

## **Prescription patterns of anti-dementia and psychotropic drugs in people living with dementia: Findings from the Clinical Pathway Study of Alzheimer's Disease in China**

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Brief summary: Using nationally representative data, we found that prescription of antimentia and psychotropic medication depended on patients' clinical symptoms, which generally concurred with clinical guidelines in memory clinics in China.

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#### Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## **Prescription patterns of anti-dementia and psychotropic drugs in people living with dementia: Findings from the Clinical Pathway Study of Alzheimer's Disease in China**

### **ABSTRACT**

*Objectives:* Evidence about prescribing patterns of dementia medication in China is lacking. This study aimed to examine prescribing rates of anti-dementia and psychotropic drugs and factors associated with drug prescription for dementia in China.

*Design:* A multi-center observational study.

*Setting and Participants:* This study employed cross-sectional data from the Clinical Pathway for Alzheimer's Disease in China study that was conducted in 28 memory clinics at tertiary hospitals across 14 provinces between 2012 and 2013. Patients aged 45 years and older with a diagnosis of dementia were included.

*Methods:* Anti-dementia and psychotropic drugs were classified according to the Anatomical Therapeutic Chemical codes. Odds ratios (ORs) of putative factors associated with prescription patterns were estimated using logistic regressions.

*Results:* A total of 751 respondents were included in this study, 77.8% of whom were prescribed anti-dementia drugs, and 33.0% were prescribed at least one psychotropic drug. The concomitant prescription rate of anti-dementia and psychotropic drugs was 24.1%. Frontotemporal dementia (OR 9.92 [99.17% CI 3.08-42.70]), severe dementia (4.25 [1.88-9.79]), and apathy (1.94 [1.18-3.20]) were significantly associated with an elevated likelihood of memantine prescription. Psychotic symptoms (1.84 [1.02-3.35]), agitation (1.91 [1.08-3.40]), and depressive symptoms (2.10 [1.12-3.94]) were significantly associated with the co-prescription of anti-dementia and psychotropic agents.

*Conclusions and Implications:* The prescribing rate of anti-dementia drugs in the study sample was higher while the rate of co-prescription of psychotropic and anti-dementia drugs was lower than reported in western studies. Dementia prescription practice was generally consistent with clinical guidelines in memory clinics in China, while the prescription of anti-dementia and psychotropic medication mainly depended on patients' clinical symptoms.

*Keywords:* Dementia, prescribing patterns, anti-dementia drugs, psychotropic drugs

Dementia is a neurodegenerative syndrome that can impose a huge burden on people living with it, their families, and society.<sup>1,2</sup> Pharmacological treatment, whilst not providing a cure for dementia, is considered effective for improving cognition and managing its behavioral symptoms and should be made available to people living with dementia.<sup>3</sup> A comprehensive situation analysis of pharmacological intervention is necessary to inform pharmacotherapy services provision and promote improved dementia treatment and care.<sup>4</sup>

First-line agents used for the symptomatic treatment of dementia include cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) (ChEIs) and memantine. ChEIs are mainly used to treat mild to moderate Alzheimer's disease and are effective in ameliorating cognition and global functioning.<sup>5-7</sup> A combination of a ChEI and memantine can be used to treat moderate to severe Alzheimer's disease, and previous studies have suggested that this combination may have additive benefits in improving cognitive, functional, and global symptoms.<sup>8</sup> In addition, randomized controlled trials have shown that these drugs may be beneficial in alleviating the behavioral symptoms of dementia.<sup>8,12</sup> In clinical practice, memantine and ChEIs are also used to treat symptoms of other dementia subtypes, such as vascular dementia and Lewy body dementia.<sup>9-11</sup> The National Institute for Health and Care Excellence (NICE) Guideline recommends memantine and ChEIs for the treatment of people living with dementia.<sup>13</sup>

Psychotropic drugs include antipsychotics, anxiolytics, hypnotics/sedatives, antidepressants, and antiepileptics that are often prescribed for the treatment of neuropsychiatric symptoms.<sup>14</sup> However, psychotropic drugs were shown to have limited efficacy in improving neuropsychiatric symptoms while side-effects include increased risks of adverse cerebrovascular events,<sup>2</sup> falls,<sup>15</sup> and all-cause mortality<sup>16</sup>. It is recommended that psychotropic drugs should be prescribed only for dementia patients at risk of self-harm or threatening others, and those with severe neuropsychiatric symptoms generating grievous distress.<sup>13</sup> The co-prescription of psychotropic and anti-dementia drugs may have deleterious effects, reduced potency, and early discontinuation of ChEIs therapy among dementia patients. Co-prescription, therefore, should be used cautiously in line with best-practice standards.<sup>17</sup>

