ORIGINAL CONTRIBUTION

Dementia Subtypes in China

Prevalence in Beijing, Xian, Shanghai, and Chengdu

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Background: Prevalences of Alzheimer disease (AD) and vascular dementia (VaD) in China reportedly differ from those in Western countries.

Objective: To estimate prevalence of AD and VaD in 4 regions of China.

Design: Cross-sectional, population-based prevalence survey with a stratified, multistage cluster sampling design.

Setting: Rural (n=99) and urbanized (n=71) communities of Beijing, Xian, Shanghai, and Chengdu.

Participants: A sample of 34 807 community residents (94% of those eligible) 55 years or older.

Main Outcome Measures: Participants were screened with the Chinese Mini-Mental State Examination. Those who screened positive (n=3950) underwent a standardized diagnostic workup. Screening sensitivity was assessed in a 3.3% random sample (n=1008 of the 30 857 who passed the screening). Diagnoses of AD and VaD were made according to National Institute of Neurological and Communicative Diseases and Stroke–Alzheimer Disease and Related Disorders Association and National Institute of Neurological Disorders and Stroke–Association Internationale pour la Recherche et l'Enseignement en Neurosciences criteria, respectively. Final diagnoses were made after a 6-month confirmation interval.

Results: We identified 732 AD cases and 295 VaD cases. Prevalence in persons 65 years or older was 3.5% (95% confidence interval, 3.0%-3.9%) for AD and 1.1% (95% confidence interval, 0.9%-1.1%) for VaD. After post hoc correction for negative screening errors, prevalence increased to 4.8% for AD and remained at 1.1% for VaD.

Conclusion: Prevalence of dementia subtypes in China is comparable with that in Western countries.

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REPORTED PREVALENCES OF Alzheimer disease (AD) and vascular dementia (VaD) in east Asia differ from those in Western countries.[1-7] Whereas AD predominates in Europe and North America, an excess of VaD over AD has been observed in Japan and northern China.[4,6] Although methodologic factors such as completeness of case ascertainment could explain this variation, some investigators believe that the underlying risk factors for AD and VaD differ in east Asia.[7,8]

To better characterize the epidemiologic patterns of AD and VaD, we conducted a population-based prevalence survey in urban and rural communities of 4 major regional centers in China by using extensive case ascertainment procedures.

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METHODS

STUDY AREAS AND SAMPLING

In 1997, we studied 4 regional centers: Beijing (northeast), Xian (northwest), Shanghai (southeast), and Chengdu (southwest) (**Figure 1**). These regions encompass 34 urban districts and 36 rural counties with a 1994 population of 39.6 million. Northern China has marked differences in geography, climate, diet, and culture from the south. Eastern China is more developed economically than the west of China.[9]

The target population included all eligible residents 55 years or older in 1997 living in the selected regions. Eligible persons were listed in the updated 1996 population census of community registry offices including those in nursing homes or residing with registered first-degree relatives.

A stratified, multistage, cluster sampling design was adopted. A random sample of 14 urban districts and 19 rural counties was se-

Figure 1. Map of China.

lected from the study regions. Within selected counties or districts, a random sample of urbanized sectors (n=37) and rural townships (n=53) was chosen, and finally 76 urban and 106 rural communities were randomly sampled.

FIELDWORK TRAINING

A total of 63 interviewers were recruited from the 4 regions, including university-hospital neurologists, psychiatrists, and medical students, of whom the majority were senior and attending clinicians. Regional team supervisors received 1 week's training in Beijing and 1 week of community practice before training fieldworkers at regional sites. Retraining was held every 6 months. All fieldworkers completed pilot interviews in a nonsampled community in their region. Interviewers' interrater reliability for the Chinese Mini-Mental State Examination (C-MMSE)[10] and other cognitive tests exceeded 0.90 with videotaped interviews. Throughout fieldwork, the principal investigator (Z.-X.Z.) and supervisors monitored interviews on site.

INFORMED CONSENT AND RECRUITMENT

Participation was voluntary, with multilevel approvals by survey hospitals and community leaders. Before interviews, informational flyers were posted and community meetings were held. Eligible residents were encouraged to participate but were free to refuse. To minimize sample attrition, household visits were repeated at least 3 times for persons temporarily away or in nursing homes.

