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The Shanghai Aging Study: Study Design, Baseline Characteristics, and Prevalence of Dementia

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Key Words
Aging, dementia · Epidemiological methods · Cohort study · Mild cognitive impairment · Prevalence rate · Neuropsychological tests

Abstract
Background: To establish a prospective cohort to enumerate the prevalence, incidence and risk factors for dementia and mild cognitive impairment (MCI) among residents aged ≥60 in an urban community of Shanghai, China. ***Methods:*** Participants received clinical evaluations including physical measurements, demographic and lifestyle questionnaires, physical and neurologic examinations, and neuropsychological testing. Urine and blood samples were collected, aliquoted, and stored. DNA was extracted for Apolipoprotein (APOE) genotyping. Diagnoses of dementia and MCI were made using standard criteria via consensus diagnosis. ***Results:*** Among 3,141 participants aged ≥60, 1,438 (45.8%) were men. The average age of participants was 72.3 years (SD 8.1), and they had an average of 11.6 years (SD 4.4) of education. The most common chronic disease of participants was hypertension (56.4%). The frequencies of APOE-ε2, ε3 and ε4 were 7.9, 82.7 and 9.4%, respectively. We diagnosed 156 (5.0%, 95% CI 4.3–5.8%) participants with dementia. The prevalence rates of Alzheimer's disease and vascular dementia were 3.6% (95% CI 3.0–4.3%) and 0.8% (95% CI 0.5–1.1%). ***Conclusions:*** The Shanghai Aging Study is the first prospective community-based cohort study of cognitive impairment in China, with a comparable study design, procedures, and diagnostic criteria for dementia and MCI to most previous cohort studies in developed countries.

Introduction

Dementia is progressive and eventually results in the need for constant care; therefore, it is one of the most burdensome diseases of the elderly in this aging society. According to a recent review of the global prevalence of dementia [1], the age-standardized prevalence of dementia for those aged ≥60 varied little: 5–7% in most world regions, with a higher prevalence in Latin America (8.5%), and a distinctively lower prevalence in the four sub-Saharan African regions (2–4%). The evidence base on the prevalence of dementia is expanding rapidly, particularly in countries with low and middle incomes. In 2012, there

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were 185 million Chinese over age 60 – the largest number of elderly people in any country in the world [2]. With a reported national prevalence of 6% [3], there are an estimated 7.4 million elderly currently living in China with dementia, and this number will grow to 18 million by 2030 if effective preventions are not identified and implemented.

Since there is currently no effective treatment for dementia, once symptoms are evident, early detection of a treatable preclinical phase is very important. Mild cognitive impairment (MCI) has been identified as an intermediate state between normal cognitive aging and dementia [4, 5]. Understanding the progression from a cognitively normal state to MCI, and from MCI to dementia is fundamental to the discovery of risk and predictive factors, and to seek effective intervention. To achieve this goal, researchers in western countries have established community-based cohorts and conducted prospective studies over the past 2 decades. However in China, studies have so far only focused primarily on enumerating prevalence. A community-based cohort in China is urgently needed to explore the incidence and risk or protective factors for cognitive decline in the elderly, by using a similar methodology, standard definitions and consensus diagnose comparable to leading western studies.

The number of people aged 60 and over in Shanghai was 3,673,200 in 2012, representing 25.7% of the city's population [6]. The Shanghai Aging Study was thus designed to establish a prospective community-based cohort aged 60 and over to examine: (1) the prevalence of dementia and prevalence of MCI; (2) the incidence of dementia and MCI; (3) conversion rates from MCI to dementia or normal cognition, and (4) risk and protective factors for these outcomes and their transitions. In the current report, we describe the rationale, study design, baseline characteristics of participants, and prevalence of dementia.

Materials and Methods

Study Site and Target Population

Jingansi community is located in the southwest part of downtown Shanghai, PR China. The target population lives in 11 neighborhoods with 5,138 registered residents aged 60 or older, according to the annual census at the end of 2009. Eligible study subjects were: (1) registered residents in this community; (2) ≥60 years; (3) without schizophrenia or mental retardation based on their medical records; or (4) able to communicate and accept physical and cognitive examinations.

This study was approved by the Medical Ethics Committee of Huashan Hospital, Fudan University, Shanghai, PR China. Written informed consent was obtained from all participants and/or their legally acceptable representative.