China, with around 9.5 million people living with dementia in 2017<sup>19</sup>, has the largest number of people living with dementia in the world.<sup>18</sup> However, current evidence about pharmacological treatment of dementia in China is lacking. Although previous studies have examined the prevalence of use or prescription of anti-dementia and psychotropic drugs for people living with dementia,<sup>20-22</sup> no research has investigated co-prescription of both in a single study or factors associated with prescription patterns in China. In this study, we aimed to address this research gap using data covering a wide geographic area in China.

## **Methods**

### *Data source, study design, and population*

The Clinical Pathway for Alzheimer's Disease (CPAD) study is an eight-week multi-center registry study conducted between November 12, 2012, and January 31, 2013, in mainland China. A total of 1010 patients aged 45 years and older with suspected cognitive impairment were recruited from 28 memory clinics at tertiary hospitals across 14 provinces

(including municipalities) located in east, central, and west China. Consenting respondents underwent eligibility screening, initial assessment, and second and third assessments at four and eight weeks, respectively. Individuals aged 45 or above, willing to attend a two-month follow-up interview, and accompanied by an informant or carer, were eligible to participate in the study.<sup>23</sup> Informed consent was obtained from all respondents.

A clinical report form (CRF) adapted from the Uniform Data Set (UDS) commonly utilized in Alzheimer Disease Research Centers (ADRCs) in the US was used to collect demographic data and information about disease history (Part A), clinical symptoms, examinations (Part B), and caregiving perceptions and attitudes toward dementia care (Part C).<sup>24</sup> Where patients themselves were unable to answer questions, their caregivers responded. Drug prescription information was recorded by healthcare professionals for each visit. The CPAD study was approved by the central ethics committee at “Blinded for Review”. This investigation comprised a subsample of 751 respondents who had a confirmed diagnosis of dementia in at least one of the three assessments. Respondents who were diagnosed as having normal cognitive function, mild cognitive impairment, or other diseases were excluded. Details of the sample selection procedure are shown in Figure 1.

#### *Outcome measures*

The coding of prescription of anti-dementia and psychotropic drugs was based on the ATC Classification.<sup>25</sup> Anti-dementia drugs were classified into two groups: acetylcholinesterase inhibitors (N06DA) and memantine (N06DX01). ChEIs included donepezil (N06DA02), rivastigmine (N06DA03), and galantamine (N06DA04). Prescription of ginkgo folium (N06DX02) was also included. Psychotropic drugs were classified into five groups: antiepileptics (N03A), antipsychotics (N05A), anxiolytics (N05B), hypnotics/sedatives (N05C), and antidepressants (N06A). Detailed information on the drugs included in each category is listed in Supplementary Table 1.

Since three assessments were administered within eight weeks, the prescription of a specific drug was coded as 1 if a prescription record was identified after dementia diagnosis, and 0 otherwise. The main outcomes of interest included the prescription of (1) ChEIs, (2) memantine, (3) both ChEIs and memantine, and (4) both anti-dementia and psychotropic drugs. Secondary outcomes of interest included the prescription of (1) any antipsychotic and (2) any antidepressant.

#### *Explanatory variables*

Patient characteristics included age, sex, whether the current visit was the patient’s first consultation due to cognitive impairment, functional status, dementia subtype, dementia severity, and neuropsychiatric symptoms at the first recording of a confirmed dementia diagnosis (baseline). For example, for patients whose diagnoses were confirmed at the second visit, personal and clinical information collected during the second visit was used in the subsequent analysis. Specifically, functional status was assessed by a general item on a four-point Likert scale, with responses ranging from 1 (can live independently without assistance with activities of daily living) to 4 (total dependence on other people). Dementia subtypes included Alzheimer’s disease, vascular dementia, frontotemporal dementia, and other types of dementia (including Lewy body dementia, Parkinson’s disease dementia, and mixed dementia).

