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# Economic burden for Alzheimer's disease in China from 2010 to 2050: a modelling study

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**ABSTRACT**

**Objectives**: We aimed to conduct a modelling study to estimate and predict the economic burden of AD to support the healthcare management of AD in China.

**Methods**: The economic burden of AD was estimated with an evaluation of the prevalence of AD patients and a simulation of annual resource use and cost per AD patient in China using a published model. Percentage of AD patients being treated was assumed to be 5% from 2010 to 2050, with three scenarios testing the value of this parameter of 10%, 20% and 40% throughout 2020 to 2050.

**Results**: The costs of AD were estimated to be from around 91 billion RMB in 2010 to 332 billion in 2050. Most of the current burden was related to private caregivers paid by families. With the percentage of patients being treated changing from 5% to 40%, costs were estimated to double. This was related to more hospitalisations and more use of care facilities, while the burden for families would decrease.

**Conclusion**: A high economic burden related to AD is predicted. The burden would be driven mainly by indirect costs related to the social support of the patients. Investment in improving awareness and care of AD patients is needed and worth it.

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Alzheimer's disease; economic burden; caregiver burden; economic model; China

## Introduction

Alzheimer's disease (AD) is a chronic progressive neurodegenerative disease, which is a common type of dementia, with symptoms of memory loss, cognitive decline and functional capacities impairment [1]. AD is also characterized by the key behaviour symptoms of agitation and aggression, which are relevant to disease severity [2]. Patients are commonly affected in daily activities, lacking independence [3]. They depend largely on their family and health systems, causing a huge burden of long-term care [4]. Usually, dementia prevalence is estimated, instead of just AD. It is estimated that 46.8 million people worldwide were living with dementia in 2015, with an economic burden of 817.9 billion US dollar [5]. In China, the number of dementia patient was 9.5 million in 2015 [5] with annual cost per dementia patient estimated to be 2,641 US dollars in 2010 [6]. And the prevalence of dementia increased among surveys from 4.2% during 2000–2009 to 5.15% during 2000–2015 [7]. It was estimated that the prevalence of AD patient was around 61.9% among dementia patient in China in 2010 [8].

The economic burden for AD patients will probably continue to increase in China. More health care resources will be needed for AD patients, since the number of AD patients will continue to increase, with the increasing life expectancy and ageing population in China. It was estimated that the number of AD patients in China was 1.93 million in 1990 and increased rapidly to 3.71 million in 2000 and 5.69 million in 2010 [8]. It was forecasted that AD prevalence would increase to 42.5 million in 2050 [9]. Additionally, cost for healthcare system will also increase due to more diagnosed and treated AD patients, since people will be more aware of the disease and the number of physicians will increase in the future. The economic burden of AD in China is huge. Therefore, it is necessary to estimate the economic impact in the following years to better plan healthcare resource allocation.

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Supplemental data for this article can be accessed here.

However, evidence on the resources use and the related cost of AD patients in China are scarce. Considering the diversity of China and the uncertainty around its economic development, it is difficult to obtain precise estimates of the cost related to AD in the coming years. So far, only one modelling study and one retrospective analysis were identified. The modelling study predicted the economic burden of AD in China from 2011 to 2050 [9]. However, they did not account for the untreated AD patients, which were estimated to be more than 90% of the AD population in China [10]. The retrospective analysis on patients provided an accurate estimate of costs of AD patients, showing how costs increase with the severity of the disease. However, this evaluation, dated from 2006, provides insight from a single hospital in Shanghai and is based on a small sample size (63 patients). It is difficult to extrapolate this to the entire population of China and to the future costs [11].

A CEA model could be an option to estimate the economic burden. CEA models usually incorporate the patients' profiles and disease progression information, which could be used to track the associated resource use and costs by patients in different levels of disease severity. Modelling also allows more flexibility for estimation as it could be easily adapted when new data were available. Therefore, to inform resource allocation decision for AD patients, a tool was adapted from a previous developed CEA model to forecast the economic burden of AD in China.

## Methods

The economic burden of AD was based on two estimates: 1) forecasted number of AD patients; 2) annual resource use and cost per AD patient.

