IBS would amount to CNY123.83 billion (USD1.99 billion). Among the IBS subtypes, total annual costs per patient of IBS-M was highest at CNY18891.18 (USD3034). Furthermore, there was significant difference in productivity loss among IBS subtypes ($P = 0.031$).

CONCLUSION

IBS imposes a huge economic burden on patients and healthcare systems, which could account for 3.3% of the total healthcare budget for the entire Chinese nation. More than two-thirds of total annual costs of IBS consist of inpatient and outpatient healthcare use. Among the subtypes, IBS-M patients appear to have the greatest economic burden but require further confirmation.

Key words: Irritable bowel syndrome; Burden of illness; Direct and indirect medical and nonmedical costs; Irritable bowel syndrome subtype; Productivity loss

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Core tip: This study was the first article to evaluate the costs of patients with irritable bowel syndrome (IBS) in China, including all costs associated with care of patients with IBS, and allowed a more reliable estimation of true costs. In addition, unlike other published studies, this study also analyzed the costs of patients with four IBS subtypes, finding a difference in indirect costs among IBS subtypes. This would provide a benchmark for other researchers engaged in studying IBS.

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INTRODUCTION

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder^[1], with the worldwide prevalence ranges from 5.7% to 34%^[2]. Prevalence estimates for IBS appear to vary widely according to the criteria used and population studied^[3]. The reported prevalence of IBS in Western countries ranges from 17%-22%^[4]; but a highly variable range between 2.3%-34% is reported in Asian countries^[5,6]. In China, most studies applying the Rome II criteria reported the IBS prevalence in adult as between 5% to 10%^[7]. According to Rome II criteria, patients diagnosed with IBS can be classified into four subtypes: IBS-constipation (IBS-C), IBS-diarrhea (IBS-D), IBS-mixed type (IBS-M) and IBS-unclassified (IBS-U)^[8]. In

western countries, the major IBS subtype is IBS-C^[4], while IBS-D is commonly encountered in China^[9]. Clinically, IBS contributes between 25% and 50% of gastroenterology outpatient caseload^[10].

The high prevalence rate and complicated clinical manifestation make IBS a serious burden for social and public health^[11]. Compared to other chronic diseases, IBS sufferer has a higher utilization rate of health resources^[12]. Vandvik *et al*^[13] had shown that patients with IBS make two to three times the number of health care visits per year compared to the general population. Likewise, Badia *et al*^[14] found patients with IBS spent 1.6 times as much on their health care as those without IBS. Additionally, many studies also showed patients with IBS have poorer quality of life (QOL) when compared to the general population as well as patients with other chronic diseases^[11,15]. Furthermore, IBS patients suffering from frequent abdominal pain for prolonged duration were reported to have increased levels of anxiety about IBS^[11,15,16]. When considering economic impact, Hungin *et al*^[4] found that nearly one-quarter of IBS respondents worked fewer hours, 11% missed work and 67% felt less productive at work because of their symptoms. Meanwhile, caregivers of IBS patients also had more lost work days, and also more worry about IBS patients^[16,17].

Currently, studies of the economic burden in IBS were mainly performed in western countries^[18]. These studies used either a societal or patients' perspective to estimate the cost impact of IBS on society or patients their families^[18]. From a societal perspective, one US national company in 2005 calculated the productivity loss attributable to IBS to be USD7737 per patient^[4]. In Denmark, the median annual cost was between USD1360 and USD1508 per patient from absenteeism^[19]. Through absenteeism and presenteeism combined, the loss per IBS patient was estimated to be USD748 in Canada^[20], and EUR995 in Germany^[21]. From the patients' perspective, studies from the US estimated the annual cost per patient with IBS as between USD4232 and USD4527^[22,23], with a projected annual cost for the nation of USD1353 million^[24]. Annual treatment cost per patient estimated in other countries included United Kingdom estimates of between GBP316 and GBP906^[25,26], Canadian estimate of USD259^[20], and Norwegian estimate of NOK954 and NOK14854^[27]. Likewise, two Asian studies estimated the costs of IBS to be USD155 million in Korea nationally^[28], and the annual cost per patient as USD90 in Iran^[29]. Generally, the costs of primary care form a large part of total burden in IBS^[18]. For example, in the United States, on average, 25%-49% of IBS patients consult a primary care physician with two to three visits per year^[30]. One United Kingdom study showed that among those newly developing IBS over a 10-year period, the median number of annual primary care consultations for IBS was only 1 but with the maximum being 14^[31]. In Germany, primary

care visits accounted for up to 30% of total direct healthcare costs for patients with IBS^[21]. In addition, a small number of studies calculated the cost of IBS for special populations. In the Netherlands, total annual costs per child was estimated to be EUR2512.31. Overall, inpatient and outpatient healthcare use were major cost drivers, accounting for up to 50% of total annual costs^[17]. However, no studies estimating the costs of IBS subtypes were found.