Sub-domains of neuropsychiatric symptoms of interest included apathy, depression, visual hallucination, auditory hallucination, delusions, disinhibition, irritability, and agitation. The presence of each specific symptom was measured based on clinical judgment. Our preliminary analysis showed that visual hallucination, auditory hallucination, and delusions were highly correlated with each other (see Supplementary Table 2). Similarly, high correlations were also observed between disinhibition, irritability, and agitation. Therefore, we followed an earlier study and collapsed highly correlated subtypes of symptoms into two general categories: psychosis and agitation.<sup>26</sup>

Caregivers' characteristics included caregiving burden and a binary variable measuring whether the caregiver had received training or guidance on dementia care services. Caregiving burden was measured by the Chinese version of the Caregiver Burden Inventory, comprising 24 items where possible scores range from 0 to 96, with higher scores indicating greater burden.<sup>27</sup> Coding details for explanatory variables are shown in Table 1.

### *Statistical analysis*

We tabulated sample characteristics at baseline and report the prevalence of anti-dementia and psychotropic drug prescriptions. Three logistic regression models were fitted to examine factors associated with the prescription of ChEIs, memantine, and their combination. Using the subsample of patients who were prescribed anti-dementia drugs, we fitted another logistic regression to examine factors associated with concomitant prescription of anti-dementia and psychotropic drugs. Two additional logistic regression models were fitted to examine the association between specific neuropsychiatric symptoms, i.e., depression and psychotic syndrome, and the prescription of antipsychotics and antidepressants. We used list-wise deletion to handle missing values. Given that the six outcomes were used, we adjusted  $p$  values ( $0.0083 = 0.05/6$ ) and confidence intervals ( $99.17\%$ ,  $1 - 0.0083 = 0.9917$ ) based on Bonferroni correction to counteract the problem of inflated Type I errors. Estimates were considered statistically significant at the 0.0083 level (two-tailed). All statistical analyses were performed using the statistical software R Version 3.6.1.<sup>28</sup>

## **Results**

Baseline sample characteristics are summarized in Table 1. The mean age of the respondents was 73 years ( $SD = 9.5$ ). Of the 751 respondents, 51.0% were female and 27.7% had consulted a doctor for cognitive problems for the first time. Most respondents were diagnosed with Alzheimer's disease (68.8%). Most respondents with dementia had moderate dementia (44.8%), needed help with instrumental activities (45.9%), and had agitation (52.1%). Less than 7% of caregivers had received training in dementia care.

Prescribing patterns of anti-dementia and psychotropic drugs are shown in Table 2. Overall, anti-dementia drugs were prescribed to 77.8% of the sample. Prescription of ChEIs and memantine accounted for 52.6% and 39.9% of the total sample, respectively, and 14.8% of respondents were prescribed both ChEIs and memantine. Very few patients were prescribed ginkgo folium (6.1%). Psychotropic drugs were prescribed to 33.0% of respondents, with the highest prevalence observed in antipsychotics (20.4%), followed by anti-depressants (12.8%). The prevalence rates of antiepileptics, anxiolytics, hypnotics, and sedatives were all lower than

5%. A quarter of patients (24.1%) were concomitantly prescribed both anti-dementia and psychotropic drugs.

Results from the logistic regression analysis of the prescription of anti-dementia and psychotropic drugs are shown in Table 3. Model 1 shows the logistic regression results for the prescription of ChEIs. People with vascular dementia (0.21; 0.10-0.41) and frontotemporal dementia (0.18; 0.06-0.48), and those with psychotic symptoms (0.53; 0.32-0.87) had lower odds of being prescribed ChEIs. Model 2 presents the logistic regression results for the prescription of memantine. People with frontotemporal dementia had almost ten times the odds of being prescribed memantine (9.92; 3.08-42.70), compared with those with Alzheimer's disease. Also, those with severe dementia had around four times (4.25; 1.88-9.79) the odds of being prescribed memantine, compared with those with mild dementia. Those with apathy were also more likely to be prescribed memantine (1.94; 1.18-3.20), whereas those having their first consultation due to cognitive impairment (0.50; 0.28-0.87) were less likely to be prescribed memantine. Model 3 shows that patients with moderate (7.10; 2.49-26.21) and severe dementia (11.20; 3.26-47.19) were strongly associated with co-prescription of ChEIs and memantine, while those with first consultation due to cognitive impairment (0.35; 0.13-0.80) were less likely to be co-prescribed both drugs.

