

2023 China Alzheimer's disease: facts and figures

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Abstract: In China, the aging population and the increasing incidence of Alzheimer's disease (AD) and other dementias have emerged as major medical concerns. Extensive research and new technologies on AD have provided possibilities for early intervention, including emerging biomarkers for detection and new drugs with disease-modifying therapy. This report includes a large amount of facts and figures to describe the understanding of patients and their families about the disease, discuss the problems they encounter in the current medical environment, and outline potential difficulties in clinical diagnosis and treatment status. Furthermore, people's concerns, the overall effect on caregivers, and the development of AD treatment are presented in this report. Overall, to increase public awareness of the disease, this report suggests early detection, screening, and intervention for AD while calling on all sectors to work together to help AD patients.

Keywords: Alzheimer's disease; Mild cognitive impairment; Biomarkers Public health administration.

INTRODUCTION

With the acceleration of population aging, the incidence of dementia diseases, mainly Alzheimer's disease (AD), continues to rise in China (Ren, 2022 #604). At present, China has become the country with the largest number of patients with AD in the world, with nearly 10 million patients (Liu *et al.*, 2013). According to a global research, the prevalence of AD and other dementias in China has increased by 5.6% from 1990 to 2016, while the global prevalence increased by 1.7% ("Global, regional, and national burden of Alzheimer's disease and other dementias, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016," 2019). It is predicted that by 2050, the number of patients with AD will reach 27.65~91.94 million (Wang *et al.*, 2019), bringing a heavy burden to elderly patients, families and society. Therefore, we urgently need effective management of AD. Meanwhile, AD is a degenerative brain disease which gets worse over time. During the progression of AD, there are three broad phases: pre-clinical AD, mild cognitive impairment (MCI) due to AD and dementia due to AD (Scheltens *et al.*, 2021). Preclinical periods usually have no symptoms. MCI stage starts with memory loss, such as occasional forgetting of details, and misplacing of items which may be attributed to other factors. When patients develop into the dementia stage, their activities of daily living are usually damaged and they rely heavily

on others. Thus, it is important to take early signs seriously in the early stage of the disease.

However, it is still a challenge to use effective diagnostic tools to confirm AD at early or mild stages. In AD, the accumulation of the soluble and insoluble aggregated beta-amyloid(A β) may contribute to the cause of the pathologic process in AD(Hardy & Higgins, 1992). Another putative cause of AD is tau protein which becomes hyperphosphorylated and aggregates into neurofibrillary tangles in brains(Avila *et al.*, 2004). In recent years, various biomarkers have been found in both MCI and AD patients which could be recognized as precursors of dementia. For example, abnormal A β 42 levels and tau levels could be detected in patients' cerebrospinal fluid (CSF) before MCI onset, and positron emission tomography (PET) imaging can identify amyloid deposition or misfolded tau in the brain at early stage. Studies have shown that CSF A β 42/A β 40 and plasma P-tau217 have a high concordance in discriminating AD from other neurodegenerative diseases (Janelidze *et al.*, 2017; Palmqvist *et al.*, 2020). Based on these findings, two type of anti-amyloid monoclonal antibody- Lecanemab and Aducanumab-have received approval by U.S. Food and Drug Administration (FDA), and one of them has been used in Hainan Lecheng international medical tourism pilot zone in China since 2022, which are aimed at removing A β from the brain and slowing the process of cognitive decline. Despite the new research progress in AD, early screening and intervention has not been applied extensively in China.

Furthermore, when it comes to the current situation in China, to what extent do patients and their families know about AD? How many patients have received more timely screening and intervention measures? There is still a huge gap between the public's understanding of the disease and prevention/cure. These problems are even more urgent in China, considering that the research on AD or other dementia based on the Chinese population is still in the initial stage, while various studies such as the Alzheimer's Disease Neuroimaging Initiative (ADNI)(Veitch *et al.*, 2023) or the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability(FINGER)(Ngandu *et al.*, 2015) have been ongoing for decades in the world.

Here, to better understand the dilemma in treating and caring for AD patients in China, we launched a national survey focusing on the major challenges encountered in the diagnosis and treatment of AD, as well as the concerns expressed by

patients and their families. Then, the results of the survey were summarized here as an annual report of 2023 China AD: facts and figures.