### *1) Forecasting number of AD patients*

The estimated total population was sourced from International Data Base [12] and the number of AD population was sourced from the simulations done by Li et al. 2014 [13]. Li et al. simulate the AD population by pooling the prevalence of AD in China from 1990 to 2014 with meta-analysis and by predicting the population >60 years old in China based on the 6th census data in 2010 and age shift algorithm. The total population was 1,336.7 million and the estimated total number of AD patients was 5.8 million in 2010 in China (Table 1).

**Table 1.** Total number of AD patients and total population.

| | 2010 | 2020 | 2030 | 2040 | 2050 |
|---|---|---|---|---|---|
| Total population in China (million) | 1,336.7 | 1,394.0 | 1,403.9 | 1,364.7 | 1,301.6 |
| Total number of AD patients (million) | 5.8 | 9.0 | 13.0 | 17.6 | 21.1 |
| Percentage of AD patients in total population | 0.4% | 0.6% | 0.9% | 1.3% | 1.6% |

AD: Alzheimer's disease

### *2) Annual resource use and cost simulation*

The resource use and costs by moderate AD patients were used to represent the associated burden by average AD patients, as indicated by a recent survey that most AD patients were in moderate severity, and the number of severe patients was not far away from the number of mild patients [14]. Annual resource use and costs per patient were calculated with a cohort Markov model adapted from a previously developed model [15]. The simulation model structure has been described in detail elsewhere [15]. In brief, this model was developed to evaluate the cost-effectiveness of a pharmacological treatment on moderate AD patient over a 5-year timeframe with a 6-month cycle duration. The model considered nine health states, including moderate AD, severe AD and death, with the former two health states each being further classified into four health states according to patients' functional independence and the presence of agitation/aggression symptoms. The model was applied to estimate the annual burden of moderate AD patients from the first year of diagnostic to the fifth year. It was assumed that the repartition of the patients over the 5 years was representative of an average AD patient, and therefore the average annual burden over the 5 years was used to represent the one-year burden of an average AD patient. The analyses were conducted for 'diagnosed and treated' patients and 'undiagnosed or untreated' patients. The transition probabilities for 'diagnosed and treated' patients and 'undiagnosed or untreated' patients were the transition probabilities for the pharmacological treatment (memantine) and no treatment, respectively, in the previous model [15].The results for both treated and untreated patients were extrapolated to estimate the results in the whole AD population in China.

The resource use for treated patients included pharmacological treatments, outpatient resources (consultation, biological analysis, brain imaging and cognitive assessment scales), hospitalisation, and care facilities (long-term care home and paid caregiver at home). Undiagnosed/untreated patients were assumed to not attend consultation for AD and to not receive treatment, but they would experience symptoms which

may require for care service. Therefore, the resource use for untreated patients included hospitalisation and care facilities.

For treated patients, the resource use inputs were mostly based on the results of a Delphi panel study in China [16]. Daily pharmacological treatment was considered with a 20% of momentary discontinuation every 6 months from expert opinion. For undiagnosed/untreated patients, the probabilities of hospitalisation and care facilities of undiagnosed/untreated patients were 20% of those of treated patients. This was based on the feedback of clinicians that undiagnosed/untreated patients were likely less engaged in their disease management, less aware of the different health care resources available for use and less able to utilise such resources but still in need for care, compared to treated patients. The amount of caregiving time was assumed to be the same as for treated patients (Table 2). The probability of professional caregiver at home was 17.5% from a cross-sectional study [17].

Inputs for costs have been adapted to reflect costs for treated and for untreated patients in China. Cost for treatments was taken from average price for all drugs (including generics) in IMS sales in 2015. Cost for consultations was calculated as the total cost of consultations/total number of consultations done in 2015 in China [18]. Cost for hospitalisation for moderate AD was assumed to be the cost of hospitalisation for diagnosis, and was derived from a Delphi panel study in China [16]. Cost for hospitalisation for severe AD was assumed to be the cost of hospitalisation for both diagnosis and treatment. This cost for treated patients was taken from a database analysis in Shanghai Insurance Bureau identifying the costs of hospitalisation for Alzheimer patients in tier 1 to 3 hospitals, by different types of insurance. We used this input and calculated a weighted average price for patients covered by all insurances (data in files) [19]. This cost for untreated patients was calculated as the total cost of admissions/total number of admissions done in 2015 in China [18], as there was no available data.

