Tools to Inform Policy
Chinese communities' Action in Response to Dementia
華人社會認知障礙症策略工具

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Prescription Patterns of Antidementia and Psychotropic Drugs in People Living With Dementia

Findings From the Clinical Pathway Study of Alzheimer's Disease in China

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Introduction

- Pharmacologic treatment for people living with dementia
  - For improving cognition and managing behavioral symptoms
  - Should be made available to people living with dementia
- First-line agents: cholinesterase inhibitors (ChEIs) and memantine
  - ChEIs: ameliorating cognition and global functioning.
  - ChEI + memantine: treating moderate to severe Alzheimer's disease; improving cognitive, functional, and global symptoms.
- Psychotropic drugs: antipsychotics, anxiolytics, hypnotics or sedatives, antidepressants, and antiepileptics
  - Limited efficacy in improving neuropsychiatric symptoms
  - Side effects include increased risks of adverse cerebrovascular events, falls, and all-cause mortality.
  - Recommendation: prescribed only at risk of self-harm or threatening others, and those with severe neuropsychiatric symptoms generating grievous distress.

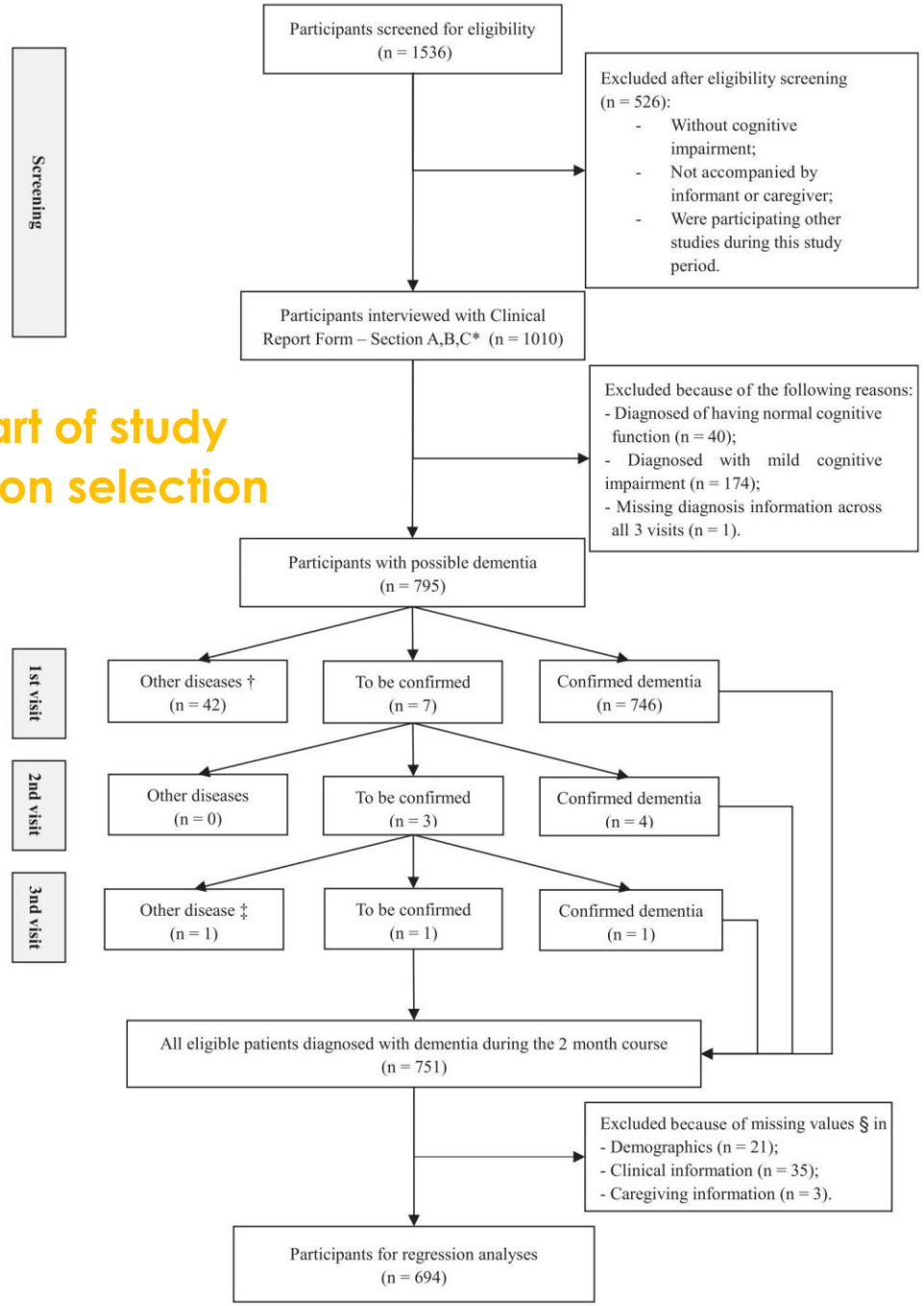
Ballard C, Gauthier S, Corbett A, et al. Alzheimer's disease. Lancet 2011;377: 1019.
National Institute for Health and Care Excellence. Dementia: Assessment, management and support for people living with dementia and their carers (NICE guideline [NG97]). Available at: https://www.nice.org.uk/guidance/ng97. Accessed March 9, 2021.