DIAGNOSTIC ASSESSMENT

We used community-based, multiphase assessments for case ascertainment (**Figure 2**).

Phase 1: Dementia Screening

A door-to-door screening survey was conducted by trained clinical interviewers. All participants were administered the C-MMSE, Activities of Daily Life,[11] demographic questionnaire, personal and medical history, dementia family history (first-degree relatives), and a brief physical and neurologic examination.

In a study completed in 1997, we established optimal C-MMSE screening cutoff points in a population-based pilot study in Beijing.[10] The cutoffs were the lowest 10th percentile for each educational group: 19 points or less for uneducated, 22 or less for those with 6 or fewer years of education, and 26 or less for

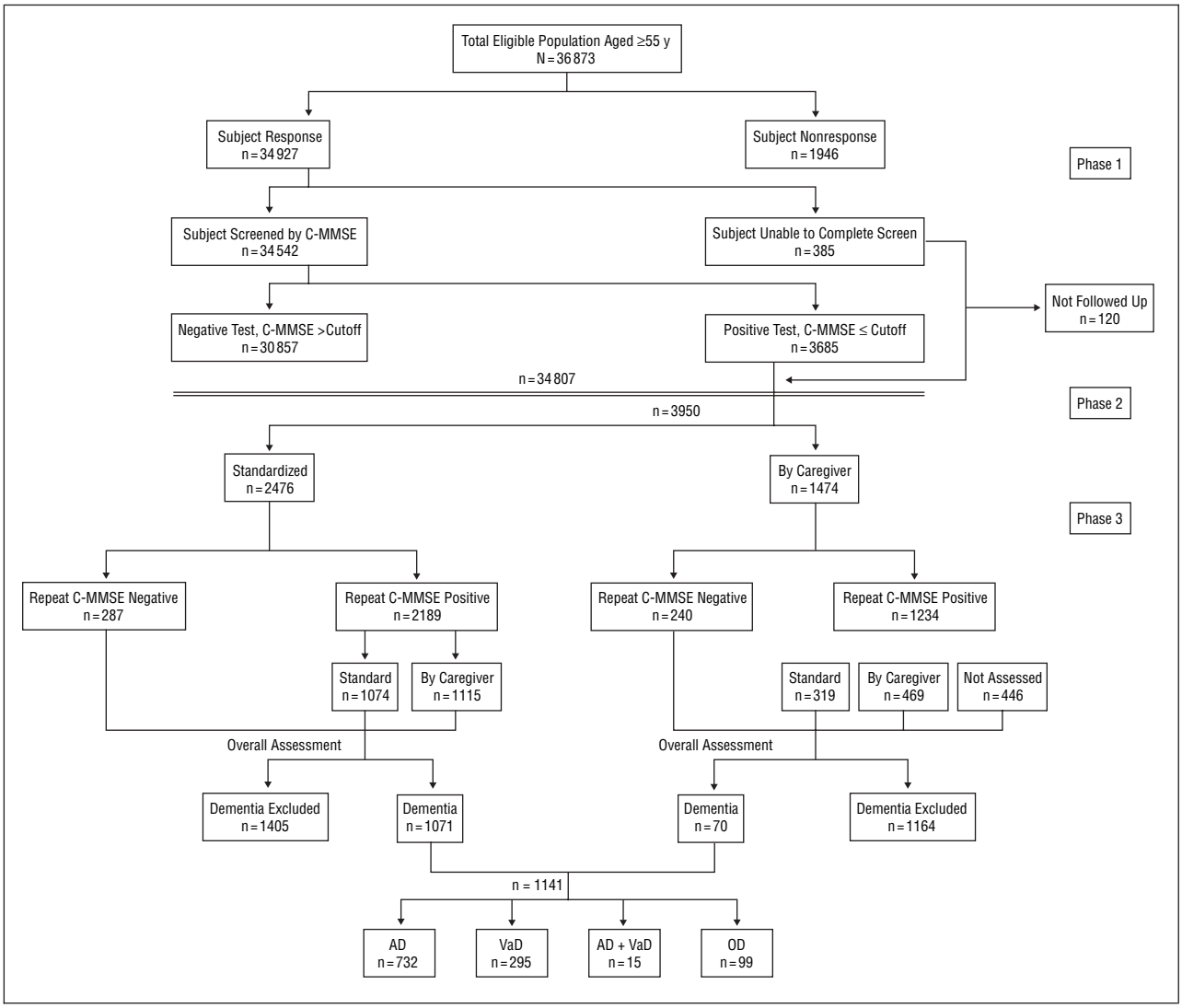

Figure 2. Flow chart of dementia assessment procedures. C-MMSE indicates Chinese Mini-Mental State Examination; AD, Alzheimer disease; VaD, vascular dementia; and OD, other types of dementia. For phases 2 and 3, the percentage traced was 88.7% ([2476+319+469+240]/3950); not followed up, 11.3% (446/3950); screened by caregiver, 11.9% (469/3950); and screened by standardized screening, 70.8% ([2476+319]/3950).

those with 7 or more years of education. Screening validity was confirmed in 76 demented patients and 1878 nondemented urban subjects (sensitivity, 90.8%; specificity, 93%; positive predictive value, 34.3%; negative predictive value, 99.6%).[10]

Phase 2: Clinical Diagnostic Assessment

All persons scoring below the C-MMSE cutoff point for their educational level and those unable to complete screening were interviewed. Detailed medical histories, standard neurologic examinations, and neuropsychological tests,[5] assessing cognitive function and behavior, as well as the Hamilton Rating Scale for Depression[12] and the Hachinski Ischemia Scale,[13] were obtained. Dementia severity was rated with the Global Deterioration Scale.[14] Proxy (caregiver) interviews and a Chinese caregiver questionnaire[15] were completed when physical impairment or illness precluded direct examination.

