Featured Article

The cost of Alzheimer's disease in China and re-estimation of costs worldwide

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Abstract

Introduction: The socioeconomic costs of Alzheimer's disease (AD) in China and its impact on global economic burden remain uncertain.

Methods: We collected data from 3098 patients with AD in 81 representative centers across China and estimated AD costs for individual patient and total patients in China in 2015. Based on this data, we re-estimated the worldwide costs of AD.

Results: The annual socioeconomic cost per patient was US $19,144.36, and total costs were US $167.74 billion in 2015. The annual total costs are predicted to reach US $507.49 billion in 2030 and US $1.89 trillion in 2050. Based on our results, the global estimates of costs for dementia were US $957.56 billion in 2015, and will be US $2.54 trillion in 2030, and US $9.12 trillion in 2050, much more than the predictions by the World Alzheimer Report 2015.

Discussion: China bears a heavy burden of AD costs, which greatly change the estimates of AD cost worldwide.

1. Background

China has become an aging society in the past 20 years. The sixth national population census in 2010 showed that 178 million people were aged ≥ 60 years, 13.26% of the total population [1]. As a result, dementia, especially Alzheimer's disease (AD), is increasing rapidly in China. It was reported that the prevalence of AD was 3.21% among people aged ≥ 65 years [2], and more than 7 million Chinese people live with AD today in China. AD tends to have a long course, various comorbidities, and requirements for long-term care. Consequently, AD confers a heavy economic burden on society and families [3]. In past decades, only two regional studies have investigated the monetary cost of AD in China, in Shanghai and Shandong province [4,5]. There has been no national-scale randomized sampling study on the economic burden in China. To date, no reliable number for the socioeconomic costs of AD in China as a whole has been established.

Most international multilateral cost-of-illness studies for dementia have been carried out in high-income countries [6], and they have provided reliable and timely information to support estimates of the global burden. Evidence has also accumulated with regard to the economic burden of dementia in some low- and middle-income countries, but not in mainland China [7–9]. Based on these studies, the World Alzheimer Report (2015) estimated the worldwide economic costs of dementia [10]. However, this estimate referred to the results of a small study that included only one hospital in one city of China, which hardly seems representative of the entire country. This may have influenced the estimated results, which might be less or greater than the true value. An accurate value for the costs of AD in China is important simply because it will have a great impact on any global estimate numerically. Thus, a large, nationwide survey to determine the true socioeconomic costs of patients with AD in China is urgently needed.

Therefore, we designed the present study to include representative hospitals, nursing homes, and care facilities in both urban and rural areas in almost all parts of mainland China to investigate the socioeconomic costs of patients with AD, and furthermore to analyze the impact of our results on the global AD economic burden.

2. Methods

2.1. Settings

For the region selection, excluding Tibet, Hong Kong, and Macao, 30 provincial, municipal, and autonomous regions in mainland China (the mainland China has a total of 33 regions) were included. For the participating site selection, tier 3 hospitals, mental health centers/psychiatric hospitals, gerontology hospitals, nursing homes, care facilities, and both urban and rural residences, were chosen randomly as study sites. Ultimately, in total, 81 sites were included in this study.

2.2. Participants

Patient were aged ≥ 60 years, and the inclusion criteria were as follows: (1) a primary diagnosis of AD according to the National Institute of Neurologic and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria [11], diagnosed by a dementia specialist; (2) complete information about the economic costs of AD and comorbidities, obtained from electronic medical records systems and face-to-face interviews. The details of the inclusion and exclusion criteria are provided in our protocol which was published in BioMed Central Neurology [12].

The institutional review board or ethics committee at each participating site approved the study protocol. Written informed consent was obtained from each participant before data collection.

2.3. Design

This is a multi-centre, cluster-randomized, cross-sectional study which was conducted from October 2015 to March 2016. As described in the published protocol [12], we design this study considering several factors. First, China has a vast territory with different economic levels in the Eastern, Central, and Western areas [13,14]. The costs of medical treatment vary from area to area [15]. Therefore, we sampled almost all provinces and autonomous regions in mainland China to accommodate all economically representative areas. Second, in each region, hospitals, nursing homes and care facilities, and both urban and rural residences, which met inclusion criteria [12], were selected randomly to ensure the study was representative of various disease stages and care practices. Third, for accuracy of the data, electronic medical record systems and electronic residence health-care systems at each site were used to calculate AD costs.