Upper and lower value of resource use and cost inputs was applied in deterministic sensitivity analysis. For resource use input, the value of ± 20% change was applied as upper and lower scenarios. For cost input, lowest and highest provincial costs were applied for consultation and hospitalisation; ± SD change was applied in costs for drug and price for patients covered by all insurances. For costs of care facility, lower value scenario applied half the base case value for treated patients, and applied 1/3 the base case value for untreated patients to reflect a potential geographical difference with more nontreated patients living in rural area based on expert opinion (Table 3).

In the base scenario, we assumed 5% of the patients were being treated in each year from 2010 to 2050, based on two studies: Chen et al. 2013 [10] estimated that less than 10% AD patients were diagnosed and Zhang et al. 2004 [20] estimated that only 26.9% of patients visiting a doctor received a diagnosis with 21.3% of them were recommended a treatment. Assuming that 5% of patients were treated in 2010, we test different scenarios of percentage of patients being treated for each decade from 2020 to 2050: with a stable proportion of treated patients (5% – base case) and proportions increased to 10% (scenario 1), 20% (scenario 2) and 40% (scenario 3), as it is expected that awareness on AD will increase and more health care practitioner will be able to diagnose and treat patients with AD. The optimal scenario (3) of 40% was based on an estimate from Europe where it was estimated that 60% of patients were diagnosed and 63% of diagnosed patients got treatment [21].

**Table 2.** Resource use input in every 6-month cycle.

| | Moderate Independent Non-Aggressive | Moderate Independent Aggressive | Moderate Dependent Non-Aggressive | Moderate Dependent Aggressive | Severe Independent Non-Aggressive | Severe Independent Aggressive | Severe Dependent Non-Aggressive | Severe Dependent Aggressive |
|---|---|---|---|---|---|---|---|---|
| **Treated patients** | | | | | | | | |
| Pharmacological treatment (day of use) | 180 | 180 | 180 | 180 | 180 | 180 | 180 | 180 |
| Consultations (number of use) | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Biological analysis (number of use) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Brain imaging (number of use) | 0 | 0 | 0 | 0 | 0 | 0 | 0.35 | 0.35 |
| Cognitive assessment scales (number of use) | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| Hospitalisations (probability) | 0% | 5% | 5% | 90% | 1% | 1% | 35% | 70% |
| Nursing home (probability) | 0% | 20% | 80% | 0% | 0% | 20% | 80% | 20% |
| Other caregiver time (hours per day) | 1 | 3 | 4 | 10 | 1 | 3 | 12 | 15 |
| **Untreated patients** | | | | | | | | |
| Hospitalisations (probability) | 0% | 1% | 1% | 18% | 0.2% | 0.2% | 7% | 14% |
| Nursing home (probability) | 0% | 4% | 16% | 0% | 0% | 4% | 16% | 4% |
| Other caregiver time (hours per day) | 1 | 3 | 4 | 10 | 1 | 3 | 12 | 15 |

Table 3. Cost input for treated in every 6-month cycle (RMB).

| Resource use | Unit price | Base case | Lower | Higher | Source |
|---|---|---|---|---|---|
| **Treated patients** | | | | | |
| Treatment | per day | 12.7 | 3.2 | 22.2 | IMS data |
| Consultations | per consultation | 236 | 123 | 441 | Annual report 2016[18] |
| Biological analysis | per use | 500 | 500 | 500 | Yu 2015[16] |
| Brain imaging | per use | 1,050 | 1,050 | 1,050 | Yu 2015[16] |
| Cognitive assessment scales | per use | 100 | 100 | 100 | Yu 2015[16] |
| Hospitalisation for moderate AD | per admission | 1,600 | 1,600 | 1,600 | Yu 2015[16] |
| Hospitalisation for severe AD | per admission | 37,087 | 29,670 | 44,505 | Yang 2017[19] |
| Nursing home | per month | 6,000 | 3,000 | 6,000 | Yu 2015[16] |
| Professional caregiver | per month (8 hour/day) | 6,000 | 6,000 | 6,000 | Yu 2015[16] |
| **Untreated patients** | | | | | |
| Hospitalisation for moderate AD | per admission | 1,600 | 1,600 | 1,600 | Yu 2015[16] |
| Hospitalisation for severe AD | per admission | 8,268 | 5,388 | 20,149 | Annual report 2016[18] |
| Nursing home (24 hour/day) | per month | 3,000 | 1,000 | 6,000 | Yu 2015[16] |
| Professional caregiver | per month (8 hour/day) | 6,000 | 6,000 | 6,000 | Yu 2015[16] |

AD: Alzheimer's disease

## Results

Figure 1 presents the clinical characteristics of AD patients at model entry and after 5 years. Undiagnosed/untreated patients were estimated to have worse outcomes after 5 years, with a higher probability of being severe, dependent and aggressive than those who received treatment. With 5% of patients being treated, the overall impact of treatment on clinical outcomes at a population level was minimal.