At each workday's end, clinical interviewers reviewed results and diagnoses were rated independently by each clinician according to the criteria of the National Institute of Neurological and Communicative Diseases and Stroke–Alzheimer Disease and Related Disorders Association[16] for probable or possible AD, and those of the National Institute of Neurological Disorders and Stroke–Association Internationale pour la Recherche et l'Enseignement en Neurosciences[17] for probable or possible VaD. When consensus was not reached, a senior clinician returned to the household the following day to reexamine respondents with supplemental neuropsychological tests.[18] If no diagnosis was reached, the participant was referred to a research hospital for further evaluation.

Phase 3: Six-Month Diagnostic Confirmation

A preliminary diagnosis of AD or VaD was confirmed by repeating all screening tests and diagnostic examinations 6 months later in every phase 2 participant who could be traced.

After phase 3 examinations, senior clinicians at each site confirmed final diagnoses on the basis of all available data, including history, examination, temporal course, and relevant medical, laboratory, or computed tomographic or magnetic resonance imaging results (if any). For respondents missing any assessment, final diagnoses were based on all available clinical data.

Table 1. Study Population Characteristics

Characteristic	Weighted %*	Sample Size (n = 34 807)
Sex		
M	46.2	15 749
F	53.8	19 058
Age, y		
55-64	43.7	14 152
65-74	39.2	13 793
75-84	14.4	5778
≥85	2.7	1084
Education, y		
<1	36.1	13 606
1-6	32.1	11 488
7-12	20.4	7061
≥13	11.5	2652
Residence		
Rural	35.7	15 170
Urban	64.3	19 637
Marital status		
Married	77.4	25 910
Widowed	20.8	8162
Other	1.6	676
Unknown	0.1	59
Ethnicity		
Han	98.6	34 393
Meng, Hui, other	1.3	413
Unknown	<0.1	1
Occupation†		
Farm laborer	32.5	13 959
Non–farm laborer	36.4	11 736
Official	11.4	3215
Professional	11.8	2928
Sales, service	2.6	1099
Housework	5.4	1863
Unknown	<0.1	7
Dementia		
AD	2.0	732
VaD	0.8	295

*Weighted for the sampling design.
†Before retirement.