METHODS

In July 2023, we conducted a national survey through web-based questionnaires which was supported by Alzheimer's Disease Chinese (ADC), the only official member of Alzheimer's Disease International (ADI) in China. This survey was designed to obtain practice and epidemiological data on the health management of cognitive impaired patients and the follow-up intervention measures. We issued it through ADC website and gained nearly 4,500 visits(<https://www.wjx.cn/vm/OeDPcL7.aspx>). The respondents came from both hospitals and communities. Each family was asked to submit only one questionnaire and answer the questions honestly. After collecting and checking the data, we excluded the ones which were not fully completed as well as duplicated ones. At the end, we collected 1,000 qualified questionnaires. Among the respondents, they are either patients diagnosed with AD (11.2%) or caregivers (88.8%) and more than half of them hold bachelor degree or higher education levels. This survey covered 31 provinces in China, almost all regions in China including Northern China, Eastern China, Southern China, Middle China, Southwest of China, Northwest of China and Northeast of China(Supplementary table 1). Finally, a statistical description is presented in this report.

	n	Proportion
subjects		
patients	112	11.2%
caregivers	888	88.8%
education years		
<9years	140	14.0%
9-12years	236	23.6%
>12years	615	61.5%
provinces		
Northern China	280	28.0%
Middle China	94	9.4%
Southern China	66	6.6%
Eastern China	330	33.0%
Southwest of China	73	7.3%
Northwest of China	120	12%
Northeast of China	37	3.7%

Supplementary table 1. Demographic characteristics of respondents.

RESULTS

1. Age distribution in AD population

AD patients in China mainly occur in elderly people, but there is a growing trend in younger people. Among the people diagnosed with AD for the first time, the proportion of people aged 60 to 79 years

old was the highest, at 62.1% (Fig.1). However, it is worth noting that 21.3% of AD patients were under 60 years old in this survey, which is higher than the 5-10% of early-onset Alzheimer's disease reported previously ("2023 Alzheimer's disease facts and figures," 2023), indicating that AD is affecting more and more younger people in China at present.

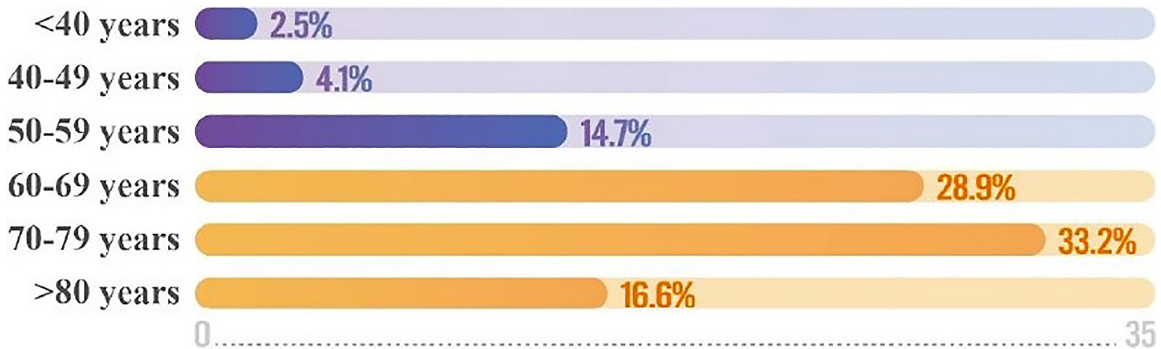


Figure 1. Patients' age when first diagnosed with AD

2. Recognition of early signs of AD and delaying the timing of the first visit

The common early symptoms of AD include amnesia and language impairment, etc. (Table 1) In the survey, most AD patients and their family members (80%) can recognize the common symptoms such as memory loss. Besides, some typical non-amnestic symptoms (including mental and behavioral symptoms, executive functions, etc.) are

also better understood among people (Weiner *et al.*, 2005).

However, even when AD-related symptoms occur, only about 30% of the respondents see a doctor within 1 year, and 70% of the respondents see a doctor within 2 years (Fig.2). Our research also showed that most patients tend to seek medical treatment until they "often forget things and have problems in judging time, location, etc." (44.1%) while the disease has progressed into next stage.

