# Epidemiology of Dementia

Jong Chul Youn, M.D.[1], Dong Young Lee, M.D.,Ph.D.[2], Ki Woong Kim, M.D.,Ph.D.[3],
Jong Inn Woo, M.D.,Ph.D.[2]

[1]Department of Neuropsychiatry, Gyeonggi Provincial Hospital for the Elderly, Yongin, Gyeonggi-do, Korea,
[2]Department of Neuropsychiatry, Seoul National University College of Medicine, and Seoul National University
Hospital, Seoul, Korea, [3]Department of Neuropsychiatry, Seoul National University College of Medicine, Seoul, Korea
and Seoul National University Bundang Hospital, Seongnam, Gyeonggi-do, Korea

**Abstract**: Dementia is one of the most important public health problems. Because of rapid increasing of old age in the world, need for prevention strategies and caring of dementia should be solved. Epidemiological studies can provide the basic data for making health policy, developing the prevention strategies. Epidemiological studies can be classified into the descriptive studies for studying the prevalence and incidence of a disease and the analytic studies for identifying risk factors of a disease. This review summarized the recent achievements in the epidemiology of dementia performed in the world and our country. The prevalence and incidence of dementia increased double by every 5 years of age over the age of 65 years in general. However, whether the prevalence rate of dementia exponentially increases in the oldest old age is uncertain.

The prevalence rates of dementia were generally lower in developing countries, but the exact mechanisms of these findings were not well understood. Although Alzheimer's disease is the most common etiology of dementia in most countries, some studies, especially from Japan, reported that vascular dementia is more common. However, recent studies suggested that the prevalence of vascular dementia decrease and Alzheimer's disease is more prevalent. Age and some genetic factors were consistently reported as the risk fac tors of dementia. In contrast, the association between most non-genetic risk factors and dementia were still controversial. The epidemiological studies for dementia should overcome some methodological difficulties such as diagnostic threshold for dementia and the diagnostic criteria of vascular dementia.

*Psychiatr Invest 2005; 2 (1): 28-39*

## Introduction

Dementia is one of the most important causes of disability in the elderly. With the rapidly growing numbers of elderly people, the numbers of dementia patients are also increasing at a very high speed in most countries. As a result, the management of dementia patients is now becoming one of the most important public health problems[1, 2]. Epidemiological studies could give the fundamentals for the development of the government policy and the strategies for the prevention of dementia.

Although the epidemiological studies on dementia and its specific type were started in 1960s in western countries, more sophisticated and refined epidemiological studies have been carried out since 1980s[3]. Till now, a number of epidemiological surveys were performed around the world. The results of the epidemiological studies can be classified into two categories: one is the descriptive study in which the prevalence and incidence of a disease can be estimated and the other is the analytic study in which the risk factors of a disease can be identified[4]. This review follows this kind of classification. First, the prevalence and incidence studies on dementia

**Correspondence**: Dong Young Lee, M.D.,Ph.D., Department of
Psychiatry & Behavioral Science, Seoul National University
Hospital, 28 Yongon-dong, Chongno-gu, Seoul, Korea (110-744)
Tel: +82-2-2072-2205, Fax: +82-2-744-7241,
E-mail: selfpsy@plaza.snu.ac.kr

and its subtype will be discussed. The recent epidemiological studies on dementia in Korea will be also reviewed briefly. Second, the recent findings on the risk factors of dementia and its subtype will be summarized. Most epidemiological studies have focused on dementia and Alzheimer's disease (AD). Much fewer studies focused on vascular dementia (VD), especially for identifying risk factors. Studies on rarer form of dementia, which are is frontotemoral dementia (FTD) and dementia with Lewy body (DLB), are few little. Thus, the major portion of this review will be devoted to overall dementia and AD.

## Descriptive Epidemiology

### Prevalence (Worldwide)

**Dementia**: Because there are so many studies on the prevalence of dementia in the world, it is very difficult to summarize the results of each study. Fortunately, several meta-analyses have been carriedout on pooled data from a number of comparable studies, which make it easier to summarize the literatures.

Jorm et al[5]. pooled 22 studies from throughout the world and reported that prevalence of dementia increased double by every 5 years of age. Hofman et al[6]. pooled 12 European studies performed from 1980 to 1990 and reported the very similar result to Jorm et al. Lobo et al[7]. pooled 11 European studies performed during 1990s and reported that the prevalence rate of dementia is 6.4%. Table 1 summarizes the age-specific prevalence rate of dementia reported from the mentioned studies. The prevalence of dementia is very low in the subjects under the age of 65 years (0.5-1.0%) and increases with age. Although Ritchie and Kildea[8] reported that the prevalence rate of dementia do not increase exponentially, this observation might be influenced by survival effect and need adequate numbers of the very old.

The geographical variation of the prevalence of dementia was also reported. The prevalence rates of dementia in North America and Europe were quite similar. In contrast, some studies performed in developing countries reported lower prevalence rate than those of western countries. For example, Li et al[9]. and Liu et al[10]. reported very low prevalence rates of dementia (1.8% and 2.0%, respectively) in China. Recently, such a lower prevalence rate of dementia in developing countries was confirmed by inter-continental studies, which might overcome some methodological differences. In the Indo-US study, the prevalence of rural community in India is only 1.1%[11]. In the Indianapolis-Ibadan project, the prevalence rate of dementia in Ibadan was 2.3%, which was much lower than that of Indianapolis (8.3%)[12]. This geographical difference might come from several factors. First, different culture and environment including rather simple activities of daily living, low-tech environment, under–reported functional impairment by family members might influence the results[10, 13]. Second, short life span and high mortality in developing countries might also influence the low prevalence of dementia. Third, true racial difference might exist. For example, APOE $\varepsilon 4$ allele, which is known as a genetic risk factor for AD in Caucasians and Asians, is not associated with a higher risk of dementia in Africans[14].