Introduction

- Co-prescription of psychotropic and antidementia drugs
  - Deleterious effects, reduced potency, and early discontinuation of ChEIs therapy among patients with dementia.
  - Coprescription, therefore, should be used cautiously in line with best-practice standards.
- Current evidence about pharmacologic treatment of dementia in China is lacking.
  - No research has investigated coprescription of the two 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.

Sverdrup Efjestad A, Ihle-Hansen H, Hjellvik V, Blix HS. Comedication and treatment length in users of acetylcholinesterase inhibitors. Dement Geriatr Cogn Dis Extra 2017;7:30e40.
Jia L, Quan M, Fu Y, et al. Dementia in China: Epidemiology, clinical management, and research advances. Lancet Neurol 2020;19:81e92.

Flow chart of study population selection



CPAD in China

- The Clinical Pathway for Alzheimer's Disease study
- 28 memory clinics at tertiary hospitals across 14 provinces.
- In this study:
  - 8- week multicenter registry study conducted between November 12, 2012, and January 31, 2013
  - Individuals aged 45 years, willing to attend a 2-month follow-up interview, and accompanied by an informant or carer
  - 751 respondents who had a confirmed diagnosis of dementia in at least 1 of the 3 assessments

Measures

- Outcome
  - Main outcomes of interest: prescription of (1) ChEIs, (2) memantine, (3) both ChEIs and memantine, and (4) both antidementia and psychotropic drugs.
  - Secondary outcomes of interest: prescription of (1) any antipsychotic and (2) any antidepressant.
  - The coding of prescription of antidementia and psychotropic drugs was based on the ATC Classification.
- Explanatory Variables
  - Age
  - Sex
  - Whether the current visit was the patient's first consultation due to cognitive impairment
  - Functional status
  - Dementia subtype
  - Dementia severity
  - Neuropsychiatric symptoms at the first recording of a confirmed dementia diagnosis (baseline).

Statistical Analysis

- Tabulated sample characteristics at baseline
- Reported the prevalence of antidementia and psychotropic drug prescriptions
- Fitted logistic regression models to examine factors associated with
  - Prescription of ChEIs, memantine, and their combination
  - Concomitant prescription of antidementia and psychotropic drugs
  - Prescription of antipsychotics and antidepressants
- Listwise deletion to handle missing values
- Given that the 6 outcomes were used, we adjusted P values (.0083 = .05/6) and confidence intervals (99.17%, 1- .0083 = .9917) based on Bonferroni correction to counteract the problem of inflated type I errors. Estimates were considered statistically significant at the .0083 level (2-tailed)
- All statistical analyses were performed using the statistical software R, version 3.6.1

Baseline sample characteristics

Variable	Valid n	n (%) or Mean (SD)
Demographic characteristics		
Female	736	375 (51.0)
Age (45-103 y)	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		79 (10.6)
Clinical information		
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)
Coexistence 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)
Caregiver characteristics		
Received training for dementia care	751	50 (6.7)
Caregiving burden (0-96)	749	26.3 (18.6)

Prescribing patterns of antidementia and psychotropic drugs

Drugs	n	%
Antidementia drugs in all 3 visits		
Cholinesterase inhibitors	395	52.6
Memantine	300	39.9
Cholinesterase inhibitors + memantine	111	14.8
Any antidementia drugs	584	77.8
Ginkgo folium in all 3 visits	46	6.1
Psychotropic drugs in all 3 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
Antidementia drugs + psychotropic drugs	181	24.1