Early Signs of AD

Memory loss	Memory loss, especially forgetting recent events, is one of the most common symptoms of Alzheimer' dementia. Others include asking family members the same questions again and again.
Decreased language function	Patients may find difficulty finding words to name objects or repeating others' words. There could be fewer active conversations between patients and others.
Confusion with time or place	Patients may be confused about specific dates, seasons or locations.
Decreased executive function	Patients may be unable to complete complex tasks or solve problems at work or family. Making decisions or judgments is also difficult for them.
Psychiatric symptoms	Such as hallucination, delusion, mania, depression
Others	Trouble with concentration, Trouble with calculating numbers, Movement disorders

Table 1. Early signs of AD in the questionnaire

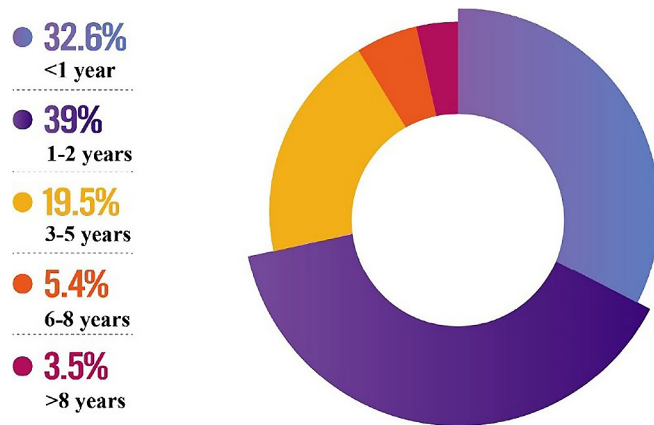


Figure 2. The time elapsed before first seeing a doctor when the first symptoms occurred.

3. Lack of early screening in the community

More than 60% of patients in communities have not yet received early cognitive screening, while 12.8% of patients rarely know about the availability of such screenings. In China, a comprehensive cognitive impairment diagnosis and treatment

system, primarily led by neurology memory clinics, has been established (Ren *et al.*, 2022). AD was mainly diagnosed in the Department of Neurology of tertiary hospitals (64.2%) (Fig.3). Departments of geriatrics and psychiatry also play crucial roles, especially in patients with geriatric comorbidities and behavioral and psychological symptoms of dementia(BPSD).

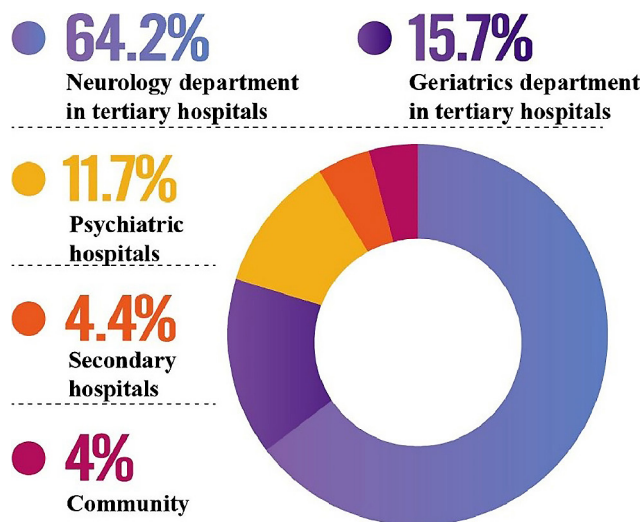


Figure 3. The clinical setting where patients were diagnosed with AD

4. The acceptance of different examinations for early screening

This survey involves three examination techniques, including blood test, CSF test, and PET neuroimaging with a relatively higher testing cost. According

to the AT(N) framework (Jack *et al.*, 2018), patients with abnormal Aβ deposition are considered as Alzheimer’s continuum and Aβ-PET is a valid surrogate Aβ deposit in the brain (Clark *et al.*, 2011; Ikonomic *et al.*, 2008). Especially, on September 15th this year, the National Medical Products Administration

(NMPA) approved (18)F-florbetaben developed by Sinotau for a novel tracer for PET imaging of Aβ(Administration, 2023). (18)F-florbetaben, also known as AV-1, is the first Aβ-PET imaging tracer approved for the diagnosis of AD in China.

All three techniques were accepted by over half of the interviewed patients and their families (Fig.4), indicating the demand for sensitive and specific diagnostic tools. More specifically, the

majority are willing to pay for examination fees below 1,000 RMB (136.7\$) or within the range of 1,000 to 3,000 RMB (410\$) (Fig.5). It's also noted that patients and their families show a high level of acceptance of the new and accurate diagnostic examinations, and half of the respondents were willing to have PET imaging. However, these functional neuroimaging tools have not yet been applied extensively across the country at present.