2.4. Outcome measures

The total socioeconomic costs in this study included direct medical, direct nonmedical, and indirect costs [12]. Direct medical costs consisted of outpatient costs, hospitalization costs, and out-of-pocket expenses for health care and medications. Direct nonmedical costs, also known as direct social sector costs [10], included cost of transportation, accommodation, and meals when visiting a physician; the cost of nourishment and health-care equipment in the patient's daily life; and formal care fees in nursing homes, care facilities, or at home. Indirect costs included monetary losses caused by the patient's inability to work, reduction in informal caregivers' income, and intangible costs, which included the treatment of the mental suffering of caregivers and unexpected injuries in patients with AD or their caregivers.

2.5. Study procedures

Before starting the study, all participating investigators attended a training program conducted in regional centers to ensure consistency and accuracy of the AD diagnosis. At the start of the study, electronic medical records systems were used to identify patients with a primary diagnosis of AD in hospitals, residences, nursing homes, and other care facilities. Those patients with AD then had their diagnoses reconfirmed clinically by dementia specialists. New participants were also enrolled during the study period. For those who were confirmed to have AD, information about costs was collected using electronic medical records systems and the electronic residence health-care system at each site. Then, questionnaires were completed by trained staff

based on information from the electronic systems. When information was not available from electronic medical records, such as informal care, out-of-pocket money, and transportation costs, we conducted face-to-face interviews to obtain the details.

2.6. Statistical analysis

Descriptive statistics were used to summarize patient characteristics, including variables of age, gender, years of education, time since AD diagnosis, marital status, and living location (urban or rural). Means ± standard deviation were used to describe quantitative variables and frequencies of qualitative variables.

We used a prevalence-based, bottom-up approach to estimate the economic costs of AD in China. (1) We first estimated the number of individuals with AD in China in 2015 by multiplying the age-specific prevalence of AD by the corresponding numbers of people in each age group in the population [16]. Age-specific prevalence in 2020, 2030, 2040, and 2050 was obtained using a regression model based on data from a comprehensive review [16]. Then the predicted numbers of people with AD in each specific year were calculated by multiplying the age-specific prevalence by the corresponding numbers of people in each age group. (2) The average annual cost of AD per capita in China was obtained by adding direct medical costs, direct nonmedical costs, and indirect costs [12]. (3) The total economic burden of patients with AD in China in 2015 was obtained, with the average annual cost per patient with AD from our results multiplied by the number of patients with AD in 2015 [12].

The average annual growth rate of the consumer price index in China was estimated as 1.030 [17]. According to this growth rate, we predicted the per capita cost of patients with AD in China in 2020, 2030, 2040, and 2050. We then multiplied the per capita cost by the predicted number of patients with AD and determined the predicted annual total AD socioeconomic costs in China for these years. According to the World Alzheimer Report of 2015 [10], the world annual growth rate of dementia patients was 1.033, and the annual growth rate of the consumer price index was 1.031. Using these growth rates, we predicted the economic burden of dementia worldwide. The cost estimates were converted to 2015 US dollars based on country-specific consumer price indexes [18] and exchange rates [19] (exchange rate: US $1 \approx 6.4$ RMB; Bank of China, December 2015) for comparison with other countries.

We compared our new results with previous data on socioeconomic costs of AD in China. We then updated Chinese and global AD current and future predicted costs based on our new data and compared them with the numbers reported in the World Alzheimer Report of 2015. Moreover, the proportion of AD socioeconomic costs in the gross domestic product (GDP) of China was compared with that of the world's average using χ^2 test. Finally, comparisons of

proportions of direct medical costs, direct nonmedical costs, and indirect costs between China and some developed countries were also conducted using χ^2 test [20–23].