**Subtypes of dementia**: The prevalence rate of AD

**TABLE 1.** Prevalence rates (%) for dementia from different meta analysis studies

| Age group | Jorm et al. (1987)[5] | Hofman et al. (1991)[6] | Ritchie and Kildea (1995)[8] | Fratiglioni et al. (1999)[15] |
|---|---|---|---|---|
| 60-64 | 0.7 | 1.0 | - | 0.5 |
| 65-69 | 1.4 | 1.4 | 1.5 | 1.5 |
| 70-74 | 2.8 | 4.1 | 3.5 | 3.0 |
| 75-79 | 5.6 | 5.7 | 6.8 | 6.0 |
| 80-84 | 11.1 | 13.0 | 13.6 | 12.0 |
| 85-89 | 23.6 (85+) | 24.5 (85+) | 22.3 | - |
| 90-94 | | | 33.0 | - |
| 95+ | | | 44.8 | - |

increases with age. Lobo et al[7]. pooled the data from European country and reported the age-specific prevalence rate of 0.6 to 0.7% at the ages fo 60-69 years, 1.5 to 2.3 at 70-74, 1.8 to 4.3 at 75-79, 6.3 to 8.4 at the age of 80-84 years, 8.8 to 14.2 at 85-89 and 17.6 to 23.6 at 90 and the more. The prevalence of AD was higher in women than in men. The prevalence of VD also increases with age. In the same study, the prevalence of VD was 1.6% in the age of 60 years and the more. The age-specific prevalence is reported as 0.5 to 0.1% at the age of 60-69 years, 0.8 to 0.6 at 70-74 years, 1.9 to 0.9 at 75-79, 2.4 to 2.3 at 80-84, 2.4 to 3.5 at 85-89 and 3.6-5.8 at 90 and the more.

The ratio between AD and VD was similar in most studies of US, Europe and Africa. AD is the most common etiology of dementia and accounts for 50-70% of total dementia cases. Second most common etiology is VD and account for 20-30% of total dementia[15]. However, two studies from Italy[16] and Sweden[17] in Europe and several studies from Japan reported higher prevalence rates of VD than those of AD[18, 19, 20]. These results might be explained by the following two factors. One is related with diagnostic criteria. Many early studies in Japan classified AD and VD by the Hachinski Ischemic Score (HIS)[21] only. HIS might overestimate the prevalence of dementia[22]. In consistent with this explanation, in two studies on Japanese immigrants, which used the Diagnostic and Statistical Manual for Mental Disorders, the third edition, revised (DSM-III-R)[23] and the criteria of the California Alzheimer's Disease Diagnostic and Treatment Centers (ADDTC)[24] for diagnosing VD, AD was more prevalent than VD[25, 26]. On the contrary, a recent study by Ikeda et al. (2001) reported

that VD was more prevalent than AD by using the Diagnostic and Statistical Manual for Mental Disorders, the fourth edition (DSM-IV) criteria[27] for VD diagnosis. More researches should be conducted for this issue. The other explanation is related with the prevalence of stroke. In the Hisayama study[28], VD/AD ratio shift 1.8: 1 to 1.1: 1 from 1984 to 1992. This result was closely matched an overall decline in stroke incidence.

Mixed of AD and VD (MXD) is a problematic entity. Many epidemiological studies on dementia did not classify mixed dementia as an independent diagnostic entity. Only a few studies classified MXD as independent entity in their studies. The reported prevalence rate of MXD is ranged from 0.2 to 4.6%[29]. Frontotemporal dementia (FTD) is less common than the other types of dementia. Two groups have attempted to find the prevalence of FTD. Ratnaavalli et al[30]. reported 15 cases/100,000 persons in the 45-64 year range of age. For this range, the ratio between FTD/AD was 1.6/1. Rosso et al[31]. reported 3.6 cases/100,000 persons in the age of 50-59 years, 9.4 at 60-69, and 3.8 at 70-79. Prevalence studies on the dementia with Lewy body (DLB) were conducted mostly in pathological studies and estimated prevalence was ranged from 15 to 35% of all dementia subjects. The clinical prevalence of DLB was 5.0%, comprising 22% of all dementia subjects in the age of 75 years and the more[32] or 0.1-0.6% in the age of 65 years and more years of age[33, 34].

## Prevalence (Korea)

**Dementia**: There have been at least seven population based studies performed on the dementia epidemiology, which were published at peer review journals in Korea

**TABLE 2.** Study method and reported prevalence of dementia in Korea.

| Author (yr) | Area | Age | Sample number | Screening tool | Criteria for dementia | Prevalence | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Male | Female | Total |
| Kim (2003)[37] | Busan | 65+ | 1230 | MMSE-K | DSM-III-R | 2.7 | 10.0 | 8.0 |
| Suh (2003)[40] | Yonchon | 65+ | 1217 | PAS-K | DSM-III-R | 6.3 | 7.1 | 6.8 |
| Lee (2002)[36] | Seoul | 65+ | 953 | MMSE-KC | DSM-IV | 4.5 | 10.4 | 8.2 |
| Shin (2002)[41] | Kwangju | 65+ | 1598 | MMSE-K | DSM-IV | - | - | 10.7 |
| Kim (1999)[35] | Kangmyung | 65+ | 1331 | K-MMSE | DSM-IV | 7.5 | 15.9 | 13.0 |
| Woo (1998)[39] | Yonchon | 65+ | 1674 | MMSE-K | DSM-III-R | - | - | 9.5 |
| Park (1994)[38] | Yongil | 65+ | 766 | MMSE-K | DSM-III-R | 7.2 | 14.5 | 10.8 |

**TABLE 3.** Age-specific prevalence rate of dementia in Korea

| Age group | Kim et al. (2003)[37] | Suh et al. (2003)[40] | Lee et al. (2002)[36] | Kim et al. (1999)[35] | Park et al. (1994)[38] |
|-----------|-----------------------|-----------------------|-----------------------|-----------------------|------------------------|
| 65-69 | 0.8 | 0.8 | 2.6 | 5.2 | 2.4 |
| 70-74 | 3.3 | 3.3 | 3.7 | 12.2 | 7.0 |
| 75-79 | 8.3 | 8.3 | 8.5 | 17.0 | 15.3 |
| 80-84 | 21.3 | 21.3 | 27.8 | 34.3 (80+) | 38.9 |
| 85-89 | 54.6 | 54.6 | 32.6 (85+) | | 10.8 (85+) |
| 90+ | 68.8 | 68.8 | | | |

since 1990. Table 2 and 3 summarized the methodology and results. Three studies were conducted in urban areas[35, 36, 37] and other three studies were in rural areas[38, 39, 40]. Only one study was done for both rural and urban area[41]. All the studies included the people with the age over 65 years, and used DSM-III-R or DSM-IV criteria for the diagnosis of dementia. Overall prevalence rate of dementia ranged from 6.8 to 13.0% of the elderly community population, comparable to the results from the studies conducted in western countries[35, 36, 37, 38, 39, 40, 41]. Dementia was more in female than in male in all studies. The prevalence rate of dementia more increased with age in female than in male in all studies. (Table 3)