In China, there were studies reporting the epidemiology^[7], and QOL^[32] of IBS. Nevertheless, the economic burden of patients with IBS in China has not been studied. This information would be invaluable to healthcare administrators and governments in making informed decision in allocating adequate and appropriate resources in managing patients with IBS. Therefore, this study aimed to estimate the economic burden of illness of patients with IBS and IBS subtypes to fill this knowledge gap.

MATERIALS AND METHODS

Study design

This study was to estimate the economic burden of IBS from the patients' perspective. We included all patients with IBS in the database from December 2014 to December 2015, beginning with the first day of medical care for each patient, at the First Hospital of Dalian Medical University. The First Hospital of Dalian Medical University is a level 3 comprehensive hospital (the equivalent of tertiary referral hospital in western countries), renowned for its management of cardiovascular and cerebrovascular diseases, metabolic diseases, gastrointestinal diseases and senile diseases. In China, patients have the freedom to choose the healthcare institution when seeking treatments. Due to the availability of advanced technology and experienced doctors, the level 3 comprehensive hospitals are usually their first choice.

For our study, trained health workers employed in rural hospitals and community health service organizations conducted face-to-face interviews. Data were collected using a standardized questionnaire adopted from a published study^[33]; and it included clinical information of IBS, usage of primary care and hospital admission due to IBS. All patients who gave written consent to participate were included in the study. The study was approved by the Ethics Committee of the hospital.

All patients with a diagnosis of IBS according to Rome III criteria were included after providing consent. All patients underwent routine laboratory testing prior to inclusion to rule out organic causes for the abdominal pain. Exclusion criteria were a concomitant organic gastrointestinal disease, infectious diarrhea, pregnant or breastfeeding women, and intellectual disability.

At baseline, patients with IBS completed the questionnaire specially designed for the study setting.

The recall period of questionnaire items was 4 wk prior to inclusion. Questionnaire items reflected the patients' perspective, referring to all significant costs related to the illness or intervention. We distinguished between direct costs of healthcare and indirect costs of productivity loss in this study. Direct costs were divided into direct medical costs and direct nonmedical costs. Indirect costs (*i.e.* productivity loss) were calculated by the human capital method^[34]. The average daily income per capita in 2015 was used as the value of lost workdays. The average daily income per capita was CNY174.27 in Dalian, according to China Statistical Yearbook^[35]. For patients who were retirees, their indirect costs were calculated by family caregivers' lost workdays; and for patients who were employed, if family caregivers indicated that they took leave from work to care for the patients, this was also considered as indirect costs. The sum of direct costs and indirect costs were the total cost per patient. As for the costs for the entire Chinese population, the average total cost per patient total costs in our study cohort was multiplied by the prevalence of IBS^[7], and the total population. The population in 2015 was 1.37 billion people^[35]. The gross domestic product (GDP) and per capita GDP in China were CNY67670.8 billion (USD10868.2 billion) and CNY51560.28 (USD8280.78)^[35]. According to the China Health Statistics Yearbook, the national health expenditures in 2015 was CNY3758.48 billion (USD603.63 billion)^[36]. All costs were expressed in CNY. The total costs per patient were also converted and presented as United States dollars to allow better international comparison (USD1 = CNY6.2265, GBP£1 = USD1.4260)^[37]. In order to compare with other studies, discount rate was used for adjusting the total costs with IBS to 2015. The discount rate applied was 3% in United States^[38], and 3.5% in United Kingdom^[39].

Direct medical costs

Direct medical costs are costs directly related to the disease, such as costs for diagnostics, therapeutics, and care^[40]. Patients with IBS were asked about the frequency and types of healthcare resources utilization (*e.g.*, outpatient attendance, pharmacy, inpatient admission, *etc.*) related to IBS. The costs and frequency of outpatient and pharmacy were captured by using the questionnaire, and detailed costs of inpatient were collected from the hospital's information system.