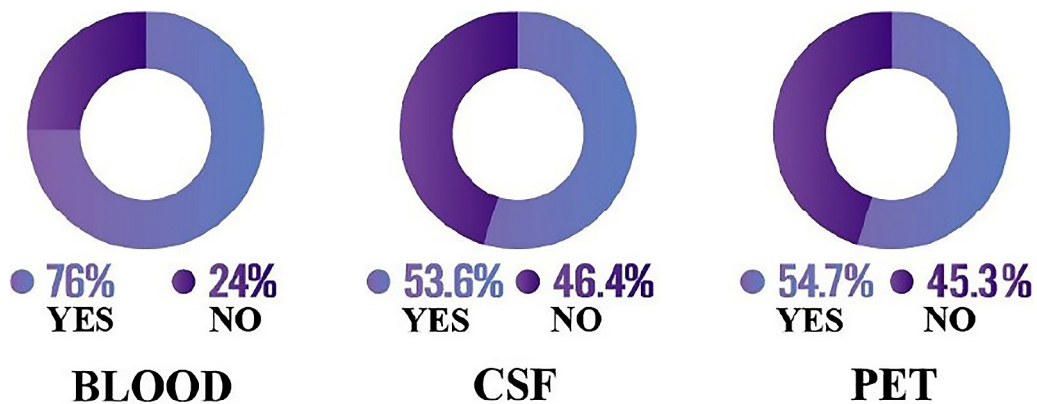


Figure 4. The acceptance of three examination techniques. CSF: cerebrospinal fluid, PET: Positron emission tomography.

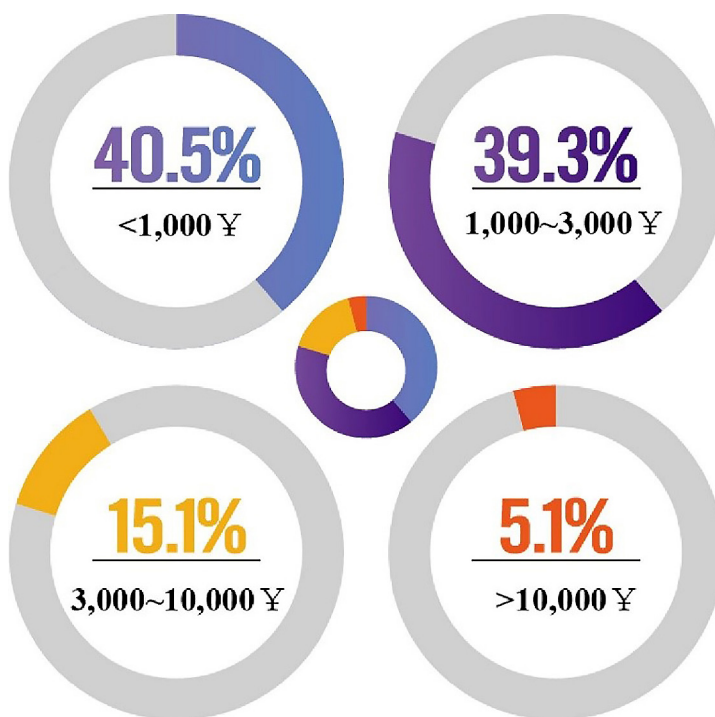


Figure 5. The examination fees: patients willing to pay

5. Caregiving

Long-term care is necessary for supporting AD. Caregiving often includes assistance with one or more activities of daily living, such as dressing and cleaning (“2023 Alzheimer’s disease facts and figures,” 2023). In China, caregivers are most likely to be the family members who can provide emotional

support to patients and help them manage other health conditions. The data indicated that 77.2% of patients were living with their families, while only 12.08% of respondents opted for professional care institutions (Fig. 6.). However, some families feel kind of exhausted and express great concern due to difficulties in caring and the lack of professional guidance.

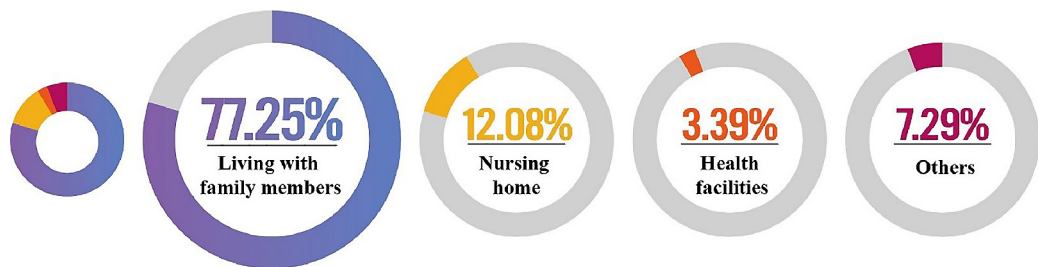


Figure 6. Places where patients lived.

