The Alzheimer's disease Burden in China (ABC) study: a nationwide multicentre cross-sectional and prospective cohort study

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1. Background

Alzheimer's disease (AD) is a devastating neurodegenerative condition characterized by a progressive decline in cognitive function, ultimately leading to significant disability or death[1]. The escalating number of AD cases represents a global public health crisis. According to Alzheimer's Disease International's 2018 estimates, the prevalence of dementia had already reached 50 million people worldwide, a number projected to triple by 2050, with two-thirds of cases anticipated to arise in low-income and middle-income countries[2]. While recent data on the epidemiology of AD in China is limited, a systematic review indicates a notable increase in AD cases from 3.71 per million people in 2000 to 5.69 in 2021, marking a 53% rise in a decade[3]. Advanced age stands out as one of the most significant risk factors for AD[4]. Given China's rapid aging population trend in recent years[5], it is inevitable that both the incidence and prevalence of AD will continue to climb.

The typical profile of a patient with Alzheimer's disease (AD) involves initial presentation with amnestic Mild Cognitive Impairment (MCI), which progresses to varying degrees of impairment in language, spatial cognition, executive function, or working memory, ultimately interfering with daily functioning (referred to as multidomain dementia). This progression significantly impacts their quality of life[4]. One particularly challenging aspect to manage is behavioral dyscontrol in individuals with dementia due to AD, often manifesting in the moderate to severe stages. The lack of effective control and treatment approaches for AD has far-reaching consequences[6, 7], exerting a broader influence on both society and the economy. The increasing number of AD patients, along with the escalating burden of care, strains the capacity of healthcare institutions[8]. Families facing this burden are often left with difficult choices, such as reducing their time commitments through hospitalization or nursing home admission. It's crucial to recognize that caring for the caregiver is as vital as caring for the patient. The quality of life for both the patient and caregiver is influenced by various factors, including comorbidities, physical limitations, hearing and visual impairments, mood disorders, pain disorders, and sleep disturbances[4]. These non-medical expenditures, encompassing time commitments and emotional stress, impose substantial burdens on families, communities, and society at large[9].

The economic impact of AD varies significantly depending on the disease stage[10]. Mild cases typically see increased medical expenditures, while moderate-to-severe cases necessitate prolonged and continuous home and social care, leading to higher nursing expenses. Despite this, there is a lack of comprehensive studies categorizing the economic burden of AD across different disease stages and providing meaningful comparisons. Additionally, individuals with AD often have a higher prevalence of comorbid conditions compared to those without dementia[11]. These additional health issues can substantially influence the calculation of AD-related costs, further complicating the economic picture. Our research aims to delve into the economic burden of AD in China, taking into account direct medical costs, direct non-medical costs, and indirect costs. By examining these factors comprehensively, investigators can better understand the financial challenges faced by individuals, families, and the healthcare system due to AD. Furthermore, our study seeks to assess the quality of life (QoL) of AD patients and their family caregivers, along with evaluating caregiver burden. Understanding these aspects is crucial for developing targeted interventions and support mechanisms to improve outcomes for both patients and caregivers.

The comprehensive understanding of how these costs are generated and their impact on AD patients, caregivers, and their families is crucial. Previous studies have highlighted that the most desired treatment outcomes for AD include memory improvement or restoration and halting disease progression[12]. Additionally, issues such as diminished personal dignity, reduced independence, and increased dependence on others have been identified as significant challenges[13, 14]. However, there are still knowledge gaps regarding how these factors contribute to the burden on families and generate economic costs. Addressing these gaps is essential for developing effective strategies to support both patients and their caregivers.

Ultimately, our research holds significant promise in guiding and supporting various aspects of AD management and policymaking in China. By shedding light on the economic impact and quality of life

implications, investigators can work towards more effective strategies for addressing the challenges posed by AD and enhancing the overall well-being of those affected by this condition.

2.1 Study Population

ABC study aims to conduct a nationwide multistage clustered sampling design into the economic burden of patients and their families with AD across various provinces and cities in mainland China. The study population not only includes patients diagnosed with AD at the dementia stage, but also prospectively incorporates individuals in the stage of amnestic mild cognitive impairment (aMCI), These patients are of decisive significance for exploring the economic value of early intervention in the disease.The inclusion and exclusion criteria of Patients is showed in Table 1.

Table 1. Inclusion and Exclusion Criteria of Patients.