Sensitivity analyses were performed to examine the robustness of the results and to explore parameters that might affect the estimated costs of AD. First, the total costs of AD were estimated using data on the prevalence of AD derived from a Chinese systematic review [24]. Then, the different distributions of AD status (mild:moderate:severe = 1:1:1 or 1:2:1) or urban versus rural (1:1) were used to estimate the AD annual total costs. Furthermore, the total costs were estimated if 50%, 70%, and 100% of the patients with AD were regarded as having received medical treatment. Finally, we estimated the annual total costs considering the different numbers of comorbidities (0∼5).

All data analyses were performed using SAS (version 9.3, 64 bit; SAS Institute, Cary, NC, USA) and "R" softwares (version 3.2.3) [25]. The level of statistical significance was set at α = 0.05.

3. Results

3.1. Participants

Of 3098 patients with AD enrolled, 3046 (54.20% women) had complete information (Table 1). Tier 3 general hospitals were the major source of patients with AD (2226 cases, 73.08%), followed by communities (341 cases; 11.19%), mental health centers/psychiatric hospitals (190 cases; 6.24%), nursing homes and care facilities (179 cases; 5.88%), and gerontology hospitals (110 cases; 3.61%).

3.2. Socioeconomic costs of AD in China in 2015 and predictions

The average cost per patient per year was US $19,144.36 (RMB 122,523) (Table 2). In 2015, given that 8.75 million people in China suffered from AD [16], the total socioeconomic costs of Chinese patients with AD were estimated to be US $167.74 billion, 5.95-fold more than the previous estimate of US $28.18 billion from the World Alzheimer Report (2015) (Fig. 1) [10], based on Wang's study in 2006 [4], demonstrating that costs of AD care in China have long been underestimated. Among the total socioeconomic costs of US $167.74 billion, direct medical costs were US $54.53 billion, accounting for 32.51% of the total costs, with direct nonmedical costs of US $26.20 billion (15.62%) and indirect costs of US $87.01 billion (51.87%). Regarding predictions based on these new results, the total costs of AD in China will be US $248.71 billion in 2020, US $507.49 billion in 2030, US $1.00 trillion in 2040, and US $1.89 trillion in 2050, in great contrast to US $40.13 billion in 2020, US $76.60 billion in 2030, US $136.99 billion in 2040, and US $217.16 billion in 2050, estimated from Wang's study by the World Alzheimer Report of 2015 [4].

Table 1
Sociodemographic characteristics of the study participants

Characteristic	No. of cases (n)	Proportion (%)
Data source		
Tier 3 hospitals	2226	73.08
Mental health centers/psychiatric hospitals	190	6.24
Gerontology hospitals	110	3.61
Nursing home or care facility	179	5.88
Communities	341	11.19
Age, years		
60–69	813	22.69
70–79	1128	37.03
80–89	981	32.21
≥90	124	4.07
Female gender	1651	54.20
Marital status		
Unmarried	17	0.56
Married	2251	73.90
Widowed	756	24.82
Divorced	22	0.72
Educational level		
No formal schooling	355	11.65
Primary school	815	26.76
Middle school	699	22.95
High school	593	19.47
College or above	584	19.17
Living locations		
Urban	2575	84.54
Rural	471	15.46
No. of children		
0	18	0.60
1	574	18.84
2	1022	33.55
3	747	24.52
≥4	685	22.49
Household income per month, RMB		
<1000	218	7.16
1000–2999	810	26.59
3000–4999	855	28.07
5000–10,000	774	25.41
>10,000	242	7.94
No steady income	147	4.83
No. of comorbidities		
0	905	29.71
1	766	25.15
2	618	20.29
3	365	11.98
4	237	7.78
≥5	155	5.09

3.3. Re-estimation of worldwide current and future costs

We found that the worldwide costs of dementia are very different if based on Wang's study versus our findings [4]. The World Alzheimer Report (2015) estimated that, using the results of Wang's study, the average per capita annual cost of dementia was US $17,478.63 and that the total costs were US $818.00 billion for 2015, of which direct medical costs were US $159.20 billion (19.46%), while the direct nonmedical costs and the indirect costs were US $327.90 billion (40.09%) and US $330.80 billion (40.44%),

