

RESEARCH ARTICLE

Prevalence, Incidence, Risk and Protective Factors of Amnestic Mild Cognitive Impairment in the Elderly in Shanghai

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Abstract: Amnestic MCI (aMCI) has notably increased in Shanghai, China. This study was designed to estimate the prevalence and incidence rates of aMCI and to determine the risk and protective factors for aMCI among persons ≥ 60 years-old in Shanghai communities. This 1-year longitudinal study, which surveyed a random sample of 1,302 individuals ≥ 60 years-old, collected baseline data about lifestyle through self-reports, and vascular and comorbid conditions from medical records and a physical examination. We also analyzed a subgroup of individuals ≥ 70 years-old. The prevalence rate of aMCI in persons ≥ 60 years-old was 22.3%, and the incidence rate (per 1,000 person-years) was 96.9. Being female was a risk factor for aMCI; protective factors included smoking, drinking tea, engaging in intellectual work before retirement, social activities and hobbies, regular reading habits, and surfing the internet. The prevalence rate of aMCI in persons ≥ 70 years was 30.3%, and the incidence rate was 145.6. Smoking, drinking tea, and surfing the internet were not protective factors for this age group (≥ 70 years). The present study indicates that aMCI is a considerable health problem in Shanghai. Preventive strategies for aMCI are needed to enhance lifestyle factors that promote brain activity.

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INTRODUCTION

Improving health conditions have led to substantial increases in life expectancy in China. The resultant aging of China's population will inevitably lead to an increased prevalence of various cognitive impairments, such as Alzheimer's disease (AD) [1]. The negative social consequences of these diseases are greater in cities like Shanghai, than in many other areas, as they have much larger elderly populations [2].

Several studies reported in 2014 that AD occurs in 3%-5% of persons aged 60 years and older and 20% of those aged 80 years and older [3, 4]. A recent meta-analysis summarizing studies on dementia that were conducted in China between 1980 and 2010 found that the prevalence of dementia was 3% among people who were at least 60 years of age, and 6% among those who were at least 65 years of age, which is somewhat lower than the prevalence reported in

developed countries [5]. A conservative estimate is that there are six million individuals currently living with AD in China, and this number is projected to reach 10 million by 2050 [5]. Dementia and cognitive impairment are already among the most significant causes of disability and death among China's elderly [5]. Amnestic mild cognitive impairment (aMCI) is generally accepted to include prodromal Alzheimer's disease (AD), as studies suggest that the majority of aMCI progress to AD [6, 7]. In contrast to the relatively recent studies of China as a whole, regional reports of cities, such as the city of Shanghai, are rare. In 1990, we reported that the prevalence rate of dementia in persons 65 years and older was 4.6%, and a clinical diagnosis of AD accounted for 65% of the patients with dementia in Shanghai, China [2]. As more than 20 years have elapsed, the data probably should be updated.

Overall, to the best of our knowledge, reports on aMCI, especially in Shanghai, have not been well documented in the literature, even though it is the one of the largest cities with the largest elderly population since 1990. Early detection of prodromal conditions is critical for the prevention and treatment of dementia [8]. Unfortunately, however, relatively little research has been conducted on prodromal conditions

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in China overall, or in Shanghai. This report describes the prevalence and incidence rates of aMCI and risk and protective factors for aMCI with the aim of providing early detection and more accurate estimates of aMCI in Shanghai, China, including urban and rural areas.

METHODS

Cross-Sectional and One Year Follow Up Survey

Four sites in Shanghai were pre-selected to participate in this research, which lasted from May 2011 to May 2012 [9]. The sites were the Huangpu, Changning, Putuo and Pudong districts, which represent urban and rural areas as a whole in Shanghai. The main coordination center (Shanghai Jiao Tong University School of Medicine, Shanghai Mental Health Center) randomly selected samples from each of these four districts using the simple random procedure in the Statistical Package for the Social Sciences version 11.0 (SPSS 11.0). The sampling rate was 10% for each selected community according to the data of Chinese census in 2010. Participation was voluntary and a informed consent form was obtained from each person who was recruited and agreed to take part in the survey.