ORs associated with the concomitant prescription of anti-dementia and psychotropic drugs are presented in model 4. Psychotic symptoms, agitation, and depressive symptoms were all positively associated with concomitant prescription, with ORs of 1.84 (1.02-3.35), 1.91 (1.08-3.40), and 2.10 (1.12-3.94), respectively. Besides, psychotic symptoms (4.43 [2.46-8.18]) and depressive symptoms (4.00 [2.01-8.04]) were significantly associated with the prescription of any antipsychotic and any antidepressant, respectively (see Supplementary Table 3).

Neither demographics (age and sex) nor caregiver characteristics (receipt of training for dementia care and caregiving burden) were significantly associated with the prescription of medication for dementia in any of the six models.

## Discussion

Using data from 28 memory clinics covering a wide geographic area, this study is one of the first to systematically report the prescribing patterns of anti-dementia and psychotropic drugs in mainland China and to investigate factors associated with the prescription of drugs for dementia. We found that almost 80% of respondents were prescribed anti-dementia drugs, one-third were prescribed psychotropic drugs, and one-quarter were prescribed psychotropic drugs in combination with anti-dementia drugs. Drug prescription practice was associated with patients' clinical features.

In China, patients who are suspected of having dementia can seek help at geriatric, neurology, or psychiatric/psychological departments in a general hospital or a specialized psychiatric hospital. However, due to stigma and inadequate training in dementia diagnosis, underdiagnosis and undertreatment of dementia are common.<sup>29</sup> With the increase in related research knowledge, standardizing the diagnosis and treatment of dementia has become possible. In this context, the first national dementia guideline for clinicians to enhance the popularization and standardization of knowledge of diagnosis and treatment of dementia was

issued by the Chinese Society of Psychiatry in 2007.<sup>30</sup> This guideline covers the standard protocol for dementia diagnosis, an algorithm for making treatment and care plans, and provides the possibility of assessing prescription practice for dementia in China. Subsequently, the Chinese Society of Neurology issued a clinical guideline on dementia, providing recommendations on the medication for Alzheimer's disease and other dementias.<sup>31</sup> However, to what extent clinical practice is consistent with the clinical guidelines remains unknown.

Overall, our study showed that the prevalence of anti-dementia drug prescription in memory clinics in China was much higher than in Germany, Sweden, and the US, where prescribing rates of anti-dementia drugs ranged from 24% to 56%.<sup>4,32,33</sup> It is possible that the high prevalence found in this study was partially attributable to the clinical characteristics of people seeking help from memory clinics, i.e., this sample might be skewed towards people at a more advanced stage of dementia. In addition, we found that the prescribing rate of ginkgo folium was low, although it was almost 70% in German clinical dementia practice.<sup>34</sup> Prescription of anti-dementia drugs generally followed the Chinese dementia guidelines that recommend drugs for dementia treatment and the need for more validation of the efficacy of ginkgo folium for treating Alzheimer's disease.<sup>30,31</sup>

The prescribing rates of psychotropic agents in western countries vary between 35% and 82%.<sup>4,26,35-39</sup> In our study, 33.0% of people living with dementia were prescribed psychotropic drugs, lower than any reported prevalence in western studies. Regarding the co-prescription rate, an earlier Japanese study reported that more than 20% of people living with dementia used donepezil concomitantly with psychotropic drugs,<sup>40</sup> and a Norwegian study showed that 60% of all dementia patients using anti-dementia drugs were prescribed psychotropic drugs.<sup>41</sup> We found a co-prescription rate of 24.1%, which is similar to the Japanese study but much lower than the Norwegian study. Given the potential side effects of psychotropic drugs and the concomitant prescription of psychotropic and anti-dementia drugs, the Chinese dementia guidelines recommend that polypharmacy should largely be avoided, and the trade-off between treating neuropsychiatric symptoms and decreasing side effects should be considered cautiously.<sup>30,31</sup>

Regression results revealed that patients' clinical characteristics were closely associated with the prescription of anti-dementia drugs. Since anti-dementia drugs are licensed for Alzheimer's disease,<sup>3</sup> the probability of prescription of anti-dementia drugs is expected to be lower in patients with other subtypes of dementia compared to patients with Alzheimer's disease. Compared with Alzheimer's disease, we found that vascular and frontotemporal dementia were significantly associated with fewer prescriptions of ChEIs. Patients with severe dementia were more likely to be prescribed memantine and its combination with ChEIs, which is consistent with the dementia guidelines.<sup>30,31</sup> The reason why dementia severity did not have a significant association with the prescription of ChEIs needs further research. Despite the potential of ChEIs and memantine for treating neuropsychiatric symptoms,<sup>8,12</sup> the study results showed that only apathy was positively associated with the prescription of any anti-dementia drugs and memantine while psychotic symptoms were associated with a decreased likelihood of the prescription of ChEIs. We also found that those having their first consultation due to cognitive impairment were less likely to be prescribed memantine and its combination with

ChEIs. Possible explanations may be that the severity of dementia in this group was milder, or that clinicians needed more time to make an accurate diagnosis.