Subject Recruitment

Potential subjects were identified using a government maintained 'residents list,' which includes the name, sex, age, address, and telephone number of every resident. Before the study, coordinators went to each home in the community to introduce the study at the door. Individuals who were eligible and willing to participate were consecutively enrolled. Nonparticipants were logged and administered a refusal questionnaire. A clinical interview (either at Huashan Hospital or at the subjects' homes) appointment was made. A reminder telephone call was also made to the subjects one day before the interview.

As shown in figure 1, among 5,138 registered residents, 4,519 were eligible, and 3,141 (70%) wished to participate in the study. Among 1,378 non-participants, 1,286 (93%) answered the refusal questionnaire, including age, sex, education, history of hypertension, diabetes mellitus, stroke, heart disease, smoking and drinking habits.

Sample Size and Power Estimation

Based on published dementia prevalence rates ranging from 4–9%, and an estimated MCI prevalence of 15–30%, we estimated that approximately 120–270 persons would have prevalent dementia and 450–900 persons would have prevalent MCI in a population of 3,000 persons. The prevalence of dementia and MCI would be estimated with 95% confidence intervals (CIs) of approximately ± (0.7–1.0%) and ± (1.3–1.6%), respectively.

Physical Measurements and Blood Pressure

Participants were examined in the morning upon testing for fasting glucose, total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), and triglycerides (TG). A research nurse measured seated blood pressure twice and anthropometry (height and weight, seated height, hip, waist and head circumference). Body mass index (BMI) was calculated dividing the weight in kilograms (kg) by height in meters (m) squared. The BMI of ≥25 was defined overweight according to the WHO standard [7].

Demographic and Lifestyle Characteristics

Demographic and lifestyle characteristics of the participants were collected via an interviewer-administered questionnaire, consisting of the following measures: (1) personal demographic data, including birth date, sex, marital status, and number of formal years of education and education level; (2) childhood environment, including number of siblings, birth order, family income, and parental education; (3) lifestyle, including occupational history, physical exercise (during the adolescent period, around 50 years old and over the past 2 years), cigarette smoking, passive smoking, alcohol consumption, tea drinking, and dietary habits measured by a food frequency questionnaire (FFQ) [8]. In the FFQ, data were obtained regarding usual dietary intake over the past 12 months. The questionnaire was designed to capture information on the consumption of major nutrients as well as specific Chinese foods, such as soy foods, fermented foods, salted foods, allium-type vegetables, and leafy vegetables; (4) the Zung Self-Rating Anxiety Scale (ZSAS) [9] and the Center for Epidemiologic Studies Depression Scale (CESD) [10] were used to determine mood for each subject. Anxiety and depression were present if ZSAS >44 and CESD ≥16; (5) the Pittsburgh Sleep Quality Index (PSQI) was used to measure the sleep quality of the participants [11]; (6) the EQ-5D was used to measure