All participants underwent a screening process that included a review of their medical history, physical and neurological examinations, laboratory tests, and MRI scans. The following data were collected from each survey participant: general demographic information (including name, gender, date of birth, home address, zip code, home phone number, ethnicity, years of education, current occupation, occupation before retirement [if retired], and permanent residence); and information about daily living (including hobbies, dietary preferences, sleeping patterns, smoking history, consumption of alcohol and tea, and physical activities). Several psychological and psychosocial assessments were performed by a psychologist: the Mini-Mental State Examination (MMSE) [10], the Montreal Cognitive Assessment (MoCA) [11], the Neuropsychological Test Battery [12] (include Wechsler Memory Scale (WMS) Verbal Associates immediate and 30-minute delayed test and digit span and picture completion, Rey Auditory Verbal Learning and 30-minute Delayed Test [2], Category Naming Test-vegetable, Clock Drawing Test, etc), and the Geriatric Depression Scale [13]. Attending psychiatrists collected information on the current and past history of diseases from each participant, conducted physical examinations, evaluated functioning, and determined diagnoses using: the Activities of Daily Living scale [14], the Clinical Dementia Rating scale [15], the Global Deterioration Scale [16], and the Hachinski Ischemia Scale [17].

Two diagnostic methods were used in this study. Clinical assessments classified participants as having or not having aMCI. The diagnostic results were used to estimate the prevalence of aMCI in the Shanghai elderly population. A diagnosis of aMCI was based on the following criteria, which were adapted from the MCI diagnostic criteria of Petersen [6]: 1) memory complaints, preferably corroborated by a spouse or relative; 2) objective memory impairment; 3) normal general cognitive function; 4) intact activities of daily living; and 5) absence of dementia. The MMSE cut-off score was adjusted to account for the low level of education of elderly Chinese people. Previous research using the Chi-

nese version of the MMSE [18] diagnosed AD patients as persons whose MMSE scores were below 18, 21 or 25, if they had no education, an elementary school education, or a middle school or higher education, respectively. A diagnosis of aMCI in the present study was characterized by MMSE scores higher than, or equal to, 18, 21 or 25 for participants who had no education, an elementary school education, or a middle school or higher education, respectively. We rated the MCI patients' cognitive impairment in seven domains: memory, attention, language, visual-spatial, orientation, calculation and executive function according to the neuropsychological battery and MMSE. Based on the assessment, we retained aMCI subjects and others were excluded such as those who had impairment in a single non-memory domain (single, non-memory domain MCI subtype) and those who had impairment in two or more domains (multiple domains, slightly impaired MCI subtype).

All of the tests described above for the baseline data also were conducted for those individuals who agreed to continue their participation with the one year follow up visit.

Data Analysis

We merged the sample of rural and urban to the whole. The sample should present the characteristic of Shanghai population. The prevalence rate of aMCI was determined by dividing the total number of cases diagnosed at baseline by the total number of participants (expressed as percentages). Incidence rates for aMCI, expressed as the number of cases per 1,000 person-years (Py), were obtained by dividing the number of newly diagnosed cases at the one year followup visit. The risk and protective factors of aMCI were analyzed by logistic regression. We used the Statistical Package for the Social Sciences version 11 to take the analysis in the study. It has significant difference when P value was less than 0.05 ($p < 0.05$).

RESULTS

Fig. (1) shows the flow diagram of the study. A total of 2,720 individuals age 60 years-old or older (out of 4,530) were randomly selected, based on the 2010 national census of persons living in the four neighborhoods, and contacted for this survey. Of these, 1,302 agreed to participate. Among them, 1,005 (77.2%) completed the baseline survey from April 2011 to July 2011 and their data were complete and valid. A followup was conducted one year later, from April 2012 to July 2012. Of the 1,005 original participants, 513 (51.4%) completed the survey at the one year follow-up and their data was complete and valid. Among the non-respondents, 329 refused to continue their participation, 152 could not be located, and 11 died (4 from Pneumonias, 3 from Cerebrovascular Diseases, 2 from Myocardial Infarction, 1 from Diabetes Complications, and 1 from Renal Failure).

The demographic characteristics of the entire baseline cohort are given in Table 1. There were no significant differences in the mean age of the males and females in total sample, or in the separate age groups, which were stratified by 10-year increments. However, there was a significant gender difference in education in all the groups. The number of years of education was significantly greater in males than in

females ($p < 0.001$). There was no significant difference between males and females on MMSE scores in the 60–69 year age group ($p = 0.203$). The age subgroups revealed significant differences between males and females for both MMSE and MoCA scores ($p < 0.001$). MoCA scores were significantly different between males and females in the entire sample: 60–90 years of age ($p < 0.001$). The MMSE and MoCA scores declined steadily across age: 60-69, 70-79, 80-89, and >90 years (Table 1).