Direct nonmedical costs

Direct nonmedical costs were the costs related to the illness, but were not spending on health resources, such as costs for traveling to the healthcare providers, having meals and accommodation when seeking treatment, *etc.*^[40]. Patients were asked about the frequency and costs for traveling, having meals when seeking treatment for IBS. In addition, patients were asked whether they paid for health food. Particularly, patients specified the frequency and amount spent in the past

Table 1 Characteristics of four irritable bowel syndrome-subtypes *n* (%)

Characteristics	IBS (<i>n</i> = 105)	IBS-C (<i>n</i> = 23)	IBS-D (<i>n</i> = 42)	IBS-M (<i>n</i> = 9)	IBS-U (<i>n</i> = 31)	<i>P</i> value
Age (yr) (mean ± SD)	57.1 ± 10.3	60.3 ± 8.7	54.9 ± 11.9	52.0 ± 9.6	59.3 ± 8.2	0.049 ¹
≤ 50	24 (22.9)	2 (8.7)	12 (28.6)	5 (55.6)	5 (16.1)	
51-60	39 (37.1)	11 (47.8)	14 (33.3)	1 (11.1)	13 (41.9)	
61-70	35 (33.3)	8 (34.8)	13 (31.0)	3 (33.3)	11 (35.5)	
≥ 71	7 (6.7)	2 (8.7)	3 (7.1)	0 (0.0)	2 (6.5)	
Disease duration (yr) (mean ± SD)	4.3 ± 5.4	3.0 ± 2.7	5.0 ± 5.7	6.8 ± 10.6	3.8 ± 4.3	0.247
< 1	33 (31.4)	8 (34.8)	11 (26.2)	3 (33.3)	11 (35.5)	
1-3	33 (31.4)	9 (39.2)	13 (31.0)	4 (44.4)	9 (29.0)	
3-5	19 (18.2)	3 (13.0)	8 (19.0)	0 (0.0)	6 (19.4)	
> 5	20 (19.0)	3 (13.0)	10 (23.8)	2 (22.3)	5 (16.1)	
Gender						< 0.001 ²
Male	37 (35.2)	6 (26.1)	24 (57.1)	4 (44.4)	3 (9.7)	
Female	68 (64.8)	17 (73.9)	18 (42.8)	5 (55.6)	28 (90.3)	
Employment Status						0.094
Retired	42 (40.0)	10 (43.5)	16 (38.1)	3 (33.3)	13 (41.9)	
Employed	63 (60.0)	13 (56.5)	26 (61.9)	6 (66.7)	8 (58.1)	
Income level						0.096
Lower income	43 (40.9)	10 (43.5)	15 (35.7)	5 (55.6)	13 (41.9)	
Middle income	55 (52.4)	12 (52.2)	25 (59.5)	2 (22.2)	16 (51.6)	
Higher income	7 (6.7)	1 (4.3)	2 (4.8)	2 (22.2)	2 (6.5)	

¹There was significant difference between age distribution of irritable bowel syndrome-constipation (IBS-C) vs IBS-diarrhea (IBS-D) vs IBS-mixed (IBS-M) vs IBS-unclassified (IBS-U) (*P* = 0.049); ²There was significant difference between gender distribution of IBS-C vs IBS-D vs IBS-M vs IBS-U (*P* < 0.001). Lower income: < 5000 yuan/mo; Middle income: 5000-10000 yuan/mo; Higher income: > 10000 yuan/mo.

4-wk. We calculated the costs of direct nonmedical costs according to the information gathered in their questionnaires.

Indirect costs

Indirect costs were defined as productivity costs in which sporadic work loss was associated with medical service use and extended work loss due to a disability or death^[40]. The time lost from work due to medical care was estimated by the type and frequency of visits to a health care institution. In our study, each day in the inpatient was considered a loss of a full work day and each outpatient visit was considered a half work day loss.

In this study, due to the nature of the disease being studied, productivity loss due to premature mortality was not included.

Total costs and data analysis

Total costs of treatment of patients with IBS according to Rome III criteria were presented as the sum of direct costs and indirect costs. To derive cost estimates per patient per year, the 4-wk recall period of the questionnaire was multiplied by 13.0446 [based on (1/28) × 365.25]. If patients reported healthcare provider consultations, but the frequency of visits was missing, the average reported consultation rate of the respective healthcare providers was used.