For factors associated with the co-prescription of anti-dementia and psychotropic drugs, this study suggested that other neuropsychiatric symptoms, psychotic symptoms, agitation, and depressive symptoms, but not apathy, were significantly associated with the concomitant prescription of anti-dementia and psychotropic drugs. This is because in clinical practice the indications for psychotropic medication are neuropsychiatric symptoms in people living with dementia.<sup>14</sup> Besides, our secondary analyses found significant associations between specific psychotropic drugs and neuropsychiatric symptoms. These findings further support the adequacy of the prescription of psychotropic drugs and also its consistency with the Chinese dementia guidelines.<sup>30,31</sup> The lack of evidence about the efficacy of psychotropic drugs on apathy might explain why apathy did not have a significant association with co-prescription.<sup>42,43</sup>

It is worth noting that frontotemporal dementia also played a very important role in prescribing decisions for dementia. We found that frontotemporal dementia was significantly associated with the prescription of memantine. Frontotemporal dementia may result in prominent frontal dysfunction while preserving the cholinergic system.<sup>44</sup> A possible reason for this is that the choice of prescription for frontotemporal dementia is absent and existing studies show that memantine may be beneficial for patients with frontotemporal dementia.<sup>45</sup> More studies about prescription practice for frontotemporal dementia are warranted.

This study has several limitations. First, detailed clinical information associated with each prescription was not available. The indications and dosages of the prescription and the severity of neuropsychiatric symptoms were therefore not available. Information regarding physicians' knowledge and experience of pharmacotherapy and neuropsychiatric symptoms, which may affect prescription practices,<sup>46</sup> was also not collected. Determination of the severity of dementia, neuropsychiatric symptoms, and functioning was based on the physician's clinical judgment, instead of validated scales, such as the Global Deterioration Scale, the Neuropsychiatric Inventory, or the Activities of Daily Living (ADL) scale. This may lead to biased estimations on their associations with prescription practices. Second, although this study has good geographic representativeness in the hospitals selected, conclusions regarding pharmacotherapy cannot be generalized to prescription practices for dementia nationwide, because the prescription data were collected from high-level (tertiary) hospitals only. Our data may overestimate the prescribing rate of anti-dementia drugs and underestimate the prescribing rate of psychotropic drugs. Third, causality between relevant factors and prescription practice cannot be proven, because of the short study duration. Fourth, the data used in this study are relatively old; over the past decade, more progress has been made including the publication of the new version of the dementia guideline in 2018 and execution of the national dementia strategy in 2020.<sup>47,48</sup> However, the study establishes very important baseline evidence on which future investigations on changes in prescription patterns can draw.