**Subtypes of dementia**: In Korea, the prevalence rate of AD is higher than that of VD in all studies. The prevalence of AD is 4.2 to 5.3% and that of VD is 2.0-4.8%. AD accounts for 39.8 to 65.4% of total dementia cases, and VD accounts for 12.0-37.5% (Table 4). The AD/VD

**TABLE 4.** Proportion (%) of dementing disorders in the world and Korea

| | Prevalent dementing cases (%) | | |
|---|---|---|---|
| | AD | VD | OD |
| **Area** | | | |
| North America | 74.5 | 15.4 | 10.0 |
| Europe | 61.4 | 27.6 | 11.1 |
| Asia | 46.5 | 38.1 | 15.4 |
| Africa | 64.3 | 28.6 | 7.1 |
| **Korea** | | | |
| Suh et al. (2003) | 61.7 | 35.3 | 3.0 |
| Lee et al. (2002) | 65.4 | 24.7 | 9.9 |
| Kim et al. (1999) | 39.8 | 37.5 | 22.5 |
| Woo et al. (1998) | 47.4 | 26.3 | 22.7 |
| Park et al. (1994) | 60.0 | 12.0 | 38 |

ratio was the highest in Park et al.'s study[38] and the lowest in Kim et al.'s study[35]. The discrepancy of AD/VD ratio among the studies might come from methodological difference, such as the diagnostic criteria for VD, the classification method of MXD, and the use of neuroimaging. Specific high prevalence of alcoholic dementia (1%) was reported in one earlier study[37], while the finding was not replicated in later studies.

## Incidence (Worldwide)

There have been relatively small numbers of study on the incidence of dementia, comparing with the studies on the prevalence. Based on existing data, overall dementia occurs at the rate of approximately 1% per year in persons with the age of 60 years and the more.

The incidence of dementia increases with age. However, the increasing pattern of incidence is not so clear. Jorm et al[42]. reported that the incidence rate for dementia increase exponentially with age up to the age of 90 years like prevalence. In contrast, in subsequent meta-analysis[43] Gao et al. reported that the incidence rate of dementia does not exponentially increase but just show slowly increasing pattern[44]. Disease-specific studies show highly consistent results with a general trend for a higher incidence of AD in women and a higher incidence of VD in men. However, Fratiglioni et al. pooled data from eight European studies which had used the same diagnostic criteria and found that there was little sex difference up to the age of 80 years[44]. In Rochester study, incidence rate of FTD was 2.2% for the age of 40-49 years, 3.3 for 50-59, 8.9 for 60-69. The ratio of FTD/AD was 1: 5.25 under the age of 70[45].

Geographical variations should be noted. In general, the lowered incidence rates were reported in European

studies than in North American studies, probably due to some methodological differences[15]. Although incidence data from other continent including Asia and Africa very limited, the recent Indo-US study[13] and Indianapolis-Ibadan study[46] reported significantly lower rate of incidence for overall dementia and AD.

The secular trend in the incidence of dementia should be mentioned. In Rochester study, the annual incidence rate of dementia declined from 11 cases /100,000 in 1960-64 years to 9.6/100,000 in 1965-69 and 5.7/100,000 in 1970-74[48]. This decline might be associated with the decline of stroke incidence.

## Incidence (Korea)

Incidence study for dementia is rare in Korea. Recently, Kim et al. (2002) reported the results of the follow up studies in Yonchon. They followed up 596 nondemented elderly for 42 months and reported that the incidence rate of dementia was 1.9%[48].

# Analytic Epidemiology: Risk Factors

## Sociodemographic factors

**Age and sex**: Old age is one of the most consistently reported risk factors of dementia. However, dementia itself is not a consequence of aging[8]. Some pathological features of AD can be found in the brain of a normal elderly individual who died without a history of AD, in spite of AD is qualitatively distinguishable to normal aging[49].

In most studies, AD is more prevalent in female than in male[44, 50, 51] although not in all studies[52, 53]. The higher incidence of AD in female may be explained by 1) the higher survival rate in women 2) the multiple exposures of risk factors of AD (ex. head trauma, smoking) in men 3) the lower estrogen level in old women. As for VD, men have been thought to be riskier, but the issue remains controversial[3].

**Education**: The relationship between education and dementia is one of the most controversial issues in the epidemiology of dementia. Stern et al[54]. reported that the relative risk of AD increased two-fold among the people with less than eight years of education comparing with those with eight or more years of education. However, other studies reported that education is not a risk factor

of AD[55, 56, 57]. The interaction between gender and education was suggested. The EURODEM analysis revealed that low education increased the risk of AD in women, but not in men[58]. Education might be an indirect risk factor. For example, lower educated people might more frequently exposure to toxic drugs or nutritional deficiency. Education is related to intelligence. Some studies reported that higher premorbid intelligence is associated with low risk of developing dementia[59, 60].

## Genetic factors

**Down syndrome**: Most of patients with Down syndrome who live up to the age of 40 years develop the pathological changes of AD[61]. The family history of Down syndrome increases the risk of AD two to three-fold[62]. Nevertheless, the prevalence of dementia in Down syndrome is much less than 100%, even at the age of 50[63]. This phenomenon is not well explained.

**Family history**: The individuals who have the first degree relatives with AD have an increased risk of AD two to four-fold and the risk might be even higher when two or more degree relatives were affected[64]. In general, family history is a strong risk factor in the early onset AD rather than in late onset AD.

**Mutation and polymorphism**: The mutations in the APP gene on chromosome 21, in the presenilin 1 on chromosome 14, and the presenilin 2 on chromosome 1 were found in the families with autosomal dominant hereditary AD[65]. The individuals with apolipoprotein (APOE) $\varepsilon$4 allele, which is located on chromosome 19, have an increased risk of AD by three to five-folds not only in western countries but also in Asian countries[66, 67]. The genetic risk factors of VD have been rarely studied despite of the existence of hereditary forms of amyloid angiopathy and CADASIL[68].

## Medical history

**Vascular risk factors**: In general, vascular risk factors are significantly associated not only with VD but also with AD. Hypertension, which is the most important risk factor for cerebrovascular disease (CVD), was reported as an important risk factor for cognitive decline and VD[69]. Recent studies suggested that hypertension also play a role in the development of AD. In the Honolulu-

Asia aging study, men with untreated hypertension in midlife had an increased risk for both VD and AD[70]. The indicators of the atherosclerosis in carotid and peripheral arteries were significantly associated with AD.