In the base case analysis with 5% patient being treated, the economic burden was around 91 billion RMB in 2010. The burden was estimated to increase to 142 billion RMB in 2020 and to 332 billion RMB in 2050. Most of the cost was related to paid caregiver (70%). The next most important cost drivers were care facilities (18%) and hospitalisation (9%) (Figure 2 and Supplement 1).

When the percentage of diagnosed and treated patients increased from 5% to 10%, 20% and 40%, the total costs in 2050 increased from 332 billion RMB to 362 billion RMB, 422 billion RMB and 540 billion RMB respectively. The increase was mainly related to increase in care facilities and hospitalisation. In total cost, the percentage of care facilities cost changed from 18% to 21%, 26% and 32% and the percentage of hospitalisation cost changed from 9% to 11%, 15% and 20%. There was a reduction in burden related to paid caregiver at home (down from 70% to 63%, 51% and 36% of total burden) (Figure 3 and Supplement 1).

In the sensitivity analyses, there was a span of approximately 3 times increase between lower and upper estimates. When lower prices were used, the burden of AD increased from 60 billion RMB in 2010 to 218 billion RMB in 2050, with a potential to increase to 370 billion RMB if 40%

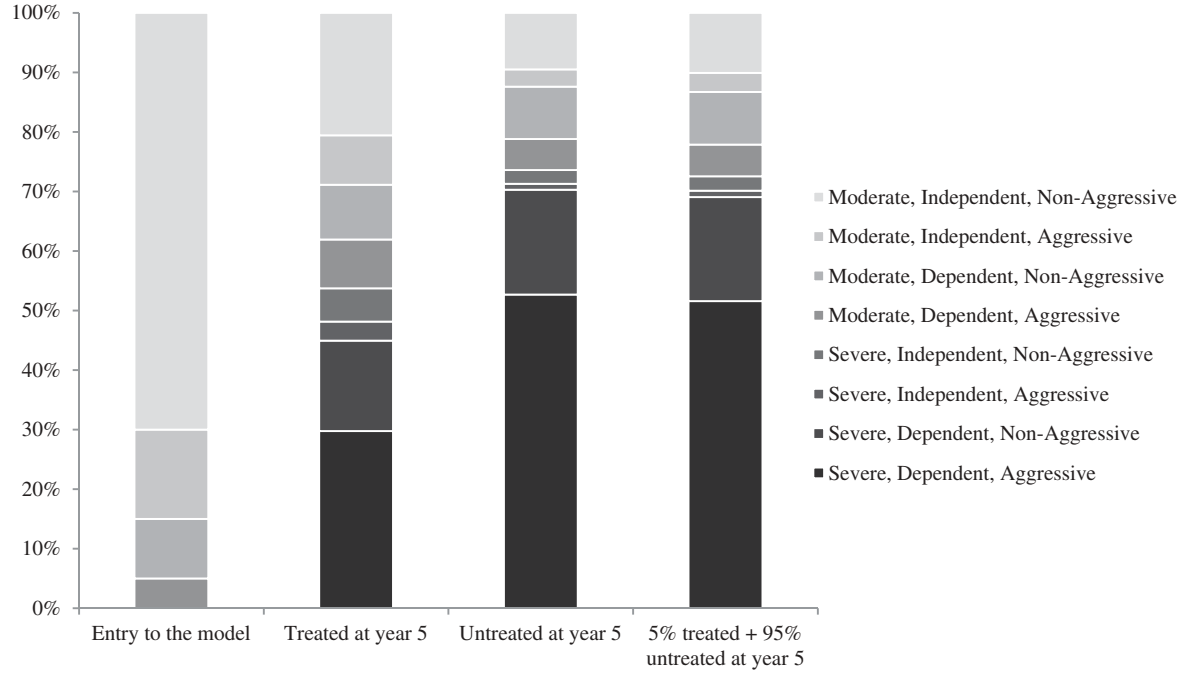


Figure 1. Clinical characteristics of AD patients at model entry and after 5 years.