Logistic regression analysis of the prescription of antidementia and psychotropic drugs

Variable	Model 1 ChEIs (n = 694)		Model 2 Memantine (n = 694)		Model 3 ChEIs + Memantine (n = 694)		Model 4 Antidementia + 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
Demographic characteristics								
Female	0.91 (0.58-1.43)	.59	0.83 (0.51-1.35)	.31	0.68 (0.36-1.26)	.10	1.23 (0.71-2.17)	.32
Age (ref = 45-59)								
60-64	1.13 (0.43-2.99)	.74	0.46 (0.16-1.30)	.05	0.71 (0.18-2.72)	.50	1.36 (0.41-4.60)	.50
65-74	1.31 (0.59-2.93)	.37	0.66 (0.28-1.58)	.21	0.90 (0.32-2.78)	.80	1.12 (0.42-3.14)	.77
75-79	1.11 (0.48-2.55)	.75	0.70 (0.29-1.70)	.29	0.85 (0.28-2.76)	.71	1.07 (0.39-3.13)	.86
80-84	1.29 (0.52-3.24)	.46	0.52 (0.20-1.38)	.08	0.84 (0.24-2.96)	.71	1.33 (0.44-4.15)	.50
≥85	1.24 (0.46-3.33)	.57	0.60 (0.21-1.69)	.19	0.61 (0.15-2.45)	.35	1.15 (0.35-3.83)	.76
Clinical information								
First consultation due to cognitive impairment	0.72 (0.44-1.19)	.09	**0.50 (0.28-0.87)**	**.001**	**0.35 (0.13-0.80)**	**.002**	0.92 (0.47-1.78)	.75
Subtype of dementia (ref = Alzheimer's disease)								
Vascular dementia	**0.21 (0.10-0.41)**	**<.001**	0.57 (0.27-1.16)	.04	0.37 (0.09-1.11)	.03	2.05 (0.80-5.22)	.04
Frontotemporal dementia	**0.18 (0.06-0.48)**	**<.001**	**9.92 (3.08-42.70)**	**<.001**	0.97 (0.24-3.13)	.94	2.53 (0.90-7.00)	.01
Other types of dementia	0.76 (0.38-1.51)	.28	0.84 (0.39-1.78)	.54	1.17 (0.43-2.92)	.65	1.35 (0.54-3.22)	.37
Severity of dementia (ref = mild dementia)								
Moderate dementia	1.45 (0.83-2.55)	.08	1.82 (0.99-3.38)	.01	**7.10 (2.49-26.21)**	**<.001**	0.75 (0.36-1.53)	.28
Severe dementia	1.41 (0.64-3.11)	.25	**4.25 (1.88-9.79)**	**<.001**	**11.20 (3.26-47.19)**	**<.001**	1.25 (0.50-3.08)	.51
Independence level (ref = independent)								
Needing help with instrumental activities	0.92 (0.48-1.75)	.73	1.19 (0.57-2.55)	.53	1.17 (0.39-4.07)	.71	2.34 (0.95-6.26)	.02
Needing help with basic daily activities	0.53 (0.22-1.28)	.06	1.36 (0.52-3.59)	.39	0.83 (0.22-3.42)	.72	2.05 (0.64-6.83)	.11
Totally dependent	0.35 (0.12-1.01)	.01	1.23 (0.40-3.78)	.63	0.73 (0.16-3.49)	.59	3.79 (1.01-14.89)	.01
Neuropsychiatric symptoms								
Psychotic symptoms	**0.53 (0.32-0.87)**	**.001**	1.21 (0.72-2.02)	.34	0.85 (0.43-1.63)	.51	**1.84 (1.02-3.35)**	**.007**
Agitation	0.92 (0.58-1.46)	.65	0.89 (0.54-1.45)	.53	0.85 (0.45-1.62)	.51	**1.91 (1.08-3.40)**	**.003**
Apathy	1.11 (0.69-1.80)	.56	**1.94 (1.18-3.20)**	**<.001**	1.76 (0.92-3.43)	.02	0.79 (0.44-1.40)	.28
Depressive symptoms	1.31 (0.76-2.28)	.20	1.16 (0.65-2.04)	.50	1.43 (0.71-2.82)	.18	**2.10 (1.12-3.94)**	**.002**
Caregiver characteristics								
Received training for dementia care	1.73 (0.70-4.65)	.12	0.84 (0.32-2.11)	.62	1.74 (0.57-4.85)	.17	0.44 (0.11-1.41)	.09
Caregiving burden	1.00 (0.98-1.02)	.99	1.01 (0.99-1.03)	.07	1.01 (0.99-1.03)	.27	1.00 (0.99-1.02)	.60

Bold text indicates that the *P* value is significant ($P < .008$).