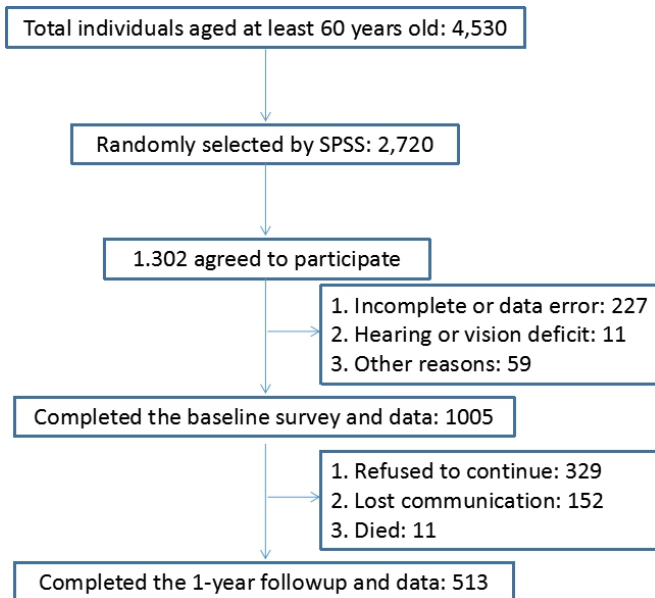


Fig. (1). Flow chart of the study.

The overall prevalence of aMCI was 22.3% (224/1,005) in persons age 60 and older and 30.3% (182/600) in persons age 70 and older (Table 2). The incidence rate (per 1,000 Py) of aMCI was 96.9 (31/320) in persons age 60 and older and 145.6 (30/206) in persons age 70 and older.

Female gender predicted aMCI (OR 2.26, $p < 0.001$) in participants who were 60 years-old or more. The risk of aMCI was reduced for participants who reported smoking (OR 0.54, $p = 0.002$), drinking tea (OR 0.59, $p = 0.002$), engaging in intellectual work before retirement (OR 0.38, $p < 0.001$), social activities and hobbies (OR 0.57, $p < 0.001$), regular reading habits (OR 0.34, $p < 0.001$), and surfing the internet (OR 0.24, $p = 0.010$). In participants who were age 70 years or older, predictors of aMCI were female gender (OR 2.13, $p < 0.001$) and parahypnosis (OR 2.90, $p = 0.028$). The risk of aMCI was reduced for participants who reported engaging in intellectual work before retirement (OR 0.39, $p < 0.001$), social activities and hobbies (OR 0.60, $p = 0.007$), and reading (OR 0.40, $p = 0.005$) (Table 2).

DISCUSSION

Our report presents the results of a longitudinal study that examined the prevalence and incidence rates of aMCI and risk and protective factors for aMCI in a population of community-dwelling elderly persons in Shanghai, China. The study revealed several interesting findings: 1) There was a very high prevalence of aMCI in persons age 60 and older, and the prevalence increased with age; 2) The incidence rate

(per 1,000 Py) of aMCI was high in persons age 60 years or older, and the incidence increased with the age; and 3) Being female was a stable risk factor for aMCI. Engaging in intellectual work before retirement, social activities and hobbies, and reading were stable protective factors for aMCI. Though smoking and drinking tea were protective factors for aMCI among individuals who were age 60 or more, these protective effects disappeared among individuals who were age 70 or more. Surfing the internet was more important as a protective factor for people who were 60-69 years-old than for people who were 70 years-old or more. The results also found that sleep quality can influence the cognitive functioning in the elderly who are 70 years of age or older.