Table 2
Estimates of annual costs per patient with AD in China in 2015

Cost by category	No. of cases	Mean cost (US $)
Direct medical costs		
Outpatient	2138	2501.18
Hospitalization	1304	9692.09
Out of pocket	3023	468.97
Direct nonmedical costs		
Transportation, accommodation, and meals	576	468.75
Nourishment	2030	1875.89
Health-care equipment	1889	156.25
Formal care	1952	2586.12
Indirect costs		
Informal care	3004	9249.51
Intangible cost	2179	781.62
Total costs	3046	1,9144.36

Abbreviation: AD, Alzheimer's disease.

respectively. Therefore, the predictions would be US $1.12 trillion in 2020, US $2.11 trillion in 2030, US $3.96 trillion in 2040, and US $7.45 trillion in 2050, based on the World Alzheimer Report (2015). However, if our new results are used, the estimated global dementia costs will increase to US $957.56 billion in 2015 (Fig. 1), US $1.33 trillion in 2020, US $2.54 trillion in 2030, US $4.83 trillion in 2040, and US $9.12 trillion in 2050, far exceeding the estimates based on the World Alzheimer Report (2015) (Fig. 2) [10].
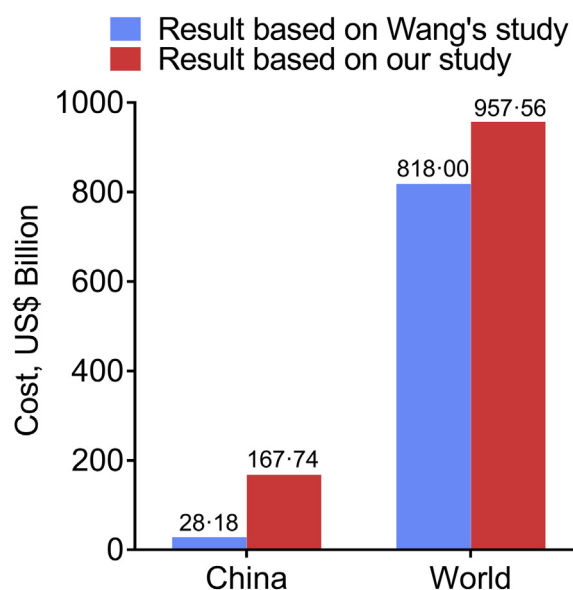
Fig. 1. Comparison between previous estimates from Wang's study and estimates from this study regarding costs of Alzheimer's disease (AD) in China and worldwide (year 2015). Note: The left two bars show that the total socioeconomic costs of Chinese patients with AD were estimated to be US $167.74 billion in 2015, 5.95-fold more than the previous estimate of US $28.18 billion from Wang's study in the World Alzheimer Report (2015). The right two bars indicate that in the same year (2015), the total costs of AD were US $818.00 billion or US $957.56 depending on the estimate from Wang's study or from our study.
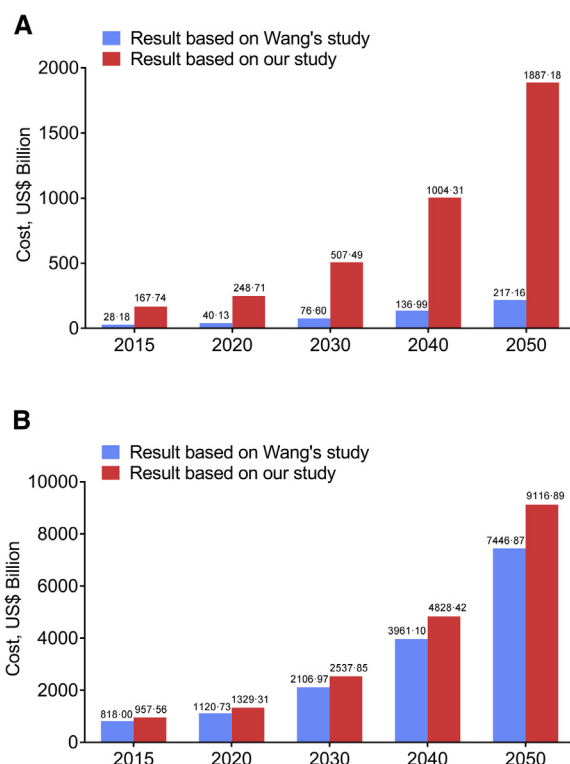
Fig. 2. Prediction of Chinese and worldwide AD costs, estimated from Wang's study or from our study. (A) Based on our new results, the total costs of AD in China will be US $248.71 billion in 2020, US $507.49 billion in 2030, US $1.00 trillion in 2040, and US $1.89 trillion in 2050, in great contrast to US $40.13 billion in 2020, US $76.60 billion in 2030, US $136.99 billion in 2040, and US $217.16 billion in 2050, estimated from Wang's study by the World Alzheimer Report of 2015. (B) For the world, based on our new results, the estimated global dementia costs will increase to US $1.33 trillion in 2020, US $2.54 trillion in 2030, US $4.83 trillion in 2040, and US $9.12 trillion in 2050, far exceeding the estimates based on the World Alzheimer Report (US $1.12 trillion in 2020, US $2.11 trillion in 2030, US $3.96 trillion in 2040, and US $7.45 trillion in 2050). Abbreviation: AD, Alzheimer's disease.