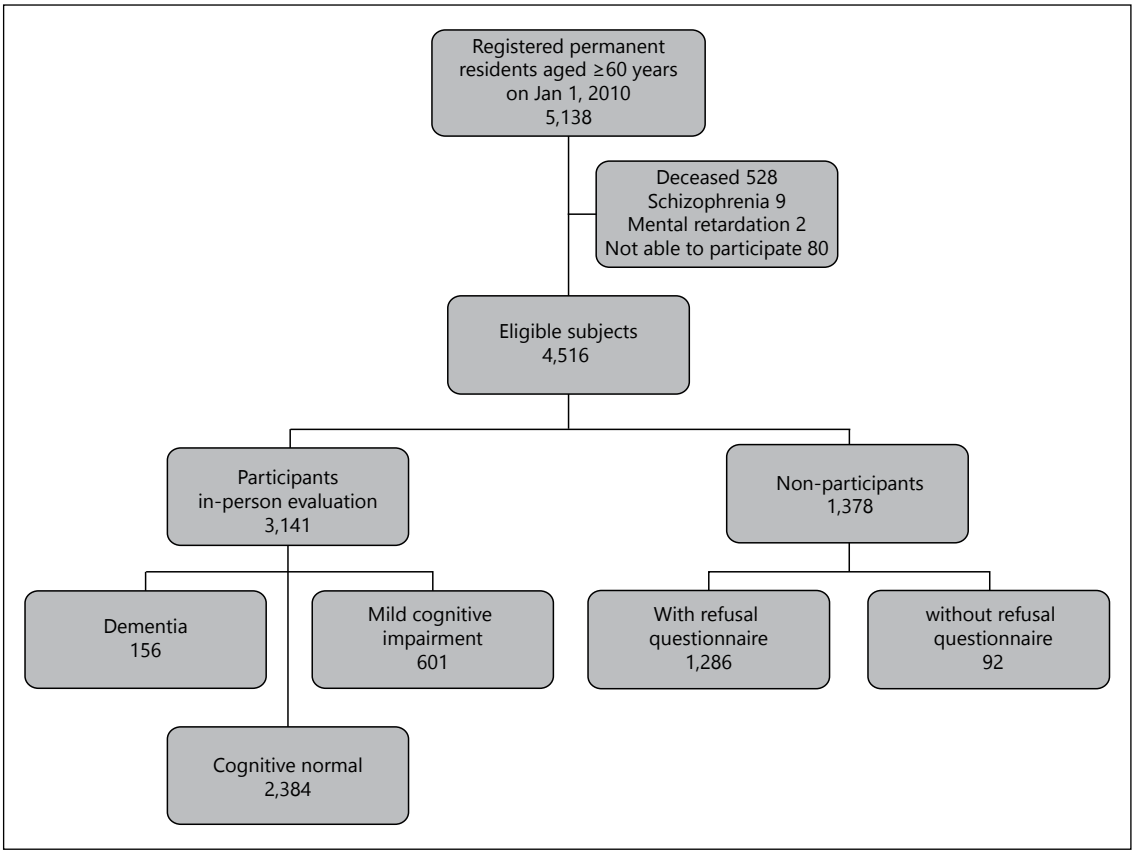

Fig. 1. Flowchart of subject recruitment for study subjects in the Jingansi community, residents aged 60 or over.

the health outcome of the participants [12]; (7) items from the Lawton and Brody Activity of Daily Living (ADL) scale-16 were used to elicit physical self-maintenance and instrumental activities of daily living, such as eating, using the telephone, preparing meals, handling money, and completing chores. Participants were considered to be functionally intact if the ADL score was over 16 [13].

Clinical Interview

Neurologists from the Department of Neurology, Huashan Hospital conducted clinical interviews for all participants. Participants were asked about their medical histories, defined by physician-diagnosed hypertension, diabetes, hyperlipidemia, stroke, head trauma, heart disease (including coronary heart disease, valvular heart disease, cardiomyopathy, heart failure, heart rhythm problems), reproductive history and hormone use (for women). Medications taken during the previous 2 weeks and during the previous year were recorded. Those subjects with a history of stroke were evaluated using the Modified Hachinski Scale [14]. The onset and subtype of stroke were queried, and the results of prior CT/MRIs were recorded. All the information was confirmed from the participants' medical records, maintained by them. An electrocardiogram was also conducted for each participant to detect undiagnosed heart disease.

The neurological examination included motor responses and reflexes for each participant. Subjects also were asked if their parents or siblings have or had been diagnosed with dementia or severe memory impairment. Neurologists administered the Clinical Dementia Rating (CDR) scale [15, 16] to a proxy and elicited memory complaints. Participants were considered to have memory complaints if they, or their proxy, a nurse or physician indicated that they had problems with memory or thinking.

Neuropsychological Battery

We translated, adapted and normed neuropsychological tests from western countries harmonized to Chinese culture, which cover the domains of global cognition, executive function, spatial construction function, memory, language, and attention. Tests used in the study were: (1) MMSE [17]; (2) Conflicting Instructions Task (Go/No Go Task) [18]; (3) Stick Test [19]; (4) Modified Common Objects Sorting Test [20]; (5) Auditory Verbal Learning Test [21]; (6) Modified Fuld Object Memory Evaluation [22]; Trail-making test A&B [23]; (8) Renminbi (official currency of China) Test, translated from the EURO test [24]. Tests (1) to (5) and (7) were used for subjects with less than 6 years of education, while tests (1) to (4) and (6) and (8) were used for subjects with at least 6 years of education. Normative data and detailed descriptions of these tests have been reported elsewhere [25]. The neuropsychological tests were administered by certified study psychometrists according to the education level of each participant. All tests were conducted in Chinese and took about 90 min.