## **Conclusion and Implications**

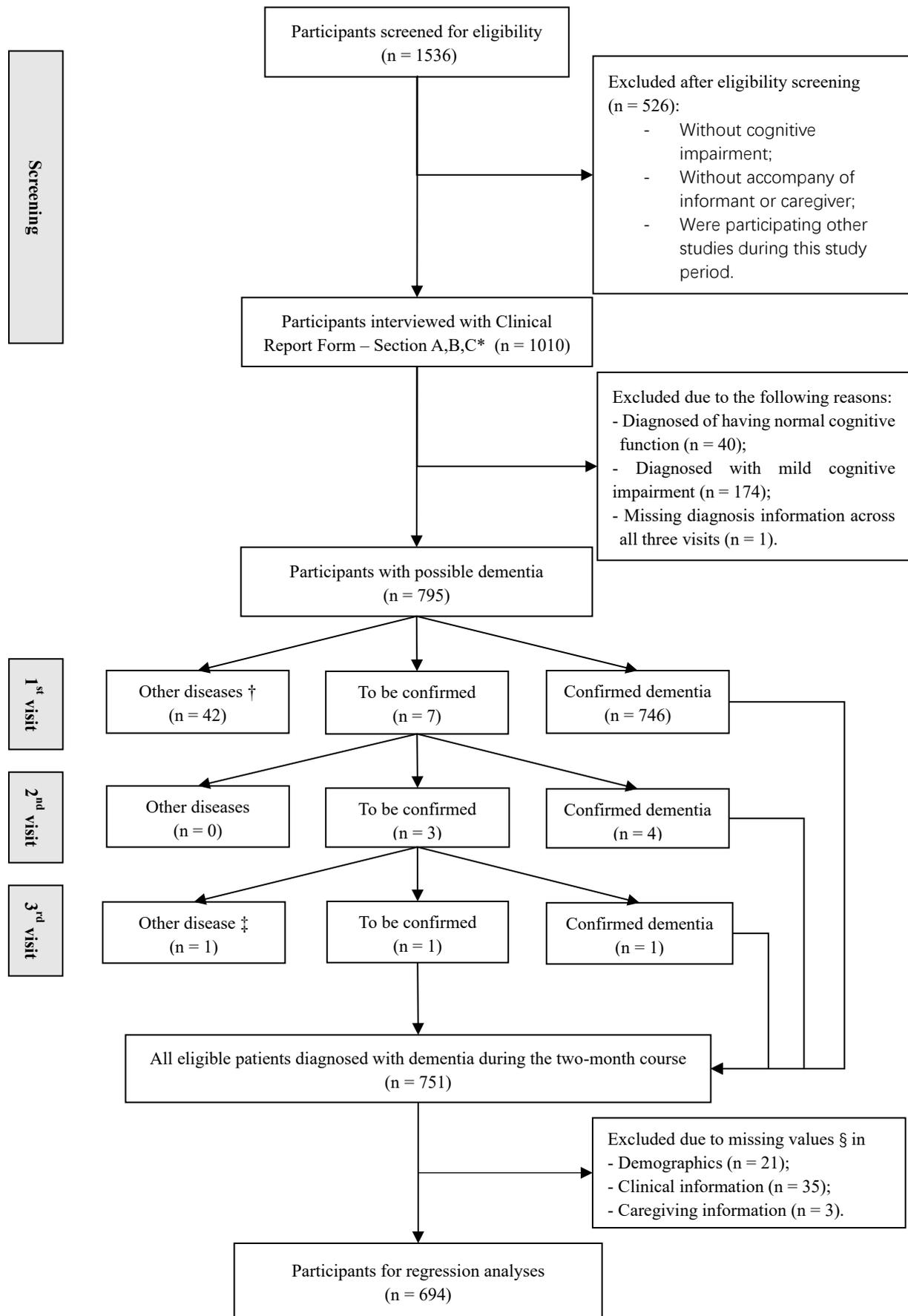
In conclusion, anti-dementia drug prescription was adequate and generally guideline-

oriented; the prescribing rates of psychotropic drugs and the co-prescription of anti-dementia and psychotropic drugs in well-established hospitals in China were kept at a low level and may be even lower than in western countries. Pharmacotherapy was mainly associated with dementia patients' clinical characteristics and was generally consistent with the Chinese dementia guidelines. To better understand prescription patterns and factors associated with drug prescription, longer longitudinal surveys are needed.

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**Fig. 1.** Flowchart of respondent selection.

*Notes:* \*Clinical Report Form – Section A, B, C indicates the clinical report form consisting of demographic (A), clinical (B), and caregiving (C) variables.

†Other diseases at the first visit include depression (n = 10), Parkinson's disease (n = 2), pseudodementia (n = 2), Creutzfeldt–Jakob disease (n = 1), transient ischemic attack (n = 1), hypothyroidism (n = 1), schizophrenia (n = 2), organic psychosis (n = 1), obsessive compulsive neurosis (n = 1), delayed encephalopathy after carbon monoxide poisoning (n = 1), normal-pressure hydrocephalus (n = 1), vascular cognitive impairment (n = 7), cognitive decline due to postoperative meningioma (n = 1), trauma (n = 2), temporal lobe epilepsy (n = 1), mild cognitive impairment (MCI) with depression and anxiety (n = 1), MCI with dyspraxia (n = 1), MCI with possible depression (n = 1), delirium (n = 1), encephalatrophy (n = 1), dysmnnesia (n = 2), and amnesia (n = 1).

‡Other disease at the third visit was MCI.