3.4. Comparison of subcosts and GDP between China and worldwide

For the subcosts in China and worldwide, US $54.53 billion (32.51%) and US $159.20 billion (19.46%) were direct costs, US $26.20 billion (15.62%) and US $327.90 billion (40.09%) were direct nonmedical costs, and US $87.01 billion (51.87%) and US $330.80 billion (40.44%) were indirect costs. These results clearly show that the proportions of subcosts between China and the rest of the world statistically differed ($P < .05$). However, there are similarities between China and developed countries regarding indirect costs. We found that the indirect costs exceeded 50% of the total costs not only in China but also in almost all developed countries (Fig. 3). In addition, the worldwide AD costs (US $818.00 billion) represent 1.09% of global GDP (US $75.05 trillion), while AD costs in China (US $167.74
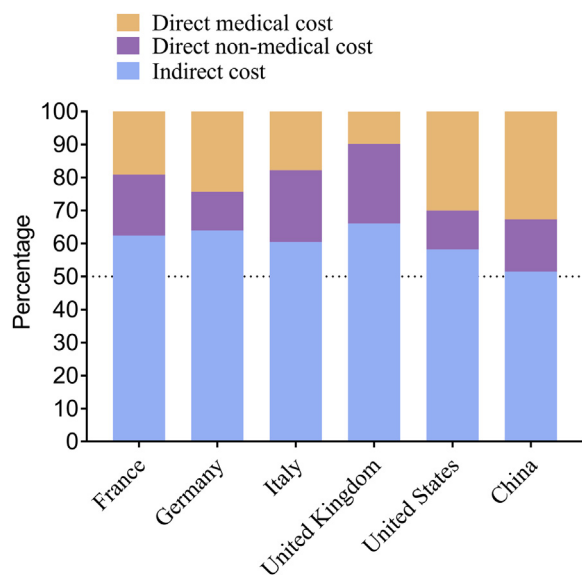
Fig. 3. Comparison of AD subcosts among China and other developed countries. Similarities between China and developed countries, such as France, Germany, Italy, the United Kingdom, and the United States of America, regarding indirect costs ($P < .05$). Abbreviation: AD, Alzheimer's disease.

Table 3
Changes in the estimated annual costs of AD according to variations in the key parameters considered in sensitivity analyses

Parameter varied	Changes in estimated annual total costs, US $ billions*	Percent (%)
Prevalence of AD[†]	−26.80	−15.98
AD status (mild:moderate:severe)		
1:1:1	−3.06	−1.82
1:2:1	−7.45	−4.44
Urban versus rural		
1:1	−20.45	−12.19
Patients with medical treatment (%)		
50	−34.62	−20.64
70	−18.30	−10.91
100	+6.19	+3.69
All AD patients with comorbidity		
None	−40.01	−23.85
One	−8.40	−5.00
Two	−7.88	−4.70
Three	60.14	35.85
Four	103.09	61.46
At least five	155.76	92.86

Abbreviation: AD, Alzheimer's disease.