Though the observed rates are similar to the rates reported in some studies, our estimate of the overall prevalence rate of 22.3% for aMCI in this population (60 years of age or older) was higher than what found in other studies [19-21]. Two studies reported that the prevalence rate of a MCI caused by prodromal Alzheimer's disease (MCI-A) was 6.1% in persons aged 65 years or older in 2014 [3] and the rate of aMCI was 13.2% in community residents ≥ 60 years of age in 2015 in China [22]. A 2001-2002 Australian study, which included 2,551 initial participants age 60-64 years-old (2,222 of whom finished the survey), found a prevalence rate of 12.9% for mild neurocognitive disorders and 7.3% for other cognitive disorders. The prevalence rate of a diagnosis of any mild cognitive impairment was 29.5% [23, 24]. We think the prevalence of MCI was underestimated in some of these studies. We suspect that the reason for the disparity in prevalence rates is probably associated with the aMCI diagnosis criteria used. The prevalence rate varies considerably (up to six-fold), according to the diagnostic criteria applied, with limited overlap between diagnoses. But this limit was also exist in our own study and our own criteria because we lacked the pathological diagnosis in the cognitive related epidemiology study. This finding emphasizes the need for standardization of the criteria. In spite of these disparities, the findings of the current study, nevertheless, suggest the seriousness of aMCI among the elderly in Shanghai.

This is the first study to report the incidence rate of aMCI in Shanghai. In the Shanghai community, the incidence of aMCI was 96.9 per 1,000 Py for individuals age 60 and over. This result is similar to the rate of 90.91 per 1,000 Py reported by De Deyn [25]. In the other studies, the incidence rates of aMCI or MCI ranged between 11.4 and 76.8 per 1,000 Py [26-30]. These variations in incidence rates might result from differences in study characteristics, like the age of the sample or the criteria used for diagnosing aMCI and MCI, and their operationalization. The incidence rate of aMCI may indicate a more serious problem among the elderly in Shanghai than in other regions of the world.

Earlier research that analyzed the effect of higher cognitive activity on the incidence of aMCI identified it as a protective factor [31]. The present study also found that engaging in intellectual work before retirement is a protective factor against suffering from aMCI. Although hypertension has been identified as a possible risk factor [27, 30], vascular and hypertension factors were not found to be the risk factors in our research because these factors are probably risks for vascular MCI or dementia. The number of cigarette packs

Table 1. Baseline demographic characteristics of all participants.

Parameter	All	Male n = 419 (41.7%)	Female n = 586 (58.3%)	P value	60–69 years			70–79 years			80–89 years			90+ years		
					Male (n = 189)	Female (n = 209)	P value	Male (n = 140)	Female (n = 221)	P value	Male (n = 84)	Female (n = 130)	P value	Male (n = 9)	Female (n = 16)	P value
Age (years)	72.72±8.46	72.22±8.43	73.07±8.46	0.117	64.22±2.78	63.97±2.74	0.359	75.04±2.81	74.83±2.82	0.505	83.25±2.79	83.08±2.51	0.638	91.22±1.48	92.06±2.49	0.367
Education	7.64±4.85	9.40±4.40	6.40±4.77	<0.001	10.56±3.54	9.39±3.04	0.001	9.13±4.76	5.66±4.89	<0.001	7.35±4.54	2.89±3.91	<0.001	9.56±5.77	2.86±4.17	0.004
MMSE	24.70±6.12	26.06±5.48	23.73±6.37	<0.001	27.91±3.33	27.51±2.88	0.203	26.02±4.95	23.50±5.56	<0.001	22.54±7.60	18.80±7.03	<0.001	21.11±7.41	15.25±9.21	<0.001
MoCA	20.66±7.28	22.46±6.54	19.39±7.51	<0.001	25.20±4.37	24.24±4.48	<0.001	22.00±6.21	18.58±6.90	<0.001	18.02±7.72	13.57±6.99	<0.001	14.78±6.89	11.38±8.53	<0.001

MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment

Table 2. Risk and protective factors for aMCI in the elderly age 60 years-old or more and 70 years-old or more.