Among the respondents, the proportion of those diagnosed with AD for more than five years currently accounts for about 30%. Considering the increasing incidence of early-onset AD, the duration of care for AD will be further extended in the future, and the cost of social care will also increase, with more than one-third of the respondents showing concern about the high financial burden of healthcare. Since home care is still the most common way of caregiving, the experts’ suggestions for home care for people with dementia based on community support have been published in 2023 (Zhu *et al.*, 2023). The documents as professional guidelines concluded four aspects of homecare guidelines: the homecare workers and facilities for dementia patients living at home, the specific content of home care, the health resources and policy support of social care, and transitional care from home to institution.

6. Drug treatment

Treatments for AD mainly include medication and non-pharmacological interventions (e.g. risk factor control, physical exercise, cognitive training, etc.). Currently, there are only a few drugs approved for clinical use in China, including cholinesterase inhibitors-donepezil, rivastigmine, galantamine, Huperzine A, the N-methyl-D-aspartate receptor-antagonist memantine, and Sodium Oligomannate Capsules (GV-971). These drugs could improve cognitive performance but almost fail to slow down the process of the disease. The result shows that

10.3% of patients do not receive any treatment even when they have been diagnosed with cognitive impairment and a part of patients (28.9%) choose to change their lifestyle instead of taking medicine (Fig.7). In China, the most frequently used oral medication is donepezil (52.4%), followed by memantine (34.6%), and GV-971(19.6%)(Fig.7). While among patients with drug treatment, nearly half of them express dissatisfaction with the effectiveness of the existing drug treatment.

The survey also asked respondents about the newly launched drugs, represented by the anti-A β monoclonal antibody. Notably, the US FDA has approved Aducanumab and Lecanemab. Lecanemab is predicted to be officially approved in China in 2024 based on evidence from amyloid clearance and potential clinical benefits(van Dyck *et al.*, 2022). Phase 3 trials of Donanemab have been initiated for its safety and efficacy, which are also recruiting participants in China at present(Huang *et al.*, 2023). Among the respondents, 42.3% knew about these new drugs and 57.7% did not. At the same time, if the drugs are approved for clinical use in hospitals in China, most respondents (81.7%) will take the initiative to see a doctor and most of them have expressed their willingness to try new drugs. The therapeutic effects and side effects are the most concerning aspects of drugs as well as the challenges faced within AD treatment (Fig.8). By further asking about the reasons for patients’ reluctance to try new drugs, lack of understanding of the medication is the main reason.

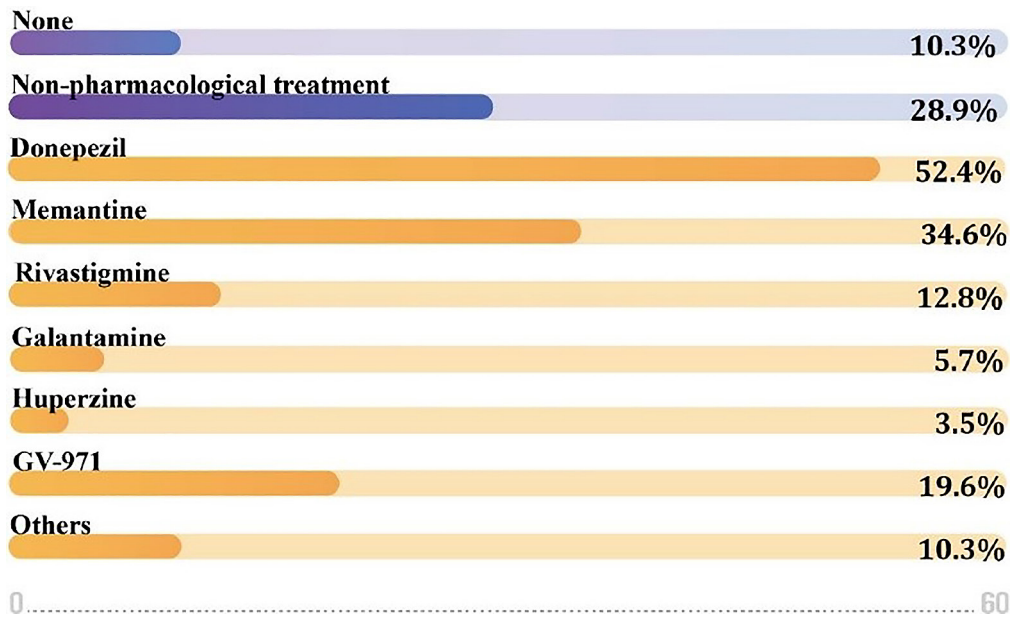


Figure 7. The proportion of most used medicine for AD patients in China.