NOTE. All the estimated costs were converted to United States dollar (US $) values in December 2015 (US $ 1 was equivalent to about 6.4 RMB).

*Compared with the estimated total socioeconomic costs of Chinese patients with AD (US $167.74 billion).

[†]Prevalence values based on groups of age given in one Chinese systematic review, that is, 0.62% in 60~64 y, 1.42% in 65~69 y, 3.06% in 70~74 y, 6.19% in 75~79 y, 11.72% in 80~84 y, and 22.86% in >85 y.

billion) accounted for 1.47% of GDP (US $11.38 trillion), roughly 2.4 times GDP per capita (~$7900) in 2015 [5]. It is significantly different ($P < .05$) between China and worldwide regarding the proportion of AD socioeconomic costs in GDP, indicating that China has a heavier burden of AD socioeconomic cost than the world average.

3.5. Sensitivity analyses

The results of our sensitivity analyses indicated that variations in prevalence of AD, ratios of patients who live in urban or rural, proportions of patients with AD who received medical treatment, and numbers of comorbidities, had a substantial impact on the estimates of the total costs of AD, whereas the proportions of AD at different degrees (mild, moderate, and severe) had relatively less impact on such estimates (Table 3).

4. Discussion

The present study showed that the annual cost of per patient with AD was US $19,144.36, and the total socioeconomic costs of Chinese patients with AD were estimated to be US $167.74 billion in 2015, 5.95-fold more than the previous estimate of US $28.18 billion from the World Alzheimer Report based on Wang's study in 2006, demonstrating that the costs of AD care in China have long been underestimated. Using our results, the global socioeconomic costs for dementia were US $957.56 billion in 2015, and will reach US $2.54 trillion by 2030, and US $9.12 trillion by 2050; these costs are much greater than the predicted US

$818.00 billion in 2015, US $2.11 trillion in 2030, and US $7.45 trillion in 2050, based on the World Alzheimer Report (2015). This study indicated that the costs of Chinese patients with AD constituted a heavy economic burden on China and worldwide.

Our study has several strengths. This is the first multicenter, cluster-randomized study on the socioeconomic costs of AD in China. It covered all hospitals and care facilities for AD patients in almost all parts of China, and the results should reflect the real economic burden due to AD cost in this country. For accuracy of the data, we collected the information using the electronic medical records systems and the electronic residence healthcare system for calculation of AD costs at each site in 2015. The data from our study have greatly changed the estimates of the economic burden of AD in China and worldwide.

Potential limitations should be considered. We estimated the costs of Chinese patients with AD in 2015 based on data obtained from a relatively short duration and small samples in this study. If the survey could have a longer duration and a larger sample size, the estimates would be more objective and accurate. In addition, patients with AD commonly have more comorbid conditions than those without dementia, and this may influence the estimate of AD costs. However, the more influential factor on the estimates of total socioeconomic costs of Chinese patients with

AD might be the proportion of patients receiving medical treatment. These limitations were discussed in Sensitivity analyses section.

In the sensitivity analysis, the parameters that affected the estimated costs of AD, such as the prevalence of AD, distribution of AD status, comorbidity conditions, proportion of patients with AD living in urban or rural areas, and proportion of patients receiving medical treatment were included. We found that the factors most strongly influencing the estimates of the total socioeconomic costs of Chinese patients with AD were the proportion of the patients receiving medical treatment, the number of comorbidities as well as the prevalence. In China, it is thought that the rates of patients with AD receiving medical treatment are lower than those of developed countries. Because the proportion of patients receiving medical treatment is unknown, we calculated the possible costs for different ratios, of 50%, 70%, or 100%, of the patients with AD who visit doctors. This helped us to understand that the true total annual cost of AD in China might be lower or higher than our estimates. As indicated, the costs are going higher as the prevalence of AD increases. In addition, we further analyzed the impact of comorbidities on the total annual cost of AD in China. In the case of patients with at least three comorbidities, the total annual costs will be increased over 35% of our estimates of US $167.74 billion. This indicates that our estimate for the cost of comorbidities in the AD population that we investigated in this study might be lower than that of the entire AD population in China.