Inclusion criteria	Exclusion criteria
Diagnosed according to the National Institute on Aging-Alzheimer's Association (NIA-AA) criteria for aMCI and AD.	History of stroke with neurological focal signs and imaging findings consistent with cerebral small vessel disease (Modified Fazekas score ≥2).
Clinical Dementia Rating (CDR) score greater than or equal to 0.5	Presence of mental or neurological developmental delay.
Have good visual, auditory, and language functions, or can complete neuropsychological assessments after correction.	Presence of other known conditions that may cause cognitive impairment.
Participants or their legal representatives sign informed consent.	Diagnosis of a disease that prevents completion of cognitive assessments.
	Refusal to sign informed consent at baseline.

2.2 Sampling Strategy

The ABC study adopted a two-stage probability sampling design to ensure data representativeness at the national level. The first stage used medical institutions as sampling units. Considering the professionalism of AD diagnosis and treatment, the study relied on 602 officially certified cognitive centers distributed across 31 provinces, autonomous regions, and municipalities as the sampling frame. This sampling based on professional centers not only ensured the reliability of diagnosis but also covered the main distribution areas of China's AD medical resources.

Since Guangxi, Qinghai, and Ningxia each have only one cognitive center qualified for AD diagnosis, these hospitals were directly included in the study through certainty selection.

Xizang currently lacks hospitals with standardized diagnostic capabilities for AD. Investigators recruited and trained locally qualified neurologists to conduct patient enrollment and data collection locally. This subset of samples will be separately labeled and subjected to sensitivity analysis.

In the sample size calculation, the study used the average annual medical expenses of AD patients as the core outcome indicator, employing a mean estimation method with relative precision calculation.

$$n_{srs} = \frac{Z^2_{1-a/2} \times \sigma^2}{\delta^2 \times \mu^2}$$

To offset the loss of independence among samples caused by Cluster Sampling, the Design Effect (DEFF) was adjusted using the intracluster correlation coefficient (rho).

$$DEFF = 1 + (m - 1)\rho$$

The study preset rho to be 0.005, which is a relatively robust parameter selection aimed at ensuring that the sample remains sufficiently representative even when there is a certain degree of homogeneity among hospitals. Under these assumptions, the design effect was approximately 1.50. Based on the China Alzheimer's Disease Report 2024 and the China Statistical Yearbook 2025, investigators estimated the number of AD patients in each administrative region, and calculate the regional distribution proportion accordingly. The number of involving hospitals in each region is allocated proportionally according to the patient scale. The largest remainder method is used to balance the deviation caused by the integer rounding to calculate the regional hospital numbers.

The number of hospitals in each region may have slight deviations due to rounding of integers. During study implementation, adjustments may be permitted without changing the regional stratification structure to ensure the overall sample size meets statistical requirements.

2.3 Follow-up

To accurately assess the indirect economic costs associated with AD, a Phase 2 follow-up survey is conducted following the completion of the Phase 1 cross-sectional survey. This involves a 12-month follow-up of patients and their informal caregivers.

2.4 Outcomes of Interest

After recruiting eligible patients, medical staff conduct face-to-face interviews with patients and their family members to collect four types of outcomes of interest: social-economic information, clinical information, economic burden, and quality of life.

2.5 Statistics Analysis

The baseline characteristics of the study population will be statistically described using the t-test for continuous variables (to be presented as mean ± standard deviation) and the chi-square test for categorical variables (to be presented as percentage). These characteristics will include age, gender, education, marital status, geographic region, place of residence (urban/rural), number of children, time of AD diagnosis, MMSE scores, ADL scores, and the number of co-morbidities. Longitudinal follow-up is designed to assess the longitudinal changes in the economic burden of patients with AD and their caregivers over time.

3. Quality Control

The survey questionnaire for this study will be meticulously designed based on insights from previous research findings and expert opinions in the field. Prior to data collection, investigators will undergo thorough training and evaluation using standardized procedures to ensure the quality and consistency

of the survey data obtained. The analysis of the study data will strictly adhere to the predefined statistical analysis plan, which outlines the specific statistical methods and techniques to be employed for data interpretation and inference.

By following these established guidelines and protocols throughout the study process, from questionnaire design to data analysis and result reporting, the study aim to uphold the highest standards of research integrity and validity. This approach not only enhances the credibility of our study but also contributes to the broader scientific understanding of the factors influencing Alzheimer's Disease and related outcomes.

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