Characteristics	60 years-old or more (aMCI 224, non-aMCI 781)			70 years-old or more (aMCI 182, non-aMCI 418)		
	OR	95% CI	P value	OR	95% CI	P value
General characteristic and living habit						
Gender (women)	2.26	1.63-3.13	<0.001	2.13	1.46-3.12	<0.001
Engaged in intellectual work before retire	0.38	0.27-0.55	<0.001	0.39	0.25-0.60	<0.001
Smoking history	0.54	0.36-0.80	0.002	0.63	0.39-1.02	0.060
Exercise history	0.86	0.63-1.17	0.335	1.35	0.94-1.96	0.108
Hobby avocation	0.57	0.42-0.78	<0.001	0.60	0.41-0.87	0.007
Reading	0.34	0.20-0.58	<0.001	0.40	0.21-0.77	0.005
Music	0.92	0.58-1.47	0.737	1.25	0.69-2.26	0.469
Painting and calligraphy	0.48	0.14-1.62	0.226	0.56	0.12-2.68	0.465
Chess and cards	1.18	0.72-1.94	0.504	1.08	0.60-1.96	0.792
Surf the internet	0.24	0.07-0.77	0.010	0.31	0.07-1.36	0.101
Photograph	0.48	0.17-1.38	0.163	0.21	0.03-1.62	0.098
Fishing	0.90	0.25-3.24	0.876	1.25	0.31-5.12	0.756
Tai Chi	1.65	0.92-2.96	0.089	1.71	0.86-3.40	0.123
Siesta in Youth (18-44 years)	1.50	0.99-2.28	0.058	1.57	0.94-2.62	0.082
Siesta in Middle age (45-59 years)	1.33	0.90-1.97	0.150	1.52	0.95-2.43	0.078
Siesta in Old age (60 years old above)	1.12	0.83-1.52	0.450	0.85	0.60-1.21	0.359
Nutrition						
Drinking history	0.80	0.51-1.22	0.295	0.88	0.52-1.47	0.611
Drink tea history	0.59	0.43-0.82	0.002	0.72	0.49-1.07	0.102
Food fish	0.74	0.49-1.14	0.172	0.86	0.53-1.39	0.538
Abnormal diet	1.12	0.50-2.52	0.786	0.51	0.06-4.56	0.543

(Table 2) contd....

Characteristics	60 years-old or more (aMCI 224, non-aMCI 781)			70 years-old or more (aMCI 182, non-aMCI 418)		
	OR	95% CI	P value	OR	95% CI	P value
Mood or sleep disorder						
Anxiety	1.35	0.47-3.88	0.579	1.08	0.27-4.25	0.915
Depression	1.49	0.93-2.37	0.094	1.38	0.80-2.38	0.248
Life events	0.61	0.61-1.22	0.401	0.90	0.56-1.44	0.660
Parahypnosis	1.09	0.68-1.49	0.968	0.35	0.13-0.93	0.028
Medical						
Hypertension	0.97	0.72-1.31	0.828	0.92	0.46-1.31	0.639
Heart disease	1.07	0.75-1.53	0.718	0.85	0.57-1.28	0.432
Endocrine and metabolic diseases	0.93	0.62-1.39	0.709	0.98	0.63-1.54	0.936
History of cerebral trauma	0.59	0.20-1.71	0.322	0.16	0.02-1.23	0.045
Handedness	1.17	0.37-3.68	0.784	0.39	0.05-3.22	0.360

Note: Values in bold-faced type indicate statistically significant differences. OR: Odd Ratio. Drinking history means drinking alcohol more than average 20 grams per day. Exercise history means exercising more than 20 minutes per day. Hobby avocation was to do some things more than average 30 minutes per day to help their own physical and mental health in spare time. Reading and photograph were more than 20 minutes per day average, respectively. We used the Life Event Scale to access the life events. Abnormal diet refer to the drinking and eating irregularly. Parahypnosis refers to an abnormal or disordered sleep.

smoked per year failed to be a significant risk factor [32], even though it is known that smoking is a risk factor for cardiovascular and cerebrovascular diseases. Smoking probably had a protective effect in the elderly 60 years-old or more in the current study because of the cholinergic effects of nicotine.

Several epidemiological studies have examined the association between smoking and risk of AD [33-37], but the findings have been inconsistent. Some case-control studies reported an inverse association between smoking and AD, whereas most population-based prospective studies have reported that smoking is a risk factor for the development of AD [35, 36]. One study revealed a positive association between smoking levels and the risk of AD [34], whereas another study, which included prevalent and incident cases of dementia, found no clear association between them [37]. It is known that oxidative damage accumulation caused by smoking may affect the development of dementia through neurodegenerative and vascular pathways. Smoking also may increase the risk of dementia by mediating cerebrovascular risk factors. As mentioned above, there is a possibility that smoking increases the risk of vascular dementia by mediating cerebrovascular risk factors. In sum, even though we found smoking was a protect factor of aMCI in the elderly age 60 or older, it does not provide much benefit for the elderly. The protect effect of smoking disappeared in the elderly who were 70 years-old or more.