Statistical analysis

We reported the details of annual costs by using bias-corrected and accelerated bootstrapping, drawing 1000 samples of the same size as the original sample. Bootstrapped independent sample *t*-tests (1000

bias corrected replications) and analysis of variance were performed to determine differences between IBS subtypes, and bias-corrected and accelerated 95%CI around the mean of the original sample were generated. All data analyses were performed using SPSS (IBM Corporation, NY, United States). Statistical significance was set at 5%.

RESULTS

A total of 140 patients with IBS according to Rome III criteria were included in this study between December in 2014 to December in 2015. Of these patients, 35 withdrew informed consent and did not complete the questionnaires. Therefore, 105 patients were included in the analyses, and 68 included patients (64.8%) were female. Table 1 shows the detailed information of the included patients. The mean age of the group was 57.1 years (SD ± 10.3). Mean duration of symptoms was 3.7 years (SD ± 5.4), with 81% having symptoms less than 5 years. Sixty percent of the patients was employed, and more than half of the patients (52.4%) reported to be in the middle income group.

When categorized according to IBS subtype, IBS-D was diagnosed in 42 patients (highest at 40%), and the number of IBS-M patients was 9 (lowest at 8.6%). The mean age of IBS-C was oldest at 60.3 years (SD ± 8.7), and IBS-M type was youngest at 52.0 years (SD ± 9.6). Patients with IBS-M had longest disease duration at 6.8 years (SD ± 10.6), while IBS-C was shortest at 3.0 years (SD ± 2.7). IBS-Ds were more prevalent in males (57.1%), and IBS-U more prevalent in females (90.3%). The proportion of employed patients in four irritable bowel syndrome subtypes

Table 2 Direct medical costs (CNY yuan)

Direct medical costs	No. of patients	Average visits per 4 wk	Average visits per year	4-wk drug cost per patient	4-wk medical cost per patient	Annual costs per patient
Outpatient	99 (94.29%)	1.01	12.42	213.57 (185.86-246.95)	112.49 (82.04-142.77)	4266.58 (3705.55-4838.44)
Pharmacy	13 (12.38%)	1.08	1.72	17.33 (7.53-28.29)	0.76 (0.34-1.25)	31.56 (13.74- 51.29)
Inpatient	105 (100%)	0.01	1.28	290.76 (261.82-320.29)	359.03 (340.65-377.07)	8476.30 (7888.07-9050.18)
Total costs				521.67 (76.32-91.09)	472.28 (437.26-507.22)	12761.14 (11885.82-13595.74)

Table 3 Direct nonmedical costs (CNY yuan)

Direct nonmedical costs	No. of patients	4-wk costs per patient	Annual costs per patient
Travel	105 (100%)	23.06 (19.65-26.57)	749.75 (645.57-867.93)
Meals	98 (93.33%)	6.49 (4.77-8.30)	79.03 (58.16-101.00)
Health food	8 (7.62%)	49.05 (14.28-97.13)	48.75 (14.20-96.55)
Total costs		78.60 (42.55-127.91)	877.54 (752.62-1022.94)

Table 4 Indirect costs (CNY yuan)

Indirect costs	4-wk lost work days	Average costs per 4 wk	Annual lost work days per patient	Annual costs per patient
Outpatient	0.62 (0.57-0.68)	108.71 (99.60-117.84)	8.14 (7.45-8.88)	1337.07 (1225.06-1449.34)
Pharmacy	0.06 (0.03-0.10)	10.79 (4.98-17.43)	0.81 (0.37-1.30)	17.42 (8.04-28.15)
Inpatient	1.10 (1.04-1.16)	190.85 (180.80-202.17)	14.29 (13.54-15.13)	2489.59 (2358.47-1637.26)
Resting at home	0.34 (0.32-0.36)	59.80 (56.87-62.98)	4.48 (4.25-4.71)	780.07 (741.90-821.56)
Total costs	2.13 (2.04-2.22)	370.15 (355.61-386.23)	27.71 (26.62-28.91)	4624.15 (4456.32-4802.13)

was between 55%-67%. Besides IBS-M patients, almost half of the patients in other subtypes reported belonging to the middle income group. Overall, there were significant differences in age distribution ($P = 0.049$) and gender distribution ($P < 0.001$) among the four irritable bowel syndrome subtypes.