Consensus Diagnoses

After each clinical assessment, study neurologists and neuropsychologists (DD, QZ, QG, HM, and ZH) reviewed the functional, medical, neurologic, psychiatric, and neuropsychological data and reached a consensus regarding the presence or absence of dementia using DSM-IV criteria [26]. Only those who were not diagnosed with dementia were considered for a diagnosis of MCI, which was defined according to Petersen's criteria [27]. We used NINCDS-ADRDA criteria to diagnose Alzheimer's disease (AD) [28]. We diagnosed vascular dementia (VaD) based on the clinical and radiological evidence of vascular diseases according to the NINDS-AIREN criteria [29].

Biological Sample Collection, Processing, and Storage

For each participant, who provided consent, a 20-ml spot urine sample was collected and aliquoted into 2 tubes with 10 ml urine each. A 12-ml fasting blood sample was drawn into 4 vacutainers. The first tube with 2 ml blood was sent to the hospital lab for biochemistry tests (fasting glucose, TC, LDL-C, HDL-C, and TG). The second serum tube with 4 ml blood was centrifuged, and 2 ml serum and 2 ml blood clot were aliquoted. The third tube with Ethylene Diamine Tetraacetic Acid (EDTA) and 4 ml blood was centrifuged, and 2 ml plasma and 2 ml red cells were aliquoted. All the aliquoted samples were stored at –80°C for future studies. The fourth tube with EDTA and 2 ml blood was stored at –80°C for DNA extraction. For those who refused the blood draw, a 10 ml mouth-rinse samples with saliva was collected and stored at –80°C for DNA extraction. The biologic sample repositories for the study are equipped with appropriate alarm system and emergency electricity backup to prevent accidental thawing.

APOE Genotype Assessment

DNA was extracted from blood or saliva samples, collected from 2,860 (91.1%) study participants. APOE genotyping was conducted by the TaqmanSNP method [30]. The presence of at least one ε4 allele was treated as being APOE-ε4 positive.

Statistical Analyses

Continuous variables are expressed as mean (SD), or median (25, 75%), and categorical variables as frequencies (%). The Student t test or one-way analysis of variance was used for comparisons for continuous variables. The χ^2 test was used for comparisons for categorical variables. The prevalence and 95% confidence intervals (CIs) for dementia, AD, and VaD were calculated for the entire population, as well as by sex, age group, education level and presence of an APOE-ε4 allele.

All p values and 95% CIs were estimated in a two-tailed fashion. Differences were considered to be statistically significant at $p \leq 0.05$. Data were analyzed using SPSS 13.0 (SPSS Inc., Ill., USA).

Results

Characteristics of Study Subjects

From January 1, 2010 through September 30, 2011, we conducted in-person interviews and clinical examinations for 3,141 participants. As shown in table 1, 1,438 (45.8%) were men, 1,373 (43.7%) and 1,191 (37.9%) were 60–69, and 70–79 years old. The average age of participants was 72.3 (SD 8.1). Participants had an average of 11.6 years (SD 4.4) of education, and the education level of the majority (67.6%) was at least high school. The majority (78.3%) was married, and only 9.4% of participants were currently living alone at home. Among all participants, only 63 (2.0%) experienced 'heavy labor' in their occupation. The average number of siblings was 3. Most (73.2%) participants grew up in a middle- or high-income family, and 37.0% of their father's education level was at least high school.

Also shown in table 1, the average BMI of participants was 24.4 (SD 3.5), and their average head circumference was 54.1 cm (SD 1.9). The average systolic and diastolic blood pressures measured on the interview day were 145.7 (SD 22.8) mm Hg and 76.3 (SD 12.9) mm Hg. The most common chronic disease of participants was hypertension (56.4%). Diabetes mellitus, stroke, and history of coronary heart disease were present in 14.6, 14.1 and 13.8% of the participants, respectively. In addition, only 9.5 and 7.9% of the participants were current smokers and alcohol drinkers. ZSAS and CESD scores showed that 2.2 and 15.1% of participants had anxiety and depression.

Urine samples were collected from 2,921 (93%) subjects. APOE genotype was missing for 281 (9%) of participants due to their refusal to be part of this study. The frequencies of the APOE-ε2, ε3 and ε4 alleles among 2,860 study subjects (with 5,720 APOE alleles) were 8.0, 82.7, and 9.3%, respectively (table 1).