§There were overlapping missing values from demographics, clinical, and caregiving information.

**Table 1**

Characteristics of study population (n = 751)

Variable	Valid N	N/M (%/SD)
<i>Demographic characteristics</i>		
Female	736	375 (51.0)
Age (45-103 years)	744	73.0 (9.5)
45-59		75 (10.1)
60-64		76 (10.2)
65-74		223 (30.0)
75-79		179 (24.1)
80-84		112 (15.1)
85 and above		79 (10.6)
<i>Clinical information</i>		
First consultation due to cognitive impairment	745	206 (27.7)
Subtypes of dementia		
Alzheimer's disease	751	517 (68.8)
Vascular dementia		114 (15.2)
Frontotemporal dementia		40 (5.3)
Lewy body dementia		8 (1.1)
Parkinson's disease dementia		5 (0.7)
Co-existence dementia *		53 (7.1)
Other types of dementia †		14 (1.9)
Severity of dementia		
Mild dementia	750	264 (35.2)
Moderate dementia		336 (44.8)
Severe dementia		150 (20.0)
Independence level of daily living		
Independent	749	151 (20.2)
Needing help with instrumental activities		344 (45.9)
Needing help with basic daily activities		162 (21.6)
Totally dependent		92 (12.3)
Neuropsychiatric symptoms		
Psychotic symptoms	728	259 (35.6)
Agitation	726	378 (52.1)
Apathy	731	334 (45.7)
Depressive symptoms	729	161 (22.1)
<i>Caregiver characteristics</i>		
Received training for dementia care	751	50 (6.7)
Caregiving burden (0-96)	749	26.3 (18.6)

Note: N = frequency, % = percentage; M = mean, SD = standard deviation; Numbers may not add exactly because of rounding.

\*Co-existence dementia includes the following combinations: Alzheimer's disease and vascular dementia (n = 11); Alzheimer's disease and frontotemporal dementia (n = 1); Alzheimer's disease and alcohol-related dementia (n = 1); the co-existence of unspecified types of dementia (n = 40).

†Other types of dementia include senile dementia (n = 1), paralytic dementia (n = 4), vascular dementia with vitamin B12 deficiency (n = 1), vascular dementia with frontotemporal lobe degeneration (n = 1), unspecified mild dementia with depressive status (n = 1), senile dementia

with possible trauma (n = 1), unspecified dementia with severe anemia (n = 1), and other unspecified dementias (n = 4).

**Table 2**

Prescribing patterns of anti-dementia drugs and psychotropic drugs (n = 751)

Drugs	<i>N</i>	%
Anti-dementia drugs in all three visits		
Cholinesterase inhibitors	395	52.6
Memantine	300	39.9
Cholinesterase inhibitors + memantine	111	14.8
Any anti-dementia drugs	584	77.8
Ginkgo folium in all three visits	46	6.1
Psychotropic drugs in all three visits		
Antiepileptics	37	4.9
Antipsychotics	153	20.4
Anxiolytics	29	3.9
Hypnotics and sedatives	15	2.0
Antidepressants	96	12.8
Any psychotropic drugs	248	33.0
Anti-dementia drugs + psychotropic drugs	181	24.1

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**Table 3**  
**Logistic regression results for prescription of anti-dementia and psychotropic drugs**