Direct medical costs

The average number of visits to utilize outpatient, inpatient and pharmacy services in the past 4 wk and the total direct medical costs were shown in Table 2. The proportion of patients using these resources was 94.29% for outpatient service, 12.38% for pharmacy service, and 100% for inpatient service. The annual frequency of visiting these healthcare facilities was 12.42 times for outpatient service, 1.72 times for pharmacy service, and 1.28 times for inpatient service. Mean annual total direct medical costs per patient was CNY12761.14 (95%CI: 11885.82-13595.74). Of this, inpatient costs comprised the highest component (66.42% of direct medical costs), at CNY8476.30 (95%CI: 7888.07-9050.18). This was followed by outpatient costs (33.43% of direct medical costs) at CNY4266.58 (95%CI: 3705.55-4838.44), and pharmacy costs (0.25% of direct medical costs) at CNY31.56 (95%CI: 13.74-51.29).

Table 2 also shows the drug costs and other medical costs per patient in the 4-wk period. The drug costs were CNY521.67 (95%CI: 76.32-91.09) in the 4-wk period, which was larger than the costs of other consumed medical resources.

Direct nonmedical costs

The total direct nonmedical costs and detailed costs were shown in Table 3. Mean annual direct nonmedical costs per patient was CNY877.54 (95%CI: 752.62-1022.94). The greatest component was travel costs (85.43% of direct nonmedical costs), at CNY749.75 (95%CI: 645.57-867.93). Most patients ($n = 98$, 93.33%) also consumed meals spending on average CNY79.03 (95%CI: 58.16-101.00) while seeking treatment. The costs were lowest in special health food (5.56% of direct medical costs) at CNY48.75 (95%CI: 14.20-96.55), with 8 patients (7.62%) only reporting this expense.

Indirect costs

All patients had worked less than usual in the past 4 wk as a consequence of their abdominal complaints. In Table 4, mean annual lost work days were 27.71 d (95%CI: 26.62-28.91), and annual cost of production loss per patient was CNY4624.15 (95%CI: 4456.32-4802.13). The annual lost work days were 14.29 in inpatient, 8.14 in outpatient, 4.48 at home, and 0.81 in pharmacy. The highest annual production loss was due to inpatient admission (53.84% of indirect costs), at CNY2489.59 (95%CI: 2358.47-1637.26).

Total costs

All direct and indirect medical and nonmedical costs were summarized in Table 5. Total annual costs per patient were CNY18262.84 (95%CI: 17326.86-19158.27), with direct medical costs accounting for 69.87% of total costs.

Table 5 Total costs (CNY yuan)

	4-wk costs per patient	Annual costs per patient
Direct medical costs	993.95 (934.37-1059.57)	12761.14 (11885.82-13595.74)
Outpatient	326.06 (285.86-372.84)	4266.58 (3705.55-4838.44)
Pharmacy	18.10 (7.77-28.25)	31.56 (13.74- 51.29)
Inpatient	649.79 (601.91-693.69)	8476.30 (7888.07-9050.18)
Direct nonmedical costs	78.60 (42.55-127.91)	877.54 (752.62-1022.94)
Travel	23.06 (19.65-26.57)	749.75 (645.57-867.93)
Meals	6.49 (4.77-8.30)	79.03 (58.16-101.00)
Health food	49.05 (14.28-97.13)	48.75 (14.20-96.55)
Indirect costs	370.15 (355.61-386.23)	4624.15 (4456.32-4802.13)
Outpatient	108.71 (99.60-117.84)	1337.07 (1225.06-1449.34)
Pharmacy	10.79 (4.98-17.43)	17.42 (8.04-28.15)
Inpatient	190.85 (180.80-202.17)	2489.59 (2358.47-1637.26)
Resting at home	59.80 (56.87-62.98)	780.07 (741.90-821.56)
Total costs	1442.70 (1356.99-1520.09)	18262.84 (17326.86-19158.27)

Table 6 Total costs for the entire Chinese population

Total costs		National health budget	Costs as % of national health budget	GDP		Total costs as % of GDP		Units
National	Per capita			National	Per capita	National	Per capita	
123.83 B (1.99 B)	18262.84 (2933.08)	3758.48 B (603.63 B)	3.29%	67670.8 B (10868.2 B)	51560.3 (8280.8)	0.18%	35%	2015CNY (2015USD)

B: Billion; GDP: Gross domestic product.