The results from Rotterdam study indicated that severe atherosclerosis could increase the risk ratio three times as comparing with those without atherosclerosis. In this study, subjects with having severe atherosclerosis and at least one APOE $\varepsilon$4 allele had nearly twenty-fold increased risk for AD[71]. Cholesterol might play a role in developing AD and VD. Recent epidemiological studies reported that statin can reduce the risk of AD and overall dementia approximately 30%[72, 73]. Homocysteine, a well known risk factor for cardiovascular and cerebrovascular disease, is a thiol-containing amino acid and produced during one-carbon metabolism[74]. During homocysteine metabolism, various cofactors including vitamin B12, B6 and folate are needed. Many studies reported that homocysteine not only increased the risk of VD[74, 75, 76, 77] but also AD[74, 76, 78, 79, 80, 81].

**Depression**: Relationship between depression and AD is much more complex. Depression may be a risk factor[82] or a symptom of dementia[83, 84]. Recent meta-analysis, Jorm et al[85]. suggested that the history of depression approximately double the risk of AD and overall dementia.

**Endocrine disease**: Most studies found that the presence of diabetes mellitus almost doubled the risk not only for overall dementia but also for AD[86, 87, 88]. Hypothyroidism might increase the risk of dementia[89, 90], but its explanatory mechanism and reversibility were still unclear.

**Head trauma**: Previous retrospective studies reported that a prior traumatic head injury can increase the risk of AD[91, 92, 93]. The association of head injury with AD might be explained by the fact that head injury can induce up-regulation of APP and neuronal loss[94]. However, selective recall bias might influence the results. Many prospective studies[51, 95, 96, 97, 98] failed to find any association between AD and head injury except the study of Schofield et al.[99].

**Drug use**: Estrogen may impact on brain functions and protect against AD. Some studies reported that Estrogen Replacement Therapy (ERT) might reduce the risk of AD by around 30%[100, 101]. However, these results should be cautiously interpreted. The recent results from the Women's Health Initiative study,[102] which is an epidemiological study on a large scale sponsored by the National Institute of Health of the United States, showed that ERT could not improve cognitive function in post-menopausal women and even increase the risk for dementia and mild cognitive impairment. The study also indicated that ERT increase the risk of breast cancer, ovarian cancer, colorectal cancer, and ischemic stroke.

The inflammatory response cbrings to the degeneration in AD. Recent longitudinal studies for association of NSAID and AD reported inconsistent results[103, 104, 105, 106]. Stewart et al.[103] supported the hypothesis that NSAID has a protective effect against AD, while Fourrier et al.[104] and Henderson et al.[105] did not. In the recent Rotterdam study, in which 6989 subjects the age of 55 years or the more were followed up approximately for 7 years, the relative risk of AD in those who use NSAIDS for more than two years was significantly reduced to 0.2. In contrast, the risk of VD was not reduced[106].

### Environmental factors

**Smoking**: Some earlier studies reported that smoking has a protective role against the development of AD. However, recent longitudinal studies did find the association between smoking and AD[108, 109, 110]. Moreover, in Rotterdam study, people who smoked cigarettes had more than two-fold increased risk of AD[110].

**Alcohol**: Moderate alcohol intake is not associated with AD[111]. In PAQUID study, protective effect of alcohol consumption on the risk of dementia was reported[112]. In contrast, alcohol abuse has been reported to increase the risk of dementia[113]. These results indicate that the alcohol consumption and cognitive performance is associated to each other according to a J shape curve pattern. It is very similar to the relationship between alcohol consumption and risk of stroke which also shows a J shape curve pattern[114].

**Diet**: Although oxidative stress is a one of the major causes of AD, the protective effect of antioxidant like Vitamin C and E is not clear. An evidence of the effect of Vitamin E comes from the study of Sano et al.[115] In this study, moderately demented patients with Vitamin E had significantly longer period in which they did not reach to several bad functional end point than those with

placebo. Heavy meat-eaters had a two-fold increased risk of dementia comparing with to vegetarians[116]. A recent study found that total fat, and saturated fat, cholesterol increased the risk of dementia up to two-fold and high fish consumption reduced the risk of dementia[117]. Fat intake might increase the risk of dementia by atherosclerosis, thrombosis, inflammation, cell membrane function, and accumulation of beta amyloid.

**Social network and activities**: Never married, living alone and those without any social ties were associated with the risk of AD[44, 118]. Low social or leisure activities were also associated with the risk of AD[119, 120, 121, 122]. For example, in Bronx Aging study, Verghese et al.[123] followed up 469 non-demented people older than the age of 75 years, and reported that leisure activities, reading, playing board game, playing musical instrument, dancing could reduce the risk of dementia. Their finding suggested that if someone participates in a cognitive activity one day per week, it can reduce the risk of AD and VD 7%.

## Discussion

We reviewed recent findings of the epidemiological studies on dementia. While many valuable findings have been reported, some issues were still controversial. Although the prevalence of dementia increases with age, whether the occurrence of dementia will exponentially increase in oldest old age or not is still unclear. In most studies, AD is more prevalent than VD, but geographical variations also exist and the exact reasons for the variation are not fully understood yet. Many risk factors of dementia and AD were also reported. However, most of them were not conclusive and the exact relationship between the risk factors and the occurrence of dementia is still not clear.

Researchers should overcome some issues on dementia in the field survey. First, more refined case finding method for dementia in the field survey is needed. The differentiation of early stage of dementia and mild cognitive impairment or normal aging is difficult in most situations. ADL impairment is difficult to evaluate in very old people who have restricted life. The presence of multiple diseases is also very common in old age, and the co-morbidity may interfere with cognitive function test[3].

These factors could be a the source of bias.

Second, the concepts and diagnostic criteria of VD should be refined. At least 5 diagnostic criteria including DSM-IV, ICD-10[124], Neuroepidemiology Branch of the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN)[125], ADDTC and HIS were used for diagnosing VD, but they are not interchangeable[126, 127]. The extent of using neuroimaging for diagnosing dementia also influenced the results. In Rochester study, among no clinical history of stroke, people of 26% were found to have vascular lesions sufficient to cause dementia and incidence of VD was increased more than double after the age of 85 years in with neuroimaging findings group than without neuroimaging findings group[3]. Whether MXD classified as VD or not was also influence the prevalence of VD.

Third, cross-cultural studies for dementia should be encouraged. Geographical variation or racial difference of the prevalence and incidence of dementia is well known. Because dementia might be caused by interaction of genetic, environmental factors, and cross cultural studies using same research method including the same case-finding method could give a powerful explanation for geographical variation. Nevertheless, cross cultural studies are still rare.