Our results differ from those of two previous studies in China. Wang's study in a single hospital in Shanghai in 2006 included only 67 patients with AD [5]. By retrospective analysis, annual costs were calculated as US $2, 384 per patient per year in this study. Xu's study in 2016 included two psychiatric hospitals in Shandong Province with 146 patients [6], and estimated that annual average cost per patient for living at home was US $6019.60, and US $5852.30 for living in nursing homes, but the total annual costs of dementia in China increased from US $0.86 billion in 1990 to US $47.20 billion in 2010. Unlike these two studies, our estimate (US $167.74 billion) is 5.95-fold that of Wang's results and 3.55-fold more than Xu's results for total annual costs. A possible reason for the different results is that our study had a much larger sample, included all types of hospitals that can make a diagnosis of AD for such patients, and that we sampled all parts of China. This ensured that our findings of the socioeconomic costs of AD in China, which have been underestimated, are reliable.

We found that indirect costs exceed 50% of total costs not only in China but also in developed countries like the USA [20], France [21], the UK [22], Sweden [26], and Italy [27]. Caregiving by society and the patient's family is the major driver of the economic burden of AD worldwide. In China,

having a person with AD is a big burden for any family. This is not because of the medications, but because of medical care overall. Currently, about 90% patients with AD live with their families [28]. This mode of care causes monetary loss for the informal caregivers who had a job but can no longer go to work. In general, our results show that indirect costs play an important role in contributing to the total cost of patients with AD. This suggests that establishing a feasible dementia care system, to reduce the burden on the family and increase the opportunities for patients' relatives to keep their jobs, should be a government imperative in China.

China has high and rapidly growing dementia-related costs [10]. Our data show that China accounts for a high proportion of the total worldwide costs of dementia, accounting for 17.52%, 18.71%, 20.00%, 20.80%, and 20.70% in 2015, 2020, 2030, 2040, and 2050, respectively. Our annual estimate per patient (US $19,144) is higher than the average level of worldwide reported in a recent study (US $15,122–17,483) [6]. Domestically, the costs of AD are much higher than those of cancer (estimated at US $2202 in 2013) and cardiovascular disease (estimated at US $13,408 in 2015). Furthermore, the total cost of AD in China in 2015 represented 1.47% of the GDP. This shows that the AD-related economic burden is heavier than the world's average (1.09%) [10]. In recent years, studies have shown that the proportions of the total costs of AD to GDP were 1.31 in Asia Pacific high-income regions, 1.30 in North America high-income regions, 0.97 in Australia, and 0.90–1.29 in Europe [29]. Therefore, the economic burden that AD brings will pose a major challenge for not only Chinese society but also worldwide, suggesting that there is an urgent need to develop an effective strategy with high feasibility for both China and worldwide. Such a strategy would ensure that we take actions to reduce the prevalence of AD, to improve its medical treatment, and to set up optimal services systems, as soon as possible.

In conclusion, the socioeconomic costs of AD are much more than expected in China and have a great impact on the global burden of dementia. The data provided in this study are useful for both China and worldwide authorities to make against dementia plans for the future.

Acknowledgments

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jalz.2017.12.006.

RESEARCH IN CONTEXT

1. Systematic review: We searched PubMed using the terms "Alzheimer's disease", "dementia", and "cost of illness" since January 1, 1990. However, there were only two small studies that were related to cost of Alzheimer's disease (AD), and there has been no national-scale randomized sampling study in this field of China.

2. Interpretation: Our study showed that the annual costs of per patient with AD were US $19,144.36. The annual national socioeconomic AD costs were US $167.74 billion, which were 5.95-fold more than the previous estimate by the World Alzheimer Report 2015, demonstrating that the costs of AD care in China have long been underestimated. Using our results, the global socioeconomic costs for dementia were US $957.56 billion in 2015, and will be US $2.54 trillion in 2030, and US $9.12 trillion in 2050, much more than the predictions by the World Alzheimer Report 2015, showing that the costs of Chinese patients with AD greatly influence the estimate of worldwide AD costs.

3. Future directions: We hope that health-care administration will establish an electronic national system in China to monitor the trends in number of patients with AD and their costs. We also hope that the World Health Organization will integrate this work within plans for a global observatory.

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