Table 7 Total costs of four irritable bowel syndrome subtypes (CNY yuan)

	IBS-C	IBS-D	IBS-M	IBS-U	P value
Direct medical costs	12036.72 (10319.41-13841.58)	12838.55 (11570.90-14221.77)	12990.03 (11094.74-14757.98)	13127.30 (11484.21-14680.82)	0.830
Direct nonmedical costs	973.31 (741.98-1252.00)	812.15 (586.09-1114.49)	986.80 (95.42-201.77)	863.34 (716.92-1025.52)	0.792
Indirect costs	4449.10 (4020.92-4893.99)	4890.66 (4648.80-5169.87)	4914.35 (4446.81-5340.35)	4308.71 (4017.27-4584.88)	0.031 ¹
Total costs	17459.12 (15369.32-19486.61)	18541.36 (17241.44-19933.29)	18891.18 (16960.86-20813.44)	18299.35 (16423.33-20269.52)	0.817

¹There was significant difference between indirect costs of irritable bowel syndrome-constipation (IBS-C) vs IBS-diarrhea (IBS-D) vs IBS-mixed (IBS-M) vs IBS-unclassified (IBS-U) ($P = 0.031$).

The total costs for the entire Chinese population are shown in Table 6. By multiplying with the prevalence of IBS^[7], and the total population^[35], the total costs for the entire Chinese population could amount up to CNY123.83 billion (USD1.99 billion), accounting for 3.29% and 0.18% of the national health budget and GDP for the entire Chinese population. And the total costs per capita would account for 35% of per capita GDP.

Total costs of four irritable bowel syndrome subtypes

As shown in Table 7, the highest total costs per patient was for IBS-M patients, at CNY18891.18 (95%CI: 16960.86-20813.44); and the costs were lowest in IBS-C, at CNY17459.12 (95%CI: 15369.32-19486.61). In all subtypes, direct costs were the major component accounting for approximately 75% of total costs. Additionally, there was significant difference between indirect costs of four IBS subtypes ($P = 0.031$), with the indirect costs in IBS-M much higher than the other subtypes.

DISCUSSION

IBS was a multi-factorial condition and the prevalence was dependent on age and gender^[41]. In most Western countries, IBS affects more women (60%-70%) than men^[42,43]. The prevalence of IBS in this study was 64.8% in females, which was similar to Western countries but higher than some Asian countries, such as India (59.69%)^[44], and Japan(50%)^[45]. Some previous studies in China had reported the prevalence of IBS in female patients as 56.50% in Shanghai^[46], and 55.56% in Guangdong province^[47]. Overall, the prevalence of IBS in female patients in our sample could be judged as similar to other Chinese studies.

When considering the age of common occurrence, one United States study found that although IBS can occur at any age, it was more prevalent in young and middle-aged groups and less common in the elderly^[48]. IBS was also reported to prevail mostly in persons below the age of 25 years (20.9%) or between 35 years to 44 years (26.1%) in Western countries^[23]. However, the age of common occurrence in some

Table 8 Economic burden per person with irritable bowel syndrome in other studies

Ref.	Country	Total costs		Units
		Direct	Indirect	
This study	China	13638.68 (2190.42) ¹	4624.15 (801.64) ¹	2015CNY (2015USD)
Dean <i>et al</i> ^[52]	United States		7737 (10398) ²	2005USD (2015USD)
Leong <i>et al</i> ^[23]	United States	3736 (6175) ²	791 (1307) ²	1998USD (2015USD)
Ricci <i>et al</i> ^[53]	United States	7547 (11758) ²		2000USD (2015USD)
Ahn <i>et al</i> ^[54]	United States	1562 (2294) ²		2002USD (2015USD)
Creed <i>et al</i> ^[55]	United Kingdom	1743 (2634) ³	334.50 (505.45) ³	2003USD (2015USD)

¹USD1 = CNY6.2265; ²The discount rate was 3% in United States; ³The discount rate was 3.5% in United Kingdom.

Asian countries was different from Western countries. In India, IBS prevails mostly in 51-61 year-old^[49]; while one Korean study reported the prevalence of IBS tended to increase with age, with 13.76% occurring in the 60-69 year age group^[28]. Similar to these countries, our current study found IBS to be more common between 51 to 60 years, accounting for 37.10%.

Furthermore, our study also found a difference with Western countries in the duration of symptoms. In our study, the proportion of patients with symptom duration less than 5 years was 81%, much higher than in United States (36%)^[50]. However, this difference would need to be interpreted with caution as it may be caused by the difference in referral systems as well as health seeking habits across different countries.