Comparison of Participants and Nonparticipants

There was no statistical difference by sex or educational attainment between the 3,141 participants and the 1,286 nonparticipants (men: 48.8%, $p = 0.064$; years of education: mean 11.3, SD 4.7, $p = 0.975$). The average age of participants, however, was significantly younger than that of nonparticipants (mean 73.3, SD 8.6, $p = 0.012$) due to the higher proportion (43.7%) of participants aged 60–69 years, and lower proportion (18.4%) of participants aged 80 years or older. Besides a history of diabetes mellitus (14.9%, $p = 0.787$), nonparticipants were less likely to have hypertension (45.7%, $p < 0.001$), heart disease (20.9%, $p < 0.001$), and stroke (8.9%, $p < 0.001$).

Dementia Subtypes

Among 156 dementia cases, we diagnosed 93 (59.6%) cases with AD, 16 (10.3%) cases with AD combined VaD, and 4 (2.6%) cases with AD combined with other dementias. Twenty-five (16.0%) cases were diagnosed with VaD, and 8 (5.1%) cases were diagnosed as other types of dementia (table 2).

Table 1. Characteristics of the cohort by selected factors at baseline

	No. of subjects (n = 3,141)	%
Sex, men	1,438	45.8
Age group, years		
60–69	1,373	43.7
70–79	1,191	37.9
≥80	577	18.4
Age, years (mean ± SD)	72.3±8.1	
Education level		
Less than primary school	134	4.3
Primary school	301	9.6
Middle school	580	18.5
High school	978	31.1
College and above	1,145	36.5
Education, years (mean ± SD)	11.6±4.4	
Marital status		
Never married	39	1.2
Married	2,459	78.3
Divorced	45	1.4
Widowed	586	18.7
Unknown	12	0.4
Currently living alone at home	295	9.4
Labor level of ever employment		
Light	2,245	71.5
Moderate	742	23.6
Heavy	63	2.0
Unknown	91	2.9
Childhood family income		
High	793	25.2
Middle	1,508	48.0
Low	821	26.1
Unknown	19	0.6
Education level of father		
Less than primary school	584	18.6
Primary school	659	21.0
Middle school	633	20.2
High school	599	19.1
College and above	563	17.9
Unknown	103	3.3
Sibling number, median (25%, 75%)	3 (2, 5)	
Physical measurements, mean ± SD		
Body mass index, kg/m^2	24.4±3.5	
Head circumference, cm	54.1±1.9	
Systolic blood pressure, mm Hg	145.7±22.8	
Diastolic blood pressure, mm Hg	76.3±12.9	
Medical history		
Hypertension	1,771	56.4
Diabetes mellitus	459	14.6
Stroke	444	14.1
Coronary heart disease	433	13.8
Lifestyle habits		
Cigarette smoking	299	9.5
Alcohol drinking	247	7.9
Mental status		
Anxiety[a]	69	2.2
Depression[b]	474	15.1
Urine sample collected	2,921	93.0
Blood sample collected	2,860	91.1
APOE allele		
ε2	455[c]	8.0[d]
ε3	4,729[c]	82.7[d]
ε4	536[c]	9.3[d]

[a] Defined by the Zung Self-Rating Anxiety Scale >44.
[b] Defined by the Center for Epidemiologic Studies Depression Scale ≥16.
[c] Numbers of known APOE alleles (ε2, ε3 or ε4).
[d] Percentage of known APOE alleles among 5,720 APOE alleles obtained from 2,860 subjects.

Table 2. Case number and proportion of different dementia subtypes

Type of dementia	n (%)
Alzheimer's disease	93 (59.6)
Alzheimer's disease + vascular dementia	16 (10.3)
Alzheimer's disease + other diseases	4 (2.6)
Vascular dementia	25 (16.0)
Other types	8 (5.1)
Parkinson's disease dementia	4
Dementia with Lewybodies	1
Frontotemporal dementia	1
Traumatic brain injury dementia	1
Cognitive dysfunction due to epilepsy	2
Unknown	10 (6.4)

Prevalence of Dementia

Among 3,141 participants, 156 were diagnosed with dementia, resulting in a prevalence of 5.0% (95% CI 4.3–5.8%). As shown in table 3, the prevalence of dementia and AD, but not VaD, was significantly higher among women compared with men. The prevalence for dementia increased significantly with age ($p < 0.001$), and decreased significantly with increasing level of education ($p < 0.001$). Compared with the prevalence of VaD, the prevalence of AD increased more rapidly with age and decreased more rapidly with higher education level. The prevalence of AD was slightly higher among APOE-ε4 carriers (3.9%, 95% CI 2.5–6.1%) compared with non-carriers (2.5%, 95% CI 1.9–3.3%), but this difference was