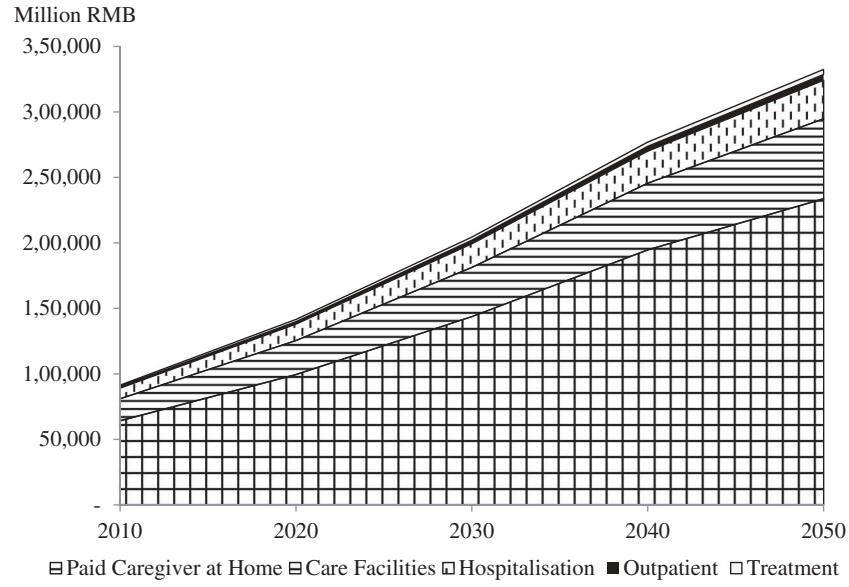


Figure 2. Evolution of annual costs related to AD patients.

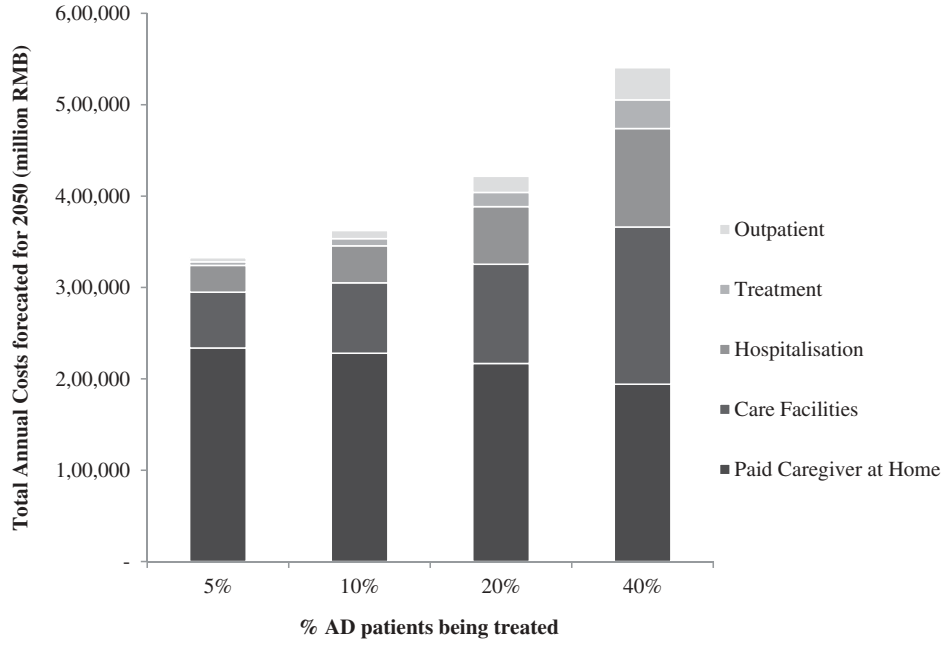


Figure 3. Estimated costs in 2050 with different scenarios of treatment rate.

of patients were diagnosed and treated. When upper prices were used, the burden of AD increases from 136 billion RMB in 2010 to 495 billion RMB in 2050, with a potential to increase to 719 billion RMB if 40% of patients were diagnosed and treated (Supplement 2, Supplement 3).