When considering the distribution of IBS subtypes, in United States, the relative proportions of IBS subtypes ranged from 5.2% to 66% for IBS-C, 0.8% to 33.9% for IBS-D, and 5.2% to 33.1% for IBS-M^[9], with the most common IBS subtypes being IBS-C. One northern Indian study found the relative proportion was 42.4% for IBS-M, 37.7% for IBS-D, 13.6% for IBS-U and 6.3% for IBS-C, with IBS-M as the most common subtypes^[44]. However, the proportions of IBS subtypes in our study was quite different from other countries with IBS-D (40%) and IBS-M (8.57%) as the most and least common IBS subtypes respectively.

Gender-specific prevalence of IBS subtypes were reported in some studies^[41]. In United States, IBS-D was more common in males (37.5%), and IBS-C more common in females (47%)^[8]. In Japan IBS-M was of similar prevalence in the females and males at 45% and 49% respectively^[51]. In South Korea, the most commonly encountered IBS subtype with similar prevalence of 38.3% and 33.8% in females and males respectively was IBS-D^[28]. Similar to United States and South Korea, IBS-D was more prevalent among males (57.1%) in our study. However, IBS-U was the predominant subtypes in our female patients (90.3%), which was quite different with other countries.

As a prevalent chronic disorder, IBS imposes a heavy economic burden on health care^[23]. In 1995, the United Kingdom spent £45.6 million (£90.73 million, which was adjusted to 2015) in managing IBS, constituting 0.1% of the total annual spending by the United Kingdom National Health Service^[25]. Similarly,

the United States spent USD1658 million (USD2740 million adjusted to 2015 value) in caring for IBS in 1998^[24]. In our study, the costs of IBS were estimated to be CNY123.83 billion (USD1.99 billion), which would account for 3.3% of the total healthcare budget for the entire Chinese population. Although the total costs of IBS were higher than United States or United Kingdom, the annual cost per patient at CNY18262.84 (USD2933.08) was lower than United States or United Kingdom^[24-26].

The direct and indirect cost per person between our study and other studies were shown in Table 8^[23,52-55]. Medical charges per patient in China were lower than that of the United States and the United Kingdom. The direct costs and indirect costs of IBS in this study were CNY13638.68 (USD2190.42) and CNY4624.15 (USD801.64) respectively. Some published review in United States reported that the annual direct costs associated with IBS ranged from USD1562 (2002 USD; adjusted to 2294 per year in 2015 USD) to USD7547 (study published in 2000; adjusted to 11758 per year in 2015 USD), while the annual indirect costs of IBS ranged from USD791 (1998 USD; adjusted to USD1307 per year in 2015) to USD7737 (study published in 2005; adjusted to USD10398 per year in 2015). Another perspective in United Kingdom reported that the direct costs were USD1743 (study published in 2003; adjusted to USD2634 per year in 2015), while the indirect costs were USD334.50 (study published in 2003; adjusted to USD505.45 per year in 2015). The difference in direct costs can be accounted by the lower price of related medical resources in China, as compared to the United States and European countries. For example, an average colonoscopy costs CNY500-1000 (USD80.30-160.60) in China, whereas it costs USD3081 in the United States^[56] and £1005-2195 in the United Kingdom^[57].

For IBS, the reported costs in outpatient costs were 12.7% to > 50% of total costs, in inpatient costs were 6.2% to 40.8%, and in pharmacy or drug costs were 5.9% to 46.6%^[58]. Despite the costs per patient of IBS were lower in China, the proportion of outpatient (23.36% of total costs) and inpatient (46.41% of total costs) costs were similar to Western countries, and in pharmacy was much lower (0.17% of total costs), because of the least number of visiting-patients. In

contrast to the western countries^[21,30,31,58], the reported share of visiting-patients of health care resource use varied widely, particularly 99 patients (94.29%) in outpatient, 105 patients (100%) in inpatient costs, and 13 patients (12.38%) in pharmacy. Additionally, this study demonstrated that IBS patients visited outpatient more frequently, at a rate of 12.42 per year compared to 1.6 in the United Kingdom and 0.9 in the United States^[59].

The indirect costs in patients with IBS accounted for two-thirds of the total in industrialized countries^[52,53]. In contrast, indirect costs were assumed to be 25.32% in the present study because the costs in China were much lower than those in United States and United Kingdom. The daily costs was 174.27 yuan (USD27.99), whereas it costs USD201.12 in the United States^[60] and £150 (USD216.51) in the United Kingdom^[61]. Furthermore, in this study, mean annual loss of work days were 27.71 d, whereas it was 8.5-21.6 d in United States^[62].