Finally, in our country, the future epidemiological studies for dementia should be performed on a large population based the sample with a longitudinal study design, in order to get an insight on the causality of various candidate risk factors for the occurrence of dementia, its specific subtypes, and the incidence data from our elderly population.

## Reference

1. Kawas C, Gray S, Brookmeyer R, Fozard J, Zonderman A. Age-specific incidence rates of Alzheimer's disease: the Baltimore Longitudinal Study of Aging. Neurology 2000 ; 54: 2072-7.

2. Brookmeyer R, Gray S, Kawas C. Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. Am J Public Health 1998; 88:1337-42.

3. Rocca Fa. Epidemiology of dementia. Handbook of Neuropsychology 2001; 6: 193-215.

4. Hendrie HC. Epidemiology of dementia and Alzheimer's dis-

ease. Am J Geriatr Psychiatry 1998; 6: S3-18.

5. Jorm AF, Korten AE, Henderson AS. The prevalence of dementia: a quantitative integration of the literature. Acta Psychiatr Scand 1987; 76: 465-79.

6. Hofman A, Rocca WA, Brayne C, et al. The prevalence of dementia in Europe: a collaborative study of 1980-1990 findings. Eurodem Prevalence Research Group. Int J Epidemiol 1991; 20: 736-48.

7. Lobo A, Launer LJ, Fratiglioni L, et al. Prevalence of dementia and major subtypes in Europe: A collaborative study of population-based cohorts. Neurologic Diseases in the Elderly Research Group. Neurology 2000; 54: S4-9.

8. Ritchie K, Kildea D. Is senile dementia "age-related" or "aging-related"? evidence from meta-analysis of dementia prevalence in the oldest old. Lancet 1995; 346: 931-4.

9. Li G, Shen YC, Chen CH, Zhao YW, Li SR, Lu M. An epidemiological survey of age-related dementia in an urban area of Beijing. Acta Psychiatr Scand 1989; 79: 557-63.

10. Liu HC, Lin KN, Teng EL, et al. Prevalence and subtypes of dementia in Taiwan: a community survey of 5297 individuals. J Am Geriatr Soc 1995; 43: 144-9.

11. Chandra V, Ganguli M, Pandav R, Johnston J, Belle S, DeKosky ST. Prevalence of Alzheimer's disease and other dementias in rural India: the Indo-US study. Neurology 1998; 51: 1000-8.

12. Hendrie HC, Osuntokun BO, Hall KS, et al. Prevalence of Alzheimer's disease and dementia in two communities: Nigerian Africans and African Americans. Am J Psychiatry 1995; 152: 1485-92.

13. Chandra V, Pandav R, Dodge HH, et al. Incidence of Alzheimer's disease in a rural community in India: the Indo-US study. Neurology 2001; 57: 985-9.

14. Kalaria RN, Ogeng'o JA, Patel NB, et al. Evaluation of risk factors for Alzheimer's disease in elderly east Africans. Brain Res Bull 1997; 44: 573-7.

15. Fratiglioni L, De Ronchi D, Aguero-Torres H. Worldwide prevalence and incidence of dementia. Drugs Aging 1999; 15: 365-75.

16. Rocca WA, Hofman A, Brayne C, et al. The prevalence of vascular dementia in Europe: facts and fragments from 1980-1990 studies. EURODEM-Prevalence Research Group. Ann Neurol 1991; 30: 817-24.

17. Skoog I, Nilsson L, Palmertz B, Andreasson LA, Svanborg A. A population-based study of dementia in 85-year-olds. N Engl J Med 1993; 328: 153-8.

18. Shibayama H, Kasahara Y, Kobayashi H. Prevalence of dementia in a Japanese elderly population. Acta Psychiatr Scand 1986; 74: 144-51.

19. Ueda K, Kawano H, Hasuo Y, Fujishima M. Prevalence and etiology of dementia in a Japanese community. Stroke 1992; 23: 798-803.

20. Ikeda M, Hokoishi K, Maki N, et al. Increased prevalence of vascular dementia in Japan: a community-based epidemiological study. Neurology 2001; 57: 839-44.

21. Hachinski VC, Iliff LD, Zilhka E, et al. Cerebral blood flow in dementia. Arch Neurol 1975; 32: 632-7.

22. Brust JC. Vascular dementia-still overdiagnosed. Stroke 1983; 14: 298-300.

23. Association AP. Diagnostic and Statistical Manual of Mental Disorders. Washington DC: APA, 1987.

24. Chui HC, Victoroff JI, Margolin D, Jagust W, Shankle R, Katzman R. Criteria for the diagnosis of ischemic vascular dementia proposed by the State of California Alzheimer's Disease Diagnostic and Treatment Centers. Neurology 1992; 42: 473-80.

25. White L, Petrovitch H, Ross GW, et al. Prevalence of dementia in older Japanese-American men in Hawaii: The Honolulu-Asia Aging Study. JAMA 1996; 276: 955-60.

26. Graves AB, Larson EB, Edland SD, et al. Prevalence of dementia and its subtypes in the Japanese American population of King County, Washington state. The Kame Project. Am J Epidemiol 1996; 144: 760-71.

27. Association AP. Diagnostic and Statistical Manual of Mental Disorders. Washington DC: APA press, 1994.

28. Kiyohara Y, Yoshitake T, Kato I, et al. Changing patterns in the prevalence of dementia in a Japanese community: the Hisayama study. Gerontology 1994; 40 Suppl 2: 29-35.

29. Zekry D, Hauw JJ, Gold G. Mixed dementia: epidemiology, diagnosis, and treatment. J Am Geriatr Soc 2002; 50:1431-8.

30. Ratnavalli E, Brayne C, Dawson K, Hodges JR. The prevalence of frontotemporal dementia. Neurology 2002; 58: 1615-21.

31. Rosso SM, Donker Kaat L, Baks T, et al. Frontotemporal dementia in The Netherlands: patient characteristics and prevalence estimates from a population-based study. Brain 2003; 126: 2016-22.

32. Rahkonen T, Eloniemi-Sulkava U, Rissanen S, Vatanen A, Viramo P, Sulkava R. Dementia with Lewy bodies according to the consensus criteria in a general population aged 75 years or older. J Neurol Neurosurg Psychiatry 2003; 74: 720-4.

33. Stevens T, Livingston G, Kitchen G, Manela M, Walker Z, Katona C. Islington study of dementia subtypes in the community. Br J Psychiatry 2002; 180: 270-6.