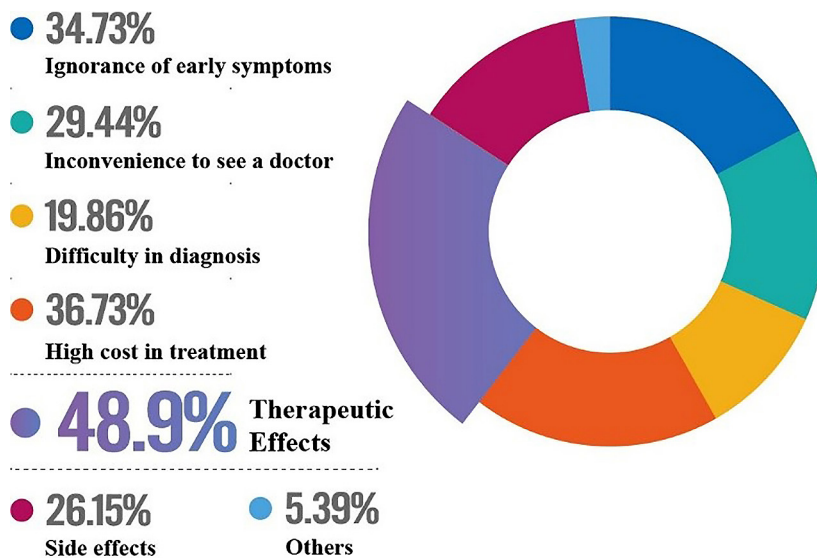


Figure 8. The difficulties and challenges patients face in the diagnosis and treatment.

7. Societal support and information acquisition

Among the respondents, more than 50% of them obtain information about AD through hospitals and others through public welfare organizations, self-media and other means (Fig.9). Meanwhile, 37% of people refuse to obtain new information (Fig.9). Considering patients' advanced age and

their cognitive decline, it is difficult for them to find and select relevant information in an active approach. Some respondents also indicate that there was a lack of opportunities and channels for the exchange of AD-related information in their regions, thus reflecting a wide gap in knowledge of the disease among different regions with imbalanced resources for patient services, which requires attention and support of the whole society.

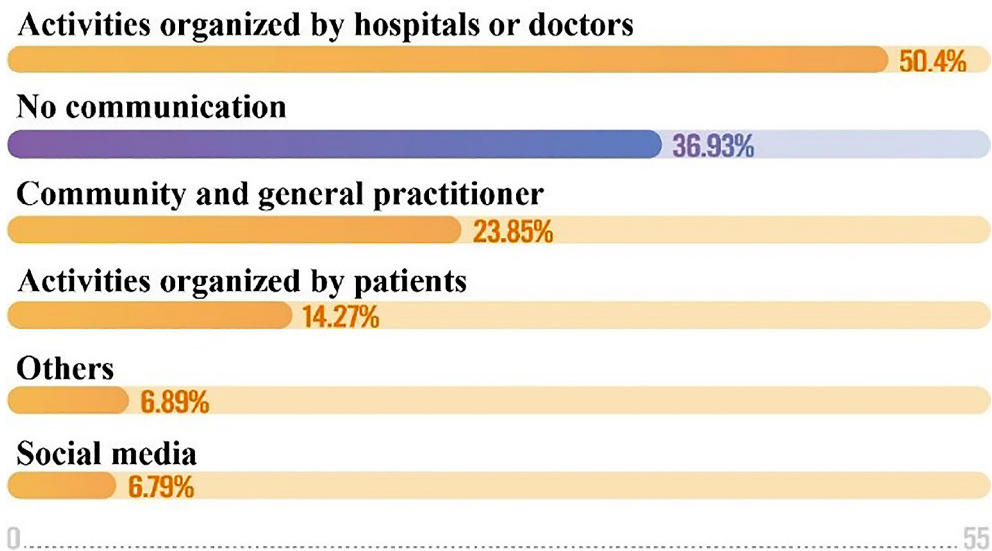


Figure 9. The pathways to access to AD related information.