So far, no published study analyzed cost outcomes for all IBS subtypes^[58]. But one United States study had reported the costs of patients with IBS-C^[51]. The total costs per patient of IBS-C were USD3856, of which 78.1% was from medical costs, and 21.9% was from productivity costs^[51]. Additionally, Guerin *et al.*^[63] found the total costs of patients with IBS-C as USD4353, of which 71.3% was from medical service costs. Although the costs per patient (CNY17459.12; USD2804) of IBS-C in our study were lower, the proportion of direct costs (74.5%) and indirect costs (25.5%) were similar to United States. However, there was significant difference among indirect costs of four irritable bowel syndrome subtypes ($P = 0.031$), with much higher indirect costs in IBS-M subtypes.

To the best of our knowledge, this was the first study to evaluate the costs for patients with IBS in China; and in our study, all costs associated with care of patients with IBS were included, thus allowing a more reliable estimation of actual costs of care for these patients. Additionally, unlike other published studies, our study also analyzed the costs of patients with four IBS subtypes, finding a difference in indirect costs among IBS subtypes. This would provide a benchmark for other researchers engaged in studying IBS.

A limitation of our current study was the extrapolation of 4-weekly costs based on the recall period of questionnaires to annual costs by simple multiplication. Although this multiplicative approach combined with bias-corrected and accelerated bootstrapping technique, the results of total costs per patient may be higher than the real value. However, when considering the similarity in the comparative proportion of direct and indirect costs between our studies and other published studies as discussed, so our approach would have produced more accurate estimate than expected. Another limitation was that the investigative sample size was relatively small, and the sample all came from the First Affiliated Hospital of Dalian Medical University.

Certainly, significant differences in lifestyle, demographics, use and access to medical facilities exist in all countries and sometimes even different regions in the same country. So there is the risk to extrapolate the results from our sample as representative of all patients from all regions of China. However, when considering the relatively lack of genetic difference, the rather standardized treatment for IBS, and the health seeking habit of the Chinese population, our cohort could be considered as typical of IBS sufferers in China if interpreted with some caution.

Finally, due to the small sample size in our study, the conclusion that patients with IBS-M subtype have a significant difference may also be risky. However, based on clinical experience, patients with IBS-M are more difficult to treat. Other published studies also supported clinical difference in the various IBS-subtypes, with patients with IBS-M subtype posing more difficulties in the management^[64-66]. Hence, there is a good chance that the difference observed would be valid. Nevertheless, due to the relatively limited sample size, our observation will need confirmation with larger studies in future.

Overall, the aforementioned limitations would somewhat affect the external validity of the results.

In conclusion, IBS imposes a huge economic burden on healthcare systems and patients, which could account for 3.3% of the total healthcare budget and 0.18% of the GDP for the entire Chinese nation. The total costs per capita could account for 35% of per capita GDP. The direct and indirect costs were lower than US and United Kingdom. More than two-thirds of total annual costs of IBS consist of inpatient and outpatient healthcare use. Among the subtypes, IBS-M patients appear to have the greatest economic burden but would need further confirmation.

COMMENTS

Background

Irritable bowel syndrome (IBS) is a significant public health issue and is considered to be prevalent in the general population, but no study on economic burden of irritable bowel syndrome in China.

Research frontiers

The objective of this study was to describe the economic burden of irritable bowel syndrome and irritable bowel syndrome subtypes in China.

Innovations and breakthroughs

This is the first published paper describing the economic burden of IBS and IBS subtypes in China. The direct and indirect costs of IBS among patients in our sample were lower than that reported in the West. This study shows that IBS imposes a huge economic burden on healthcare systems and patients, which could account for 3.3% of the total healthcare budget and 0.18% of the gross domestic product (GDP) for the entire Chinese nation.

Applications

Findings from this study have important implications for programs intended to understand the economic burden with patients suffering from IBS in China and analyze the reasons of the difference with the economic burden of IBS among other countries.

Terminology

IBS is the most common functional gastrointestinal disorder characterized by abdominal pain or discomfort along with alteration of bowel habits in absence of an organic cause. Based on predominant bowel habit, it is further divided into IBS-diarrhea, IBS-constipation, IBS-mixed and IBS-unspecified. The economic burden of IBS is equal to the cost of various resources (such as medical and nonmedical resources) and the waste of productivity.

Peer-review

This is a socio-economic study of a group of IBS patients seen at one hospital in China. It is interesting and well researched and well written.

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