## Discussion

Our study proposed the use of a previously developed model to efficiently forecast the AD economic burden information for decision-maker. The model was firstly developed for a cost-effectiveness analysis which was published in English in 2015 [15] and in Chinese in 2016 [22]. It was flexible to address multiple health policy issues upon pharmaceutical adoption at different stages of disease and different penetration rates. It could also easily incorporate modules such as caregiver contribution and loss of productivity, and simulate patient management from simple to complex in acute and long-term care facilities.

Our results for the economic burden were similar to the previous studies. An evaluation by AD international 2010 estimated that the economic burden of AD in China was 2,641 US dollars per patient (around 18,000 RMB) [6], which was higher than our estimate of 15,765 RMB (91 billion RMB for 5.8 million AD patients) but within the upper case. Our results were also similar to the estimate of a recent modelling study of the economic burden of AD which estimated a cost of US$15 billion (around 100 billion RMB) in 2011. Our estimate for the cost of AD in 2050 was much lower than the estimate of that modelling study [US$1.07 trillion (7.1 trillion RMB for 2050)] [9]. However, this was related to more prevalent patients were used in their models (28 million vs. 21 million) and different approaches they have used which estimated the impact of AD on the GDP and therefore values also the indirect impact from work loss related to caregiving for AD by the family members.

The costs of AD were found to develop from an existing burden around 91 billion RMB in 2010 to 332 billion in 2050 owing to an increase in patient population from around 6 to 21 million patients. Most of the current burden was related to use of private caregivers paid by families. In the scenarios where awareness and education around the disease increased and the proportion of diagnosed and treated patients increased, the costs increased considerably. Going from a scenario of a limited percentage of patients being treated (5%) to a Europe-like scenario (40%), costs were estimated to double. The increased costs were mainly due to better awareness of health care resource and follow-up assessment, resulting in more hospitalisation and more use of care facilities, though lower need for care at home. However, if the cost (or a substantial part) related to hospitalisation and nursing home are supported by families, this will dramatically impact the family economic burden and it will be a major issue of affordability and equity.

Our analysis also shows the importance of better management of AD patients with pharmacological treatments. The increased cost for AD patients is not attributable to pharmacological treatments, but is rather a consequence of bringing back an increasing number of patients to the health system. Pharmacological treatments were associated with improved health outcomes and subsequent reduction of caregiver burden, therefore should be emphasized more and earlier to avoid the large caregiver cost in the future.

Last, our analysis highlights the changes in the structure of costs to come, such as increasing costs in care facilities and hospitalisation, if nothing is done proactively in the management of AD patients to accompany these changes. These findings are consistent with the recent modelling studies [9]. It would be necessary for China to develop an array of services and train caregivers to enter the workforce and support the elderly population, which would benefit China even beyond AD patients.

### *Limitations*

However, limitations exist in our analysis. The basis of our assumptions was to consider patients either as treated, i.e. being managed within the healthcare system during the 5-year period of modelling, or as undiagnosed and untreated. We assumed that even though these patients were not diagnosed or not treated, they were not necessarily outside of the healthcare system which has led to the use of health care resources. The assumptions we have used may lead to imprecise estimation of the economic burden of AD.

Additionally, forecasting for the future is a difficult exercise especially in the context of China considering its vast diversity and ultra-rapid development. As indicated in the China Cognition and Aging Study (China Coast), large regional differences were seen for AD between rural areas and urban areas [23]. While we could use precise estimates for national prevalence, it was difficult to identify estimates for resource use or costs that would correspond to treated or undiagnosed and untreated patients at the local or national level. Considering the scarce data and heterogeneity of resource use and costs in China, we had to make assumptions and developed sensitivity analyses to take uncertainty into consideration. Our results have then to be read in line with those assumptions. However, rather than proving accurate evaluations of the burden related to AD in China, our intention was to provide elements of information that would give additional insight into the burden of AD and provide elements to support reflexion of finance allocation around the AD patients, at a time when China develops pilot project to better care for their elderly population.

## Conclusion

Our analysis showed a high economic burden related to AD that would be driven mainly by indirect costs related to the social support of the patients. Despite the limitations inherent to forecasting based on the current situation with wide variations in the management of patients and uncertainties in its future development, the model shows that investment in improving awareness and care of AD patients is needed and worth it. It can be used as a tool to test different scenarios and to support decision-making.

## Disclosure statement

No potential conflict of interest was reported by the authors.