34. Yamada T, Hattori H, Miura A, Tanabe M, Yamori Y. Prevalence of Alzheimer's disease, vascular dementia and dementia with Lewy bodies in a Japanese population. Psychiatry Clin Neurosci 2001; 55: 21-5.

35. Kim DH, Na DR, Yeon BG, Kang YW, Min KB, Lee SH, Lee

SS, Lee MR, Pyo OJ, Kim SM, B SS. Prevalence of dementia in the elderly of an urban community in Korea. Korean J Prev Med 1999; 32: 306-316.

36. Lee DY, Lee JH, Ju YS, et al. The prevalence of dementia in older people in an urban population of Korea: the Seoul study. J Am Geriatr Soc 2002; 50: 1233-9.

37. Kim J, Jeong I, Chun JH, Lee S. The prevalence of dementia in a metropolitan city of South Korea. Int J Geriatr Psychiatry 2003; 18: 617-22.

38. Park J, Ko HJ, Park YN, Jung CH. Dementia among the elderly in a rural Korean community. Br J Psychiatry 1994; 164: 796-801.

39. Woo JI, Lee JH, Yoo KY, Kim CY, Kim YI, Shin YS. Prevalence estimation of dementia in a rural area of Korea. J Am Geriatr Soc 1998; 46: 983-7.

40. Suh GH, Kim JK, Cho MJ. Community study of dementia in the older Korean rural population. Aust N Z J Psychiatry 2003; 37: 606-12.

41. Shin IS, Kim JM, Yoon JS, Kim SJ, Yang SJ, Kim WJ, Lee SH, Kang SA, Kwak JY, Lee HY. Prevalence and risk factors of dementia compared between urban and rural communities of metropolitan Kawangju area. J Korean Neuropsychiatr Assoc 2002; 4: 1165-1173.

42. Jorm AF, Jolley D. The incidence of dementia: a meta-analysis. Neurology 1998; 51: 728-33.

43. Gao S, Hendrie HC, Hall KS, Hui S. The relationships between age, sex, and the incidence of dementia and Alzheimer disease: a meta-analysis. Arch Gen Psychiatry 1998; 55: 809-15.

44. Fratiglioni L, Launer LJ, Andersen K, et al. Incidence of dementia and major subtypes in Europe: A collaborative study of population-based cohorts. Neurologic Diseases in the Elderly Research Group. Neurology 2000; 54: S10-5.

45. Knopman DS, Petersen RC, Edland SD, Cha RH, Rocca WA. The incidence of frontotemporal lobar degeneration in Rochester, Minnesota, 1990 through 1994. Neurology 2004; 62: 506-8.

46. Hendrie HC, Ogunniyi A, Hall KS, et al. Incidence of dementia and Alzheimer disease in 2 communities: Yoruba residing in Ibadan, Nigeria, and African Americans residing in Indianapolis, Indiana. Jama 2001; 285: 739-47.

47. Kokmen E, Chandra V, Schoenberg BS. Trends in incidence of dementing illness in Rochester, Minnesota, in three quinquennial periods, 1960-1974. Neurology 1988; 38: 975-80.

48. Kim JK KS, Hahm BJ, Lee JY, Cho MJ. Three and half year follow up study on a rural elderly cohort. Journal of Korean Geriatric Association 2002; 6: 88-96.

49. Price JL, McKeel DW, Jr., Morris JC. Synaptic loss and pathological change in older adults--aging versus disease?

Neurobiol Aging 2001; 22: 351-2.

50. Zhang MY, Katzman R, Salmon D, et al. The prevalence of dementia and Alzheimer's disease in Shanghai, China: impact of age, gender, and education. Ann Neurol 1990; 27: 428-37.

51. Launer LJ, Andersen K, Dewey ME, et al. Rates and risk factors for dementia and Alzheimer's disease: results from EURODEM pooled analyses. EURODEM Incidence Research Group and Work Groups. European Studies of Dementia. Neurology 1999; 52: 78-84.

52. Rocca WA, Cha RH, Waring SC, Kokmen E. Incidence of dementia and Alzheimer's disease: a reanalysis of data from Rochester, Minnesota, 1975-1984. Am J Epidemiol 1998; 148: 51-62.

53. Bachman DL, Wolf PA, Linn RT, et al. Incidence of dementia and probable Alzheimer's disease in a general population: the Framingham Study. Neurology 1993; 43: 515-9.

54. Stern RG, Mohs RC, Davidson M, et al. A longitudinal study of Alzheimer's disease: measurement, rate, and predictors of cognitive deterioration. Am J Psychiatry 1994; 151: 390-6.

55. Beard CM, Kokmen E, O'Brien PC, Kurland LT. The prevalence of dementia is changing over time in Rochester, Minnesota. Neurology 1995; 45: 75-9.

56. Cobb JL, Wolf PA, Au R, White R, D'Agostino RB. The effect of education on the incidence of dementia and Alzheimer's disease in the Framingham Study. Neurology 1995; 45: 1707-12.

57. Katzman R. Education and the prevalence of dementia and Alzheimer's disease. Neurology 1993; 43: 13-20.

58. Letenneur L, Launer LJ, Andersen K, et al. Education and the risk for Alzheimer's disease: sex makes a difference. EURODEM pooled analyses. EURODEM Incidence Research Group. Am J Epidemiol 2000; 151: 1064-71.

59. Schmand B, Smit JH, Geerlings MI, Lindeboom J. The effects of intelligence and education on the development of dementia. A test of the brain reserve hypothesis. Psychol Med 1997; 27: 1337-44.

60. Alexander GE, Furey ML, Grady CL, et al. Association of premorbid intellectual function with cerebral metabolism in Alzheimer's disease: implications for the cognitive reserve hypothesis. Am J Psychiatry 1997; 154: 165-72.

61. Williams RS, Matthysse S. Age-related changes in Down syndrome brain and the cellular pathology of Alzheimer disease. Prog Brain Res 1986; 70: 49-67.

62. Berr C, Borghi E, Rethore MO, Lejeune J, Alperovitch A. Absence of familial association between dementia of Alzheimer type and Down syndrome. Am J Med Genet 1989; 33: 545-50.

63. Zigman WB, Schupf N, Sersen E, Silverman W. Prevalence of dementia in adults with and without Down syndrome. Am J

Ment Retard 1996; 100: 403-12.

