

# A comparison of sociobehavioral impact on cognitive preservation in Alzheimer's disease between Taiwan and Korea

# A cross-national study

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## Abstract

Both Taiwan and Korea are developed countries with different cultures. When encountering the issue of dementia, such sociobehavioral factors have various and different impacts on dementia. We aim to assess the cross-national difference of sociobehavioral impact on cognitive preservation in Alzheimer's disease (AD) between Taiwan and Korea.

A uniformed data set was administered regarding AD. We evaluated annual cognitive function using the Mini-Mental State Examination (MMSE), Clinical Dementia Rating sum of box (CDR-SB), and CDR for 2 continuous years. Annual change of scores compared with the baseline indicated cognitive change as preservation or decline. We recorded the sociodemographic variables of interest, including education duration, level of independence, living situation, and marital status. Step-wise regression analyses were performed to determine the independent factors for cognitive preservation.

In total, 503 participants in Taiwan and 77 participants in Korea were recruited from 2011 to 2014. The baseline demographic characteristics were different in levels of education, living situation, level of independence, and dementia severity between the 2 countries. With follow-up for 2 years, cognitive preservation was associated with CDR staging at baseline and independence [adjusted odds ratio (OR) = 1.657, 95% confidence interval (95% Cl) = 1.109-2.477, P = .014] in the Taiwanese population, whereas cognitive preservation was related to living alone (adjusted OR=3.316, 95% Cl=1.135-9.687, P = .028) in the Korean population. The levels of education showed inconsistency in cognitive preservation in both countries.

Cognitive preservation was associated with independence in the Taiwanese population, whereas cognitive preservation was related to living alone in the Korean population. By practicing relevant socioeconomic support, this might contribute to lessening the negative impact of dementia and preserving cognition in different countries.

**Abbreviations:** AD = Alzheimer's disease,  $APOE_{\epsilon}4 = Apolipoprotein E gene with allele <math>\epsilon 4$  genotyping, CDR = Clinical Dementia Rating, CDR-SB = CDR scale Sum of Boxes, DSM-IV = Diagnostic and Statistical Manual of Mental Disorder 4th edition, MMSE = Mini-Mental Status Examination, NINCDSADRDA = National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association, UDS = uniform data set.

Keywords: Alzheimer's disease, clinical dementia rating, Korea, mini-mental state examination, Taiwan

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# 1. Introduction

According to the World Health Report in 2003, there is increasing prevalence of dementia and its global burden.<sup>[1]</sup> Dementia contributes to health status in people aged over 60 and living with a disability other than stroke and cancer.<sup>[1]</sup> The Delphi consensus estimated that 24.3 million people had dementia in 2005, with 4.6 million new dementia cases reported every year, with numbers projected to double every 20 years to 81.1 million by 2040.<sup>[2]</sup> Although there are different increasing rates of dementia between countries. 60% of people with dementia lived in developing countries in 2001 and this will increase to 71% by 2040. It will increase by 100% between 2001 and 2040 in developed countries, but by more than 300% in India, China, and South Asian and Western Pacific regions.<sup>[2]</sup> Globally, Asia contains 48% of the patients with dementia and the estimated percentage will grow to 59% by 2050.<sup>[3]</sup> In Asia, the majority of people with dementia live in China and the developing western Pacific area, and these areas are where the majority of this population live globally.<sup>[2]</sup>

Taiwan and Korea are developed countries located in the western Pacific area. Both countries share several similarities in history, religions, politics, "Confucianism" philosophy, <sup>[4,5]</sup> economy, <sup>[6]</sup> and education. <sup>[7]</sup> As socioeconomics has rapidly developed, Taiwan and Korea have both faced the issue of dementia. Treatment of patients with dementia and distress from caregivers are great burdens of dementia, and as the majority of patients with dementia are living at home,<sup>[8]</sup> relatives or family members are commonly the caregivers, suffering from substantial practical, psychological, and economic strains. [9-11] Currently, both dementia disease course and caregiver support have common features in clinical practice. Furthermore, cultural background and socioeconomic conditions are considered to have impact on dementia and caregiver support. [12-14] Asian countries, especially in western Pacific areas, might have the majority of such patients globally with a heterogeneous clinical status, so to address this heterogeneity, Yang et al<sup>[13]</sup> conducted studies using a uniform data set (UDS) to enhance collaboration and study cohesiveness, demonstrating differences in dementia