DISCUSSION

It is the first time to issue an annual report on AD from ADC with data collected from the national web-based survey in China. Previously, there was the China Alzheimer Report analyzing the epidemiological trends, economic burden and current clinical diagnosis and treatment status in China (Ren *et al.*, 2022). Therefore, this report is quite a good supplement to the former report series which complement each other. Recently, China has published national plans. In June 2023, the General Office of the National Health and Health Commission issued the Notice on the Promotion of Dementia Prevention and Treatment, announcing that dementia prevention and treatment will be organized and carried out across the country from 2023 to 2025 to prevent and slow down the incidence of dementia. Overall, to increase public awareness of the disease, this report suggests early detection, screening, and intervention for AD while calling on all sectors to work together to help AD patients in China.

1. Early recognition

Currently, the age of patients diagnosed with AD or MCI due to AD in China is getting younger, resulting in the increasing incidence of early-onset Alzheimer's disease (EOAD). One possible reason may be contributed to neuroimaging advances particularly multimodal neuroimaging techniques and other biomarkers, which have the potential to identify

the pathological features in subjective cognitive decline (SCD) (Karki *et al.*, 2021; Wang *et al.*, 2020). More studies on genetic and phenotypic heterogeneity as well as clinical heterogeneity in EOAD can help us better discriminate the early stages of AD (Cacace *et al.*, 2016; Sirkis *et al.*, 2022). Besides, more and more people are suffering from mental disorders nowadays, and these factors such as depression and mental inactivity are also risk factors for cognitive decline (Crous-Bou *et al.*, 2017). Most of EOAD patients are still in their working age. This not only impacts their professional and personal lives but increases the social burden. Therefore, it is crucial to pay attention to this phenomenon and emphasize the importance for individuals under 60 to be vigilant and take early preventive measures, as well as timely detection to delay the decline of their cognitive and social functions.

Despite many patients and their families recognizing some typical early symptoms such as memory loss and language problems, followed by other cognitive dysfunctions and behavioral impairments, only a minority of patients seek medical treatment within one year after noticing these symptoms. This indicates that there is still limited understanding among patients and their families regarding the disease, which may be influenced by economic and social factors. Consequently, this status results in missing out on the optimal window for treatment interventions. In the future, there remains substantial room for improvement in terms of early diagnosis of AD in China.

2. Early screening

Cognitive screening is less common in the community while most patients are diagnosed with cognitive impairment in tertiary hospitals. Previous study has shown that outpatients have a higher annual conversion rate from MCI to AD than community-based patients (Chen *et al.*, 2017), which means that the latter are probably at more advanced stages of the disease. Therefore, it is important to detect mild symptoms at the early stage especially in the community before the symptoms get worse. One study found that there was not enough evidence supporting the Mini-Mental State Examination (MMSE) as a stand-alone single-administration test in the identification of MCI patients who could develop dementia (Arevalo-Rodriguez *et al.*, 2021). Another research suggests that the Montreal Cognitive Assessment (MoCA) could be a promising screening test in memory clinics as well as for population screening, while its specificity to detect early AD is relatively low (De Roeck *et al.*, 2019). Furthermore, computer-assisted analysis of speech silence character can also be recognized as a diagnostic biomarker of early cognitive decline by analyzing the percentage of silence duration (Wang *et al.*, 2022). These relatively simple tests in the community could screen suspected patients, and then referrals go to specialized hospitals for confirming diagnosis (Laske *et al.*, 2015).

Interestingly, the data also reveal that a greater number of patients and their families are inclined to accept examinations with relatively lower prices, with fewer showing willingness to pay for higher-priced but more accurate ones. Most of them prefer cost-effective and non-invasive testing methods. CSF sampling and PET imaging are relatively invasive and/or expensive, uncomfortable, and time-consuming procedures which are not commonly applied in medical practice (Citron *et al.*, 1997; Hampel *et al.*, 2022). These factors lead to more research on blood biomarkers screening for pre-AD and MCI. Therefore, effective blood biomarkers need to be further tested in the Chinese population cohort to verify their predictive power. Recently, Zhao and her colleagues found that MCI patients with low A β 42/A β 40 and high p-tau181 may have higher risks of converting into AD through an 8-year cohort (Xiao *et al.*, 2022). Meanwhile, another Chinese research group established an optimal diagnostic model which combined the apolipoprotein E (APOE) genotype with plasma

p-Tau and serum GFAP (Gao *et al.*, 2023). Further, our research group has conducted a META analysis suggesting that blood biomarkers such as P-tau217, P-tau 181, and GFAP hold promising potential in predicting MCI conversion. The combination of different biomarkers may help us catch the disease at an early stage for preventative interventions.