64. Devi G, Marder K, Schofield PW, Tang MX, Stern Y, Mayeux R. Validity of family history for the diagnosis of dementia among siblings of patients with late-onset Alzheimer's disease. Genet Epidemiol 1998; 15: 215-23.

65. Hardy J. Toward Alzheimer therapies based on genetic knowledge. Annu Rev Med 2004; 55: 15-25.

66. Farrer LA, Cupples LA, Haines JL, et al. Effects of age, sex, and ethnicity on the association between apolipoprotein E genotype and Alzheimer disease. A meta-analysis. APOE and Alzheimer Disease Meta Analysis Consortium. JAMA 1997; 278: 1349-56.

67. Kim KW, Jhoo JH, Lee KU, et al. Association between apolipoprotein E polymorphism and Alzheimer's disease in Koreans. Neurosci Lett 1999; 277: 145-8.

68. Thomas NJ, Morris CM, Scaravilli F, et al. Hereditary vascular dementia linked to notch 3 mutations. CADASIL in British families. Ann N Y Acad Sci 2000; 903: 293-8.

69. Skoog I, Lernfelt B, Landahl S, et al. 15-year longitudinal study of blood pressure and dementia. Lancet 1996; 347: 1141-5.

70. Launer LJ, Ross GW, Petrovitch H, et al. Midlife blood pressure and dementia: the Honolulu-Asia aging study. Neurobiol Aging 2000; 21: 49-55.

71. Hofman A, Ott A, Breteler MM, et al. Atherosclerosis, apolipoprotein E, and prevalence of dementia and Alzheimer's disease in the Rotterdam Study. Lancet 1997; 349: 151-4.

72. Wolozin B, Kellman W, Ruosseau P, Celesia GG, Siegel G. Decreased prevalence of Alzheimer disease associated with 3-hydroxy-3-methyglutaryl coenzyme A reductase inhibitors. Arch Neurol 2000; 57: 1439-43.

73. Jick H, Zornberg GL, Jick SS, Seshadri S, Drachman DA. Statins and the risk of dementia. Lancet 2000; 356: 1627-31.

74. McIlroy SP, Dynan KB, Lawson JT, Patterson CC, Passmore AP. Moderately elevated plasma homocysteine, methylenetetrahydrofolate reductase genotype, and risk for stroke, vascular dementia, and Alzheimer disease in Northern Ireland. Stroke 2002; 33: 2351-6.

75. Miller JW, Green R, Mungas DM, Reed BR, Jagust WJ. Homocysteine, vitamin B6, and vascular disease in AD patients. Neurology 2002; 58: 1471-5.

76. Lehmann M, Gottfries CG, Regland B. Identification of cognitive impairment in the elderly: homocysteine is an early marker. Dement Geriatr Cogn Disord 1999; 10: 12-20.

77. Fassbender K, Mielke O, Bertsch T, Nafe B, Froschen S, Hennerici M. Homocysteine in cerebral macroangiography and microangiopathy. Lancet 1999; 353: 1586-7.

78. Quadri P, Fragiacomo C, Pezzati R, et al. Homocysteine,

folate, and vitamin B-12 in mild cognitive impairment, Alzheimer disease, and vascular dementia. Am J Clin Nutr 2004; 80: 114-22.

79. Religa D, Styczynska M, Peplonska B, et al. Homocysteine, apolipoproteine E and methylenetetrahydrofolate reductase in Alzheimer's disease and mild cognitive impairment. Dement Geriatr Cogn Disord 2003; 16: 64-70.

80. Seshadri S, Beiser A, Selhub J, et al. Plasma homocysteine as a risk factor for dementia and Alzheimer's disease. N Engl J Med 2002; 346: 476-83.

81. Clarke R, Smith AD, Jobst KA, Refsum H, Sutton L, Ueland PM. Folate, vitamin B12, and serum total homocysteine levels in confirmed Alzheimer disease. Arch Neurol 1998; 55: 1449-55.

82. Kessing LV, Olsen EW, Mortensen PB, Andersen PK. Dementia in affective disorder: a case-register study. Acta Psychiatr Scand 1999; 100: 176-85.

83. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. JAMA 2002; 288: 1475-83.

84. Lyketsos CG, Sheppard JM, Steinberg M, et al. Neuropsychiatric disturbance in Alzheimer's disease clusters into three groups: the Cache County study. Int J Geriatr Psychiatry 2001; 16: 1043-53.

85. Jorm AF. Is depression a risk factor for dementia or cognitive decline? A review. Gerontology 2000; 46: 219-27.

86. Xu WL, Qiu CX, Wahlin A, Winblad B, Fratiglioni L. Diabetes mellitus and risk of dementia in the Kungsholmen project: a 6-year follow-up study. Neurology 2004; 63: 1181-6.

87. Arvanitakis Z, Wilson RS, Bienias JL, Evans DA, Bennett DA. Diabetes mellitus and risk of Alzheimer disease and decline in cognitive function. Arch Neurol 2004; 61: 661-6.

88. Ott A, van Rossum CT, van Harskamp F, van de Mheen H, Hofman A, Breteler MM. Education and the incidence of dementia in a large population-based study: the Rotterdam Study. Neurology 1999; 52: 663-6.

89. Smith CL, Granger CV. Hypothyroidism producing reversible dementia. A challenge for medical rehabilitation. Am J Phys Med Rehabil 1992; 71: 28-30.

90. Ganguli M, Burmeister LA, Seaberg EC, Belle S, DeKosky ST. Association between dementia and elevated TSH: a community-based study. Biol Psychiatry 1996; 40: 714-25.

91. Katzman R, Kang D, Thomas R. Interaction of apolipoprotein E epsilon 4 with other genetic and non-genetic risk factors in late onset Alzheimer disease: problems facing the investigator. Neurochem Res 1998; 23: 369-76.

92. Rasmusson DX, Brandt J, Martin DB, Folstein MF. Head injury as a risk factor in Alzheimer's disease. Brain Inj 1995;

9: 213-9.

93. van Duijn CM, Hofman A. Risk factors for Alzheimer's disease: the EURODEM collaborative re-analysis of case-control studies. Neuroepidemiology 1992; 11 Suppl 1: 106-13.

94. Williams DB, Annegers JF, Kokmen E, O'Brien PC, Kurland LT. Brain injury and neurologic sequelae: a cohort study of dementia, parkinsonism, and amyotrophic lateral sclerosis. Neurology 1991; 41: 1554-7.