Table 3. Prevalence and 95% confidence intervals for dementia, Alzheimer's disease, and vascular dementia by sex, age, education, and APOE-ε4 allele

	Dementia			Alzheimer's disease			Vascular dementia		
	n	% (95% CI)	p value	n	% (95% CI)	p value	n	% (95% CI)	p value
Total	156	5.0 (4.3–5.8)		113	3.6 (3.0–4.3)		25	0.8 (0.5–1.1)	
Sex									
Male	57	4.0 (3.0–5.0)	0.012	33	2.3 (1.5–3.1)	<0.001	13	0.9 (0.4–1.4)	0.530
Female	99	5.8 (4.7–6.9)		80	4.7 (3.7–5.7)		12	0.7 (0.3–1.1)	
Age, years									
60–64	6	0.8 (0.3–1.7)	<0.001	2	0.3 (0.04–1.0)	<0.001	3	0.4 (0.04–1.0)	0.001
65–69	4	0.7 (0.2–1.7)		2	0.3 (0.06–1.4)		0	0.0	
70–74	12	2.2 (1.2–3.9)		7	1.3 (0.6–2.7)		3	0.5 (0.1–1.7)	
75–79	40	6.3 (5.0–8.5)		29	4.6 (3.1–6.6)		8	1.3 (0.6–2.6)	
80–84	41	11.4 (8.4–15.2)		35	9.7 (7.0–13.4)		5	1.4 (0.5–3.4)	
≥85	53	24.5 (19.1–31.0)		38	17.6 (12.9–23.5)		6	2.8 (1.1–6.2)	
Education									
Less than primary school	33	24.6 (17.8–33.0)	<0.001	24	17.9 (12.0–25.7)	<0.001	6	4.5 (1.8–9.9)	<0.001
Primary school	33	11.0 (7.8–15.2)		29	9.6 (6.7–13.7)		4	1.3 (0.4–3.6)	
Middle school	24	4.1 (2.7–6.2)		18	3.1 (1.9–5.0)		5	0.9 (0.3–2.1)	
High school	30	3.1 (2.1–4.4)		18	1.8 (1.1–3.0)		5	0.5 (0.2–1.3)	
College and above	33	2.9 (2.0–4.1		22	1.9 (1.2–3.0)		4	0.3 (0.1–1.0)	
APOE-ε4 allele									
ε4(+)	24	4.7 (3.1–7.0)	0.137	20	3.9 (2.5–6.1)	0.076	3	0.6 (0.2–1.9)	0.823
ε4(–)	79	3.4 (2.7–4.2)		59	2.5 (1.9–3.3)		12	0.5 (0.3–0.9)	

APOE = Apolipoprotein; CI = confidence interval.

not significant (p = 0.076). The prevalence of dementia and VaD in subjects carrying one or two APOE-ε4 alleles was similar to non-carriers.

Discussion

The Shanghai Aging Study was designed as a prospective community-based study of cognitive impairment in elderly Chinese. This is an epidemiologic study conducted in China with a comparable study design, procedures, and diagnostic criteria of dementia and MCI to most previous cohort studies, such as the Sydney Memory and Ageing Study [31], the Kolkata Indian Study [32], the Leipzig Longitudinal Study of the Aged in Germany [33, 34], the Italian Longitudinal Study on Aging [35], the German Study on Ageing, Cognition and Dementia in Primary Care Patients [36], the Kungsholmen Project in Sweden [37], the North Manhattan WHICAP study [38], Cardiovascular Health Study [39], and the Mayo Clinic Study of Aging [40, 41]. It is also the largest prospective study in which all participants were evaluated by comprehensive epidemiologic, neurologic, and neuropsychological in-person assessments with consensus diagnostic criteria being applied to all participants. Our study will merge the gap of data, which is lacking in the Chinese population.

In Shanghai, there is an extensive government-sponsored infrastructure supporting the health and wellness of seniors. More and more seniors are coming to care about their physical and mental health and agree to participate in health-related projects. In our study, we obtained a 70% participation rate, comparable to many previous studies (62–78%) [40]. Seniors in Shanghai also have characteristics that are different from those of western populations. This is useful to examine the risk and protective factors for cognitive decline in the Chinese population. For example, many seniors grew up under difficult economic conditions, including limited opportunities for education that may have predisposed them to a higher risk of dementia. A large number of elderly regularly participate in group-based physical and social activities in the community. Physical exercises, such as Tai Chi and Qi Gong are widely performed by the elderly. The traditional Chinese diet, focused on tea, rice, and soy, also offers an opportunity to study the etiology of incident

memory disorders. Thus, we collected all of these data through a well-designed questionnaire, which took 1.5 h to complete.