Our study found that drinking tea, social activities and hobbies, reading, and surfing the internet were important lifestyle factors that can protect the people age 60 years and older against aMCI. There is accumulating evidence from epidemiological studies that consumption of beverages or foods enriched with polyphenols is related to a lower risk of

dementia, such as AD; green tea (2 cups per day) can reduce the risk of dementia and cognitive impairment up to 50% [38]. This evidence is corroborated by animal studies showing that peripheral administration of epigallocatechin gallate reduces cognitive impairment and A β /tau pathology in Alzheimer transgenic mice and in mice treated with an intracerebroventricular injection of A β [39-42].

A higher level of brain activity also has been found to be associated with a decreased risk for incident AD [43]. Nearly all people over 60 years of age have disrupted sleep patterns and decreased slow wave sleep, which is critical for the appropriate consolidation of long-term memory. Furthermore, aging is associated with regional brain atrophy in midline frontal lobe regions that are associated with cognitive decline [44, 45]. A recent study showed that these factors may be linked, since age-related atrophy of the gray matter of the medial prefrontal cortex (mPFC) is associated with reduced Non-REM slow wave activity (SWA), which appears to statistically account for the impairment of overnight sleep-related memory consolidation. Together, these results support a model in which age-related mPFC atrophy decreases SWA, which disrupts long-term memory consolidation. Such findings suggest that sleep disruption in the elderly, accompanied by structural brain changes, represents a contributing factor for age-related cognitive decline in older individuals [46]. Sleep is also thought to serve a variety of physiological functions, including the restoration of tissues and brain-metabolite clearance.

Smoking, drinking tea, and surfing the internet were not the protective factors for aMCI in the participants who were 70 years of age or older. However, reading was still a protective factor in this group. Greater brain activity, such as en-

gaging in intellectual work before retirement and reading are important for older persons to avoid aMCI.

Women seem to be affected more often by dementia than men are [47]. Our research found that the prevalence of aMCI was higher in females than males for all age groups, which seems to be inconsistent with an explanation that the gender difference in prevalence reflects the slow progression of dementia combined with the longer life expectancy for women [48]. Our data, in contrast, seem to support the notion that the higher prevalence of aMCI in females was mainly associated with their lower educational level. As shown in our study, the educational level was lower in females than males for all age groups. However, some findings regarding gender are consistent with those from many prevalence studies showing a lack of association between gender and prevalence of MCI [32, 49]. Cognitive performance, as assessed by the MMSE, steadily decreased with increasing age among participants in the present study. In fact, we found that the mean MMSE scores declined slowly with increasing age. Our results are consistent with the empirical finding that the proportion of the elderly with cognitive impairment increases with age.

In summary, the overall prevalence of aMCI is high among people age 60 years or older in Shanghai. Particular attention has to be paid to the prevention of aMCI in females. Engaging in intellectual work before retirement, hobbies and other avocations, and reading are stable protective factors of aMCI. Promoting intellectual activity is important for preventing aMCI in the elderly of all ages. Sleep quality can protect brain function and influence cognitive function in the elderly who are above 70 years-old. As dementia is the most common medical condition leading to institutionalization of the elderly, homecare services and informal caregivers should be provided with the necessary support to prevent the need for institutional care. Based on our findings, an increasing number of elderly individuals will be affected by aMCI in the future; thus, the government should take steps to address these issues.

CONCLUSION

The present study supports the view that aMCI - majority progress to the AD - is a considerable health problem. Special attention should be given to preventing the development of new cases of aMCI or to postponing the occurrence of its symptoms. Promoting intellectual activity and sleep quality are probably effective methods of prevention.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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Shifu Xiao designed and was responsible for the study. Tao Wang carried out the research, statistical analysis, and drafted the paper, while Shifu Xiao supervised the data collection, statistical analysis, and modified the paper. Kewei Chen supervised the statistical analysis and modified the paper. Cece Yang, Shuhui Dong, Yan Cheng, Xia Lia, Jinghua Wang, Minjie Zhua, Fuzhong Yanga, Guanjun Lia,

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