95. Breteler MM, de Groot RR, van Romunde LK, Hofman A. Risk of dementia in patients with Parkinson's disease, epilepsy, and severe head trauma: a register-based follow-up study. Am J Epidemiol 1995; 142: 1300-5.

96. Mehta KM, Ott A, Kalmijn S, et al. Head trauma and risk of dementia and Alzheimer's disease: The Rotterdam Study. Neurology 1999; 53: 1959-62.

97. Nandoe RD, Scheltens P, Eikelenboom P. Head trauma and Alzheimer's disease. J Alzheimers Dis 2002; 4: 303-8.

98. Schofield PW, Logroscino G, Andrews HF, Albert S, Stern Y. An association between head circumference and Alzheimer's disease in a population-based study of aging and dementia. Neurology 1997; 49: 30-7.

99. Gentleman SM, Nash MJ, Sweeting CJ, Graham DI, Roberts GW. Beta-amyloid precursor protein (beta APP) as a marker for axonal injury after head injury. Neurosci Lett 1993; 160: 139-44.

100. Hogervorst E, Yaffe K, Richards M, Huppert F. Hormone replacement therapy for cognitive function in postmenopausal women. Cochrane Database Syst Rev 2002: CD003122.

101. LeBlanc ES, Janowsky J, Chan BK, Nelson HD. Hormone replacement therapy and cognition: systematic review and meta-analysis. JAMA 2001; 285: 1489-99.

102. Mulnard RA, Cotman CW, Kawas C, et al. Estrogen replacement therapy for treatment of mild to moderate Alzheimer disease: a randomized controlled trial. Alzheimer's Disease Cooperative Study. JAMA 2000; 283: 1007-15.

103. Stewart WF, Kawas C, Corrada M, Metter EJ. Risk of Alzheimer's disease and duration of NSAID use. Neurology 1997; 48: 626-32.

104. Fourrier A, Letenneur L, Begaud B, Dartigues JF. Nonsteroidal antiinflammatory drug use and cognitive function in the elderly: inconclusive results from a population-based cohort study. J Clin Epidemiol 1996; 49: 1201.

105. Henderson AS, Jorm AF, Christensen H, Jacomb PA, Korten AE. Aspirin, anti-inflammatory drugs and risk of dementia. Int J Geriatr Psychiatry 1997; 12: 926-30.

106. in t'Veld BA, Ruitenberg A, Hofman A, et al. Nonsteroidal antiinflammatory drugs and the risk of Alzheimer's disease. N Engl J Med 2001; 345: 1515-21.

107. Wang HX, Fratiglioni L, Frisoni GB, Viitanen M, Winblad B. Smoking and the occurrence of Alzheimer's disease: cross-sectional and longitudinal data in a population-based study. Am J Epidemiol 1999; 149: 640-4.

108. Lerner A, Koss E, Debanne S, Rowland D, Smyth K, Friedland R. Smoking and oestrogen-replacement therapy as protective factors for Alzheimer's disease. Lancet 1997; 349: 403-4.

109. Hebert LE, Scherr PA, Beckett LA, et al. Relation of smoking and alcohol consumption to incident Alzheimer's disease. Am J Epidemiol 1992; 135: 347-55.

110. Ott A, Slooter AJ, Hofman A, et al. Smoking and risk of dementia and Alzheimer's disease in a population-based cohort study: the Rotterdam Study. Lancet 1998; 351: 1840-3.

111. Fratiglioni L, Ahlbom A, Viitanen M, Winblad B. Risk factors for late-onset Alzheimer's disease: a population-based, case-control study. Ann Neurol 1993; 33: 258-66.

112. Orgogozo JM, Dartigues JF, Lafont S, et al. Wine consumption and dementia in the elderly: a prospective community study in the Bordeaux area. Rev Neurol (Paris) 1997; 153: 185-92.

113. Thomas VS, Rockwood KJ. Alcohol abuse, cognitive impairment, and mortality among older people. J Am Geriatr Soc 2001; 49: 415-20.

114. Sacco RL, Elkind M, Boden-Albala B, et al. The protective effect of moderate alcohol consumption on ischemic stroke. JAMA 1999; 281: 53-60.

115. Sano M, Ernesto C, Thomas RG, et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. The Alzheimer's Disease Cooperative Study. N Engl J Med 1997; 336: 1216-22.

116. Giem P, Beeson WL, Fraser GE. The incidence of dementia and intake of animal products: preliminary findings from the Adventist Health Study. Neuroepidemiology 1993; 12: 28-36.

117. Kalmijn S. Fatty acid intake and the risk of dementia and cognitive decline: a review of clinical and epidemiological studies. J Nutr Health Aging 2000; 4: 202-7.

118. Helmer C, Damon D, Letenneur L, et al. Marital status and risk of Alzheimer's disease: a French population-based cohort study. Neurology 1999; 53: 1953-8.

119. Wang HX, Karp A, Winblad B, Fratiglioni L. Late-life engagement in social and leisure activities is associated with a decreased risk of dementia: a longitudinal study from the Kungsholmen project. Am J Epidemiol 2002; 155: 1081-7.

120. Laurin D, Verreault R, Lindsay J, MacPherson K, Rockwood K. Physical activity and risk of cognitive impairment and dementia in elderly persons. Arch Neurol 2001; 58: 498-504.

121. Wilson RS, Bennett DA, Bienias JL, et al. Cognitive activity and incident AD in a population-based sample of older persons. Neurology 2002; 59: 1910-4.

122. Wilson RS, Mendes De Leon CF, Barnes LL, et al. Participation in cognitively stimulating activities and risk of incident Alzheimer disease. JAMA 2002; 287: 742-8.

123. Verghese J, Lipton RB, Katz MJ, et al. Leisure activities and the risk of dementia in the elderly. N Engl J Med 2003; 348: 2508-16.

124. Organization WH. ICD-10 Classification of Mental and Behavioral Disorders: Diagnostic Criteria for research. Geneva: WHO, 1993.

125. Roman GC, Tatemichi TK, Erkinjuntti T, et al. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology 1993; 43: 250-60.

126. Pohjasvaara T, Mantyla R, Ylikoski R, Kaste M, Erkinjuntti T. Comparison of different clinical criteria (DSM-III, ADDTC, ICD-10, NINDS-AIREN, DSM-IV) for the diagnosis of vascular dementia. National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences. Stroke 2000; 31: 2952-7.

127. Chui HC, Mack W, Jackson JE, et al. Clinical criteria for the diagnosis of vascular dementia: a multicenter study of comparability and interrater reliability. Arch Neurol 2000; 57: 191-6.