Logistic Regression Results for Prescription of Antipsychotic and Antidepressant

Variable	Any Antipsychotic		Any Antidepressant	
	OR (99.17% CI)	*P* Value	OR (99.17% CI)	*P* Value
Demographic characteristics				
Female	1.06 (0.59-1.89)	.80	1.82 (0.93-3.67)	.021
Age, y (ref = 45-59)				
60-64	1.44 (0.40-5.38)	.45	1.09 (0.25-4.82)	.87
65-74	1.02 (0.35-3.27)	.96	1.62 (0.52-5.84)	.29
75-79	1.23 (0.41-4.04)	.63	1.13 (0.34-4.28)	.80
80-84	1.09 (0.33-3.85)	.85	1.12 (0.29-4.62)	.83
≥85	1.76 (0.53-6.26)	.22	0.78 (0.13-4.04)	.69
Clinical information				
First consultation due to cognitive impairment	0.96 (0.48-1.87)	.88	0.80 (0.36-1.71)	.46
Subtype of dementia (ref = Alzheimer's disease)				
Vascular dementia	1.80 (0.83-3.84)	.043	1.22 (0.42-3.18)	.60
Frontotemporal dementia	1.14 (0.28-3.72)	.78	**5.06 (1.62-15.24)**	**<.001**
Other types of dementia	0.97 (0.37-2.37)	.94	2.21 (0.82-5.58)	.028
Severity of dementia (ref = mild dementia)				
Moderate dementia	1.26 (0.57-2.82)	.45	0.74 (0.32-1.66)	.32
Severe dementia	1.47 (0.55-3.97)	.30	0.61 (0.18-1.90)	.26
Independence level of daily living (ref = independent)				
Needing help with instrumental activities	1.42 (0.54-4.10)	.35	2.24 (0.83-6.73)	.040
Needing help with basic daily activities	1.38 (0.41-4.86)	.49	2.04 (0.52-8.36)	.17
Totally dependent	2.48 (0.65-9.87)	.08	2.63 (0.52-13.34)	.11
Neuropsychiatric symptoms				
Psychotic symptoms	**4.43 (2.46-8.18)**	**<.001**	0.84 (0.40-1.73)	.54
Agitation	1.60 (0.88-2.96)	.04	**2.19 (1.10-4.51)**	**.003**
Apathy	0.56 (0.30-1.04)	.014	1.59 (0.79-3.23)	.08
Depressive symptoms	1.23 (0.62-2.38)	.42	**4.00 (2.01-8.04)**	**<.001**
Caregiver characteristics				
Received training for dementia care	0.71 (0.18-2.22)	.46	0.14 (0.00-1.03)	.06
Caregiving burden	1.01 (0.99-1.03)	.14	0.99 (0.97-1.01)	.22

Bold text indicates that the *P* value is significant ($P < .008$).

Discussion

- 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.
  - *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.*

- The Chinese Society of Neurology issued a clinical guideline on dementia in 2010.
  - *Providing recommendations on the medication for Alzheimer's disease and other dementias.*

- However, to what extent clinical practice is consistent with the clinical guidelines remains unknown.

Zhang M. Guideline for Prevention and Management of Dementia. Beijing: Peking University Medical Press; 2007.
Jia J. Chinese Guideline for the Diagnosis and Treatment of Dementia. Beijing: People 's Medical Publishing House; 2010.

Discussion

1 Antidementia drug prescription was **adequate** and generally **guideline-oriented.**

2 The prescribing rates of psychotropic drugs and the co-prescription of antidementia and psychotropic drugs in well-established hospitals in China were kept **at a low level** and may be even lower than in western countries (35-82%).

3 **Pharmacotherapy** was mainly associated with the **clinical characteristics** of patients with dementia and was generally **consistent** with **the Chinese dementia guidelines.**

4 The study establishes very important **baseline evidence** on which future investigations on changes in prescription patterns can draw.
To better understand prescription patterns and factors associated with drug prescription, **longitudinal surveys are needed.**

Thank You

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Limitations

- *First, detailed clinical information associated with each prescription was not available.*

- *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.*

- *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.*