We assessed those who screened negative in a random sample of 3.3% (454 men and 554 women) of the 30 857 participants who passed the C-MMSE. They were enrolled in phase 2/3 examinations and were diagnosed without knowledge of their screening status. The negative predictive value of the C-MMSE screen was 97.6% for AD and 99.7% for VaD.

STATISTICAL ANALYSIS

We used *SUDAAN* 8.0 software for analyses.[19] Weights were calculated by multiplying the inverse of selection probabilities at all 3 sampling stages together with the inverse of the proportion participating in each sampled community. Clusters with weights exceeding the 95th percentile were combined with neighboring clusters to smooth weight distributions. Prevalence estimates were weighted to the target population. Variances were estimated by means of Taylor series, consistent with sample design. We used the direct method for age standardization with the total population of the United States in 2000 and China in 1999 in SUDAAN Proc DESCRIPT. We adjusted for C-MMSE false-negative results by correcting post hoc the age-, sex-, and education-specific prevalence for the corresponding stratum-specific C-MMSE false-negative rate, and then calculating an overall corrected prevalence.

RESULTS

Figure 2 summarizes the participation in each study phase. From a total of 36 873 eligible persons sampled, including 80 (0.2%) in nursing homes, 34 807 completed screening interviews. Community participation ranged from 73% to 100% and averaged 94.5% for all sampled communities. Phase 2 enrolled 3950 persons who screened positive. About two thirds of these cases (n=2476 [62.7%]) received the standardized phase 2 neuropsychological assessment; the remainder were assessed with caregiver interviews (n=1474 [37.3%]). Phase 3 clinical reassessments were completed at least 6 months later for 3504 persons (88.7%).

Table 1 summarizes major characteristics of the study population. The majority were Han Chinese, laborers, and married. Uneducated and rural respondents each composed one third of the study population.

A total of 732 cases of AD and 295 cases of VaD were identified, which represented weighted proportions of 70% and 22% of all dementia, respectively. The mean score on the C-MMSE was 13.7 for AD cases and 13.2 for VaD cases; around one quarter of patients with AD (23.8%) and VaD (29.4%) were classified as grades 6 or 7 on the Global Deterioration Scale. The mean age at onset of AD was 76.9 years, and that for VaD was 9 years earlier (67.7 years). Mean duration from onset to diagnosis in the study for AD (2.4 years) was longer than that for VaD (1.8 years). Mean Hachinski Ischemia Scale score for AD (1.5; n=531) was lower than that for VaD (10.4; n=230).

Table 2 shows the weighted prevalence of AD and VaD by sex for each region and the total study population. **Figure 3** and **Figure 4** present sex- and age-specific trends for AD and VaD, respectively, for the combined centers. **Table 3** gives the age- and sex-specific prevalence of AD and VaD for the total study population. Alzheimer disease displayed exponential increases in 5-year age intervals, but VaD showed a weak and inconsistent age trend. In all regions combined, the weighted crude prevalence of AD among persons 65 years or older was 2.2% (95% confidence interval [CI], 1.8%-2.6%) for men, 4.6% (95% CI, 3.9%-5.3%) for women, and 3.5% (95% CI, 3.0%-3.9%) for both sexes. For VaD, the corresponding figures were 1.2% (95% CI, 0.9%-1.4%) for men, 1.1% (95% CI, 0.8%-1.3%) for women, and 1.1% (95% CI, 0.9%-1.3%) for both sexes.

After post hoc correction for C-MMSE screening sensitivity, VaD prevalence remained unchanged, and AD prevalence in persons 65 years or older rose to 2.9% for men, 6.6% for women, and 4.8% for both sexes.

Standardizing the overall crude prevalence for persons 55 years or older to China's 1999 population yielded a projected total of 3.1 million elderly individuals with AD and 1.4 million with VaD. With age standardization to the US 2000 total population, AD prevalence in persons 65 years or older in China was 3.4% (95% CI, 0.8%-4.0%) (men), 7.7% (95% CI, 6.8%-8.9%) (women), and 5.9% (95% CI, 5.3%-6.4%) (both sexes). For VaD, the corresponding figures were 1.4% (95% CI, 1.0%-1.7%), 1.2% (95% CI, 0.9%-1.5%), and 1.3% (95% CI, 1.0%-1.5%), respectively.