Variable	Model 1 ChEIs (n = 694)		Model 2 Memantine (n = 694)		Model 3 ChEIs + Memantine (n = 694)		Model 4 Anti-dementia + psychotropic drugs (n = 544)	
	OR (99.17% CI)	p value	OR (99.17% CI)	p value	OR (99.17% CI)	p value	OR (99.17% CI)	p value
<i>Demographic characteristics</i>								
Female	0.91 (0.58-1.43)	0.589	0.83 (0.51-1.35)	0.312	0.68 (0.36-1.26)	0.098	1.23 (0.71-2.17)	0.320
Age (Ref = 45-59)								
60-64	1.13 (0.43-2.99)	0.737	0.46 (0.16-1.30)	0.049	0.71 (0.18-2.72)	0.502	1.36 (0.41-4.60)	0.494
65-74	1.31 (0.59-2.93)	0.373	0.66 (0.28-1.58)	0.209	0.90 (0.32-2.78)	0.795	1.12 (0.42-3.14)	0.765
75-79	1.11 (0.48-2.55)	0.745	0.70 (0.29-1.70)	0.287	0.85 (0.28-2.76)	0.705	1.07 (0.39-3.13)	0.859
80-84	1.29 (0.52-3.24)	0.456	0.52 (0.20-1.38)	0.079	0.84 (0.24-2.96)	0.707	1.33 (0.44-4.15)	0.502
85 and above	1.24 (0.46-3.33)	0.570	0.60 (0.21-1.69)	0.191	0.61 (0.15-2.45)	0.352	1.15 (0.35-3.83)	0.762
<i>Clinical information</i>								
First consultation due to cognitive impairment	0.72 (0.44-1.19)	0.085	<b>0.50 (0.28-0.87)</b>	<b>0.001</b>	<b>0.35 (0.13-0.80)</b>	<b>0.002</b>	0.92 (0.47-1.78)	0.748
Subtype of dementia (Ref = Alzheimer's disease)								
Vascular dementia	<b>0.21 (0.10-0.41)</b>	<b>&lt;0.001</b>	0.57 (0.27-1.16)	0.042	0.37 (0.09-1.11)	0.031	2.05 (0.80-5.22)	0.041
Frontotemporal dementia	<b>0.18 (0.06-0.48)</b>	<b>&lt;0.001</b>	<b>9.92 (3.08-42.70)</b>	<b>&lt;0.001</b>	0.97 (0.24-3.13)	0.940	2.53 (0.90-7.00)	0.016
Other types of dementia	0.76 (0.38-1.51)	0.283	0.84 (0.39-1.78)	0.544	1.17 (0.43-2.92)	0.654	1.35 (0.54-3.22)	0.372
Severity of dementia (Ref = Mild dementia)								
Moderate dementia	1.45 (0.83-2.55)	0.077	1.82 (0.99-3.38)	0.009	<b>7.10 (2.49-26.21)</b>	<b>&lt;0.001</b>	0.75 (0.36-1.53)	0.278
Severe dementia	1.41 (0.64-3.11)	0.252	<b>4.25 (1.88-9.79)</b>	<b>&lt;0.001</b>	<b>11.20 (3.26-47.19)</b>	<b>&lt;0.001</b>	1.25 (0.50-3.08)	0.514
Independence level (Ref = Independent)								
Needing help with instrumental activities	0.92 (0.48-1.75)	0.727	1.19 (0.57-2.55)	0.526	1.17 (0.39-4.07)	0.714	2.34 (0.95-6.26)	0.016
Needing help with basic daily activities	0.53 (0.22-1.28)	0.058	1.36 (0.52-3.59)	0.393	0.83 (0.22-3.42)	0.719	2.05 (0.64-6.83)	0.108
Totally dependent	0.35 (0.12-1.01)	0.009	1.23 (0.40-3.78)	0.625	0.73 (0.16-3.49)	0.587	3.79 (1.01-14.89)	0.009
Neuropsychiatric symptoms								
Psychotic symptoms	<b>0.53 (0.32-0.87)</b>	<b>0.001</b>	1.21 (0.72-2.02)	0.335	0.85 (0.43-1.63)	0.505	<b>1.84 (1.02-3.35)</b>	<b>0.007</b>
Agitation	0.92 (0.58-1.46)	0.649	0.89 (0.54-1.45)	0.530	0.85 (0.45-1.62)	0.510	<b>1.91 (1.08-3.40)</b>	<b>0.003</b>
Apathy	1.11 (0.69-1.80)	0.559	<b>1.94 (1.18-3.20)</b>	<b>&lt;0.001</b>	1.76 (0.92-3.43)	0.023	0.79 (0.44-1.40)	0.276
Depressive symptoms	1.31 (0.76-2.28)	0.197	1.16 (0.65-2.04)	0.494	1.43 (0.71-2.82)	0.175	<b>2.10 (1.12-3.94)</b>	<b>0.002</b>
<i>Caregiver characteristics</i>								
Received training for dementia care	1.73 (0.70-4.65)	0.122	0.84 (0.32-2.11)	0.618	1.74 (0.57-4.85)	0.165	0.44 (0.11-1.41)	0.086
Caregiving burden	1.00 (0.98-1.02)	0.987	1.01 (0.99-1.03)	0.073	1.01 (0.99-1.03)	0.272	1.00 (0.99-1.02)	0.604

Note: ChEIs = Cholinesterase inhibitors. Bold and italic text indicates that the p value is significant ( $p < .0083$ ).

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