Surprisingly, the recognition of PET examination for diagnosis has also increased. Since the AV-1 from Sinotau has been approved in China, the subsequent commercialization will promote the construction of A β -PET nuclear medicine centers, which is expected to further increase the number of AD patients diagnosed by A β -PET in China.

3. Early intervention and treatment

Considering the growing trend of early-onset AD, the time of caregiving will be further extended in the future, and the social care costs will also increase. A recent study predicts that the total annual cost of AD in China will exceed 3 trillion yuan by 2030 and reach 11.77 trillion yuan by 2050 (Jia *et al.*, 2018). In China, AD has been included in outpatient chronic disease management in most provinces and cities. The long-term treatment of AD needs the support of the whole society and joint management. It is believed that an information platform for international exchange and cooperation could be established to better provide support for the prevention and treatment of AD (Ren *et al.*, 2022).

Meanwhile, the current medication still fails to satisfy patients and their families. There is no sufficient data on clinical effects at later stages of the disease, probably because the damage in neurons has become inevitable and irreversible. Therefore, new drugs, including the antibody targeting β -amyloid, should be initiated in patients with MCI or mild dementia stage of AD. Additionally, the clinical trials of the new drugs are still investigating whether amyloid clearance protects patients from cognitive and functional decline in the long run (Jucker & Walker, 2023). Whether these drugs would be cost-effective for early AD is also a problem that needs to be thought about (Ross *et al.*, 2022). Inspiringly, we have initiated the real world study of aducanumab for early-stage Alzheimer's Disease in Ruijin Hainan Hospital in 2022. The trial has enrolled more than ten patients including mild AD and MCI due to AD receiving monthly doses of aducanumab of up to 10mg/kg. In October 2023,

a 31-year-old female familial EOAD patient was treated with Aducanumab for the first time, who might be the youngest case in clinical use in the world so far.

4. Risk factor: COVID-19

At the end of 2022, with changes in prevention policy for the Coronavirus disease 2019 (COVID-19), China suffered from an epidemic impact dominated by the Omicron BA.5.2 and BF.7. In February 2023, we also conducted a web-based national survey for the health management of cognitive impaired patients during COVID-19. Our results show that cognitively impaired patients have a higher infection rate of COVID-19, and COVID-19 also leads to a cognitive decline in cognitively impaired patients. The deterioration rate of the overall cognitive level and other cognitive domains is all around 25%. Therefore, better and more comprehensive management and healthcare should be the key issue for vulnerable groups represented by AD and other dementia patients in the post-epidemic era in the world (Wang J-T, 10th July 2023.).

5. Limitations

It must be pointed out that the reported data comes from an online survey rather than epidemiology research. Maybe patients and their family members who have no access to the network are likely to be ignored in the survey, which leads to the subject bias. On the other hand, most of them come from cities without rural areas, which may also cause regional bias and limit its representativeness for the overall situation in China. Therefore, the results must be analyzed comprehensively and combined with related statistical reports and other data. Future research should conduct more investigations to assess the medical willingness among patients and provide valuable data to support for early detection and development of appropriate diagnosis and treatment strategies.

CONCLUSION

The report aims to further understand the current needs of patients and the problems that occur in China, thus trying to call on the whole society to take action to raise the public's awareness of early management of AD. In future, the government as well as medical institutions, pharmaceutical

companies and other social forces will work together to establish a more comprehensive and effective project for AD control. Importantly, the report will be released annually to promote the information exchange and policy formulation step by step.

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Conflict of Interest Disclosures

Competing interests: None declared.

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List of abbreviations

AD: Alzheimer's disease
MCI: mild cognitive impairment
A β : beta-amyloid
CSF: cerebrospinal fluid
PET: Positron emission tomography
FDA: Food and Drug Administration
ADC: Alzheimer's Disease Branch of Chinese Aging Well Association
NMPA: National Medical Products Administration
EOAD: early-onset Alzheimer's disease
SCD: subjective cognitive decline
MMSE: Mini-Mental State Examination
MoCA: Montreal Cognitive Assessment
APOE: apolipoprotein E

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