Table 2. Prevalence of AD and VaD by Sex for Each Region and the Total Study Population*

	Beijing		Xian		Shanghai		Chengdu		Total	
	AD	VaD	AD	VaD	AD	VaD	AD	VaD	AD	VaD
Men										
Weighted %	1.3	1.2	1.4	1.1	1.4	0.6	1.3	0.5	1.3	0.9
SE	0.2	0.2	0.3	0.3	0.2	0.1	0.2	0.1	0.1	0.1
No. of cases	61	63	26	24	96	48	35	15	**218**	**150**
Women										
Weighted %	2.3	1.0	2.6	1.2	2.8	0.5	3.1	0.4	2.6	0.7
SE	0.4	0.1	0.3	0.2	0.3	0.1	0.4	0.2	0.2	0.1
No. of cases	116	58	73	27	232	50	93	10	**514**	**145**
Both sexes										
Weighted %	1.8	1.1	2.0	1.2	2.2	0.6	2.2	0.4	2.0	0.8
SE	0.2	0.2	0.2	0.2	0.2	0.1	0.2	<0.1	0.1	0.1
No. of cases	177	121	99	51	328	98	128	25	**732**	**295**

Abbreviations: AD, Alzheimer disease; VaD, vascular dementia.
*Prevalences per 100 population.

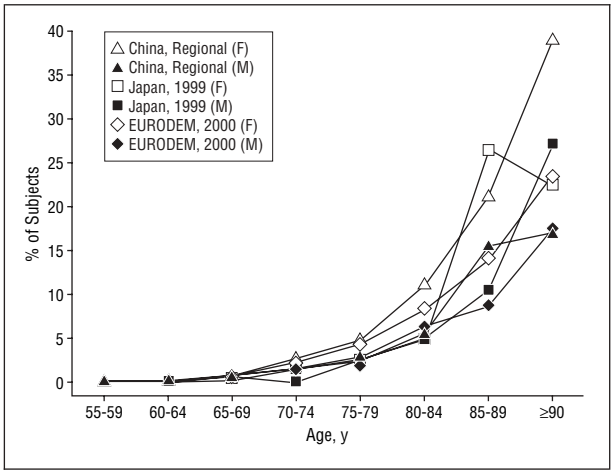

Figure 3. Age- and sex-specific prevalence of Alzheimer disease in China (present study) compared with east Asian (Japan, 1999)[20] and Western (European Community Concerted Action on the Epidemiology and Prevention of Dementia Group [EURODEM], 2000)[3] studies.

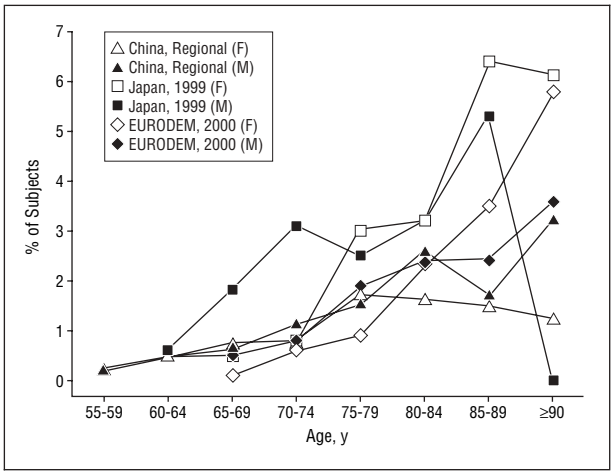

Figure 4. Age- and sex-specific prevalence of vascular dementia in China (present study) compared with east Asian (Japan, 1999)[20] and Western (European Community Concerted Action on the Epidemiology and Prevention of Dementia Group [EURODEM], 2000)[3] studies.