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## References

[1] Fox NC, Rossor MN. Diagnosis of early Alzheimer's disease. Rev Neurol (Paris). 1999;155(Suppl 4):S33–7.
[2] Li XL, Hu N, Tan MS, et al. Behavioral and psychological symptoms in Alzheimer's disease. Biomed Res Int. 2014;2014:927804.
[3] Prince M, Albanese E, Guerchet M, et al. World Alzheimer Report 2014. Dementia and Risk Reduction - an analysis of protective and modifiable factors. London; 2014.
[4] Wimo A, Winblad B, Grafstrom M. The social consequences for families with Alzheimer's disease patients: potential impact of new drug treatment. Int J Geriatr Psychiatry. 1999;14:338–347.
[5] Prince M, Wimo A, Guerchet M, et al. World Alzheimer Report 2015.The global economic impact of dementia. London; 2015.
[6] Wimo A, Prince M. World Alzheimer Report 2010. The global economic impact of dementia. London; 2010.
[7] Liu BY, Wang JL, Xiao YZ. [Prevalence of senile dementia in people aged >/=60 years in China: a Meta-analysis]. Zhonghua Liu Xing Bing Xue Za Zhi. 2016;37:1541–1545.
[8] Chan KY, Wang W, Wu JJ, et al. Epidemiology of Alzheimer's disease and other forms of dementia in China, 1990-2010: a systematic review and analysis. Lancet. 2013;381:2016–2023.
[9] Keogh-Brown MR, Jensen HT, Arrighi HM, et al. The impact of Alzheimer's disease on the Chinese economy. EBioMedicine. 2016;4:184–190.
[10] Chen R, Hu Z, Chen RL, et al. Determinants for undetected dementia and late-life depression. Br J Psychiatry. 2013;203:203–208.
[11] Wang G, Cheng Q, Zhang S, et al. Economic impact of dementia in developing countries: an evaluation of Alzheimer-type dementia in Shanghai, China. J Alzheimers Dis. 2008;15:109–115.
[12] USA Census Bureau. International Data Base. Available from https://www.census.gov/data-tools/demo/idb/region.php?N=%20Results%20&T=13&A=separate&RT=0&Y=2010,2020,2030,2040,2050&R=-1&C=CH. Assess on 2019 Sep 05.
[13] Li A Dementia in China (2010-2050) Estimated Using the 2010 Census: suzhou University; 2015.
[14] Ban CX, Xiao SF, Lin X, et al. Clinicians' prescription preferences for treating patients with Alzheimer's disease in Shanghai. Transl Neurodegener. 2016;5:8.
[15] Hu S, Yu X, Chen S, et al. Memantine for treatment of moderate or severe Alzheimer's disease patients in urban China: clinical and economic outcomes from a health economic model. Expert Rev Pharmacoecon Outcomes Res. 2015;15:565–578.
[16] Yu X, Chen S, Chen X, et al. Clinical management and associated costs for moderate and severe Alzheimer's disease in urban China: a Delphi panel study. Transl Neurodegener. 2015;4:15.
[17] Tang B, Harary E, Kurzman R, et al. Clinical characterization and the Caregiver Burden of Dementia in China. Value Health Reg Issues. 2013;2:118–126.
[18] 2016 annual statistics report of China health and family planning commission. China Peking Union Medical University Press; [cited 2017 Oct 08]. Available from http://cnki.heinfo.gov.cn/csydkns/navi/YearBook.aspx?id=N2015110062&floor=1
[19] Yang Y, He J, Kang Q, et al. Analysis of the medical service utilization and expenses of the hospitalized patients with Alzheimer's Disease in Shanghai. ISPOR 22th Annual International Meeting; Boston; 2017.
[20] Zhang ZX, Chen X, Liu XH, et al. [A caregiver survey in Beijing, Xi'an, Shanghai and Chengdu: health services status for the elderly with dementia]. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2004;26:116–121.
[21] Alzheimer's A. 2016 Alzheimer's disease facts and figures. Alzheimers Dement. 2016;12:459–509.
[22] Hu S, Yu X, Chen S, et al. Pharmacoeconomic model for Memantine for treatment of Alzheimer's disease patients in China. China J Pharm Econ. 2016;9:7–17. Article in Chinese.
[23] Jia J, Wang F, Wei C, et al. The prevalence of dementia in urban and rural areas of China. Alzheimers Dement. 2014;10:1–9.