Collection and aliquoting of blood and urine samples at baseline will also serve as an opportunity in our study, since we will be able to study the causal relationships between certain biomarkers and incident cognitive impairment in our study's incidence waves. The APOE-ε4 allele has been confirmed to be a strong risk factor of dementia in western studies. However, there is great ethnic variation in APOE frequencies. The frequency of the APOE-ε4 allele in our population is 9.3%, which is in the range of that in Asian (including Chinese) populations (6.3–9.3%) [42–44], but lower than that in Caucasian and African American populations (11–27%) [45]. Multivariate analyses did not explore the presence of APOE-ε4 as an independent risk factor of dementia. If APOE-ε4 has synergistic effects with other risk or protective factors for cognitive decline in the Chinese population, this necessitates our further study.

From the 1980's on, there have been a number of prevalence studies of dementia in the Chinese population [46–48]. These studies used a two-stage procedure, with cognitive screening using the MMSE and clinical evaluations in a subsample of individuals who failed the screening test. In the first study of dementia prevalence in China, Zhang MY et al. surveyed 5,055 people aged 55 years or older and demonstrated a dementia prevalence of 2.57% [17]. In late 1990's, Zhang ZX et al. surveyed 34,807 people aged 55 years or older in 4 populations around China and estimated the prevalence of dementia as 2.95% [3]. The two-stage procedure to enumerate prevalence has the advantage of decreasing personnel and time necessary to complete the study, but it may underestimate the prevalence when there is no sampling of screen-negatives to estimate the false-negative rate. In the late 2000's, Jia J et al. conducted a multicenter prevalence survey of dementia in 10,276 Chinese individuals, by using a one-stage procedure, which was the design that we have used in this study. The prevalence of dementia was 4.38% among 6,069 urban residents aged 65 and older [49]. Our study found a higher prevalence of 6.27% among 2,391 elderly aged 65 and older. Therefore, in addition to the one-stage procedure, the current study used more sensitive batteries to identify MCI cases, which may help to identify more early-stage dementia cases.

Clinical and radiologic evidence of cerebrovascular disease is necessary for the diagnosis of VaD. For those participants who had cerebrovascular events, we need to carefully evaluate the chronologic order of the event onset time and subsequent cognitive decline. If the subject or proxy cannot recall the information correctly, the diagnosis would be difficult. This might be the reason that 6.4% of dementias in our population were of the unknown type. Some subclinical cerebrovascular events, such as multiple lacunar infarcts and white matter lesions related to small vessel disease [50] may have a high prevalence among the elderly, but this cannot be known without a radiologic examination. For those who could not provide the image, text results of their prior CT/MRIs are not sufficient enough for the diagnosis of dementia subtypes. Not every subject in our study was able to be re-scanned due to limited funding; thus, some VaD cases might have been misdiagnosed as AD in our study.

In the current study, we excluded individuals who were not able to communicate, and who were living in nursing homes or institutions. This means that we could have missed some potentially severe dementia cases and underestimated the prevalence of dementia. Comparing with the national census, the prevalence of dementia in our study was estimated in a younger population with no institutionalized persons, a higher distribution of education, a good economic level, and good living environment. Therefore, the prevalence cannot be generalized to the whole Chinese population.

Individuals without dementia in our study cohort will be scheduled to be actively followed up during 2014–2016 by the same study team, and through the same evaluation procedure. Each of them will receive physical and neurologic examinations and neuropsychological testing. New onset of stroke, hypertension, diabetes, hyperlipidemia, stroke, head trauma, and heart diseases will also be recorded. Diagnoses of incident dementia and MCI (4 types) are made using standard criteria via consensus diagnosis.

Conclusion

The Shanghai Aging Study is the first prospective community-based cohort study of cognitive impairment in China, with a comparable study design, procedures, and diagnostic criteria for dementia subtypes and MCI to most previous cohort studies in developed countries. Further studies in our population will follow our population to examine the progression of disease states from cognitively normal to MCI, and from MCI to dementia and to identify risk factors and biomarkers for preclinical detection of incipient cognitive disorders.

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