Table 3. Age- and Sex-Specific Prevalence of AD and VaD for the Total Study Population*

	Age Group, y				
	55-64	65-74	75-84	≥85	All Ages
Men					
AD					
Weighted %	0.1	0.9	4.0	16.3	1.3
SE	0.0	0.1	0.6	1.9	0.1
No. of cases	8	52	97	61	**218**
VaD					
Weighted %	0.4	0.9	1.9	2.1	0.9
SE	0.1	0.2	0.4	0.9	0.1
No. of cases	32	60	49	9	**150**
Women					
AD					
Weighted %	0.3	1.5	7.2	27.0	2.6
SE	0.1	0.2	0.7	2.4	0.2
No. of cases	21	103	231	159	**514**
VaD					
Weighted %	0.4	0.8	1.7	1.4	0.7
SE	0.1	0.1	0.4	0.4	0.1
No. of cases	27	59	48	11	**145**
Both Sexes					
AD					
Weighted %	0.2	1.2	5.7	23.3	2.0
SE	<0.1	0.1	0.5	1.6	0.1
No. of cases	29	155	328	220	**732**
VaD					
Weighted %	0.4	0.8	1.8	1.7	0.8
SE	0.1	0.1	0.3	0.3	0.1
No. of cases	59	119	97	20	**295**

Abbreviations: AD, Alzheimer disease; VaD, vascular dementia.
*Prevalences per 100 population.

COMMENT

The prevalence of dementia subtypes in this multicenter study in China closely approximates Western reports.[3,20] Similar to most Western studies, the age-specific AD prevalence roughly doubled at 5-year intervals,

leveling after age 85 years for men. Similarly, lower prevalence of VaD than AD was observed in all age groups and across all regions.

Several factors may explain why the prevalence in this study is more similar to Western estimates than previously reported for east Asia. Most previous studies conducted in China, Japan, Korea, and Singapore investigated prevalence in comparatively small, homogeneous geographic areas that yielded relatively few dementia cases on screening.[1,2,4-7] Because of small sample sizes, earlier prevalence estimates from east Asian studies had wide standard errors, particularly in the oldest ages. By comparison, the present prevalence study in China is, to our knowledge, the first to be conducted in diverse regions with a large sample and high participation. To reduce losses from screening errors, we increased the sensitivity C-MMSE cutoff (2 points higher than in previous studies), and we assessed screening errors in a random sample of screen-negative persons. Moreover, we used standardized case-ascertainment and sampling procedures across sites. The 6-month diagnostic confirmation served both to verify the progressive deterioration of cognitive function and to decrease diagnostic errors in preliminary assessments.

Although the present investigation had more access to computed tomography or magnetic resonance imaging (50.9% for VaD and 6.8% for AD) than all previous studies in east Asia, the limited use of such imaging may have affected the relative frequencies of dementia subtypes and contributed to underdiagnosis of VaD. However, several factors suggest that misclassification did not play a major role. Diagnosis of VaD was based on a standardized, multiphase diagnostic algorithm that included a 6-month confirmation interval, using the National Institute of Neurological Disorders and Stroke–Association Internationale pour la Recherche et l'Enseignement en Neurosciences criteria. These criteria have low sensitivity but are highly specific for VaD.[21] In addition, the 6-month clinical evaluations increased the diagnostic accuracy. The observed regional variation of VaD was consistent with the regional patterns of the Hachinski Ischemia Scale and the north-south variation in stroke prevalence in China.[22] In summary, the clinical and epidemiologic features of VaD and AD subtypes observed in this study appear to represent the actual pattern of dementia in China.

Our prevalence findings have important implications for other developing countries and for the worldwide estimates of the number of persons with AD and VaD. Because of the growth of the elderly population in many developing countries,[23] the societal burden of dementia will continue to increase during the next decades and can be expected to be particularly devastating for nations with limited resources.

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Correction

Error in Affiliations. In the Original Contribution by Huang et al titled "*APOE* Genotype, Family History of Dementia, and Alzheimer Disease Risk: A 6-Year Follow-up Study," published in the December issue of the ARCHIVES (2004;61:1930-1934), an error occurred in the affiliations paragraph on page 1930. That paragraph should have read as follows: "**Author Affiliations:** Aging Research Center, Division of Geriatric Epidemiology and Medicine, Department of Neurotec, Karolinska Institutet and Stockholm Gerontology Research Center, Stockholm, Sweden. Dr Huang is now with the Department of Public Health, Guiyang Medical College, Guiyang, Guizhou, People's Republic of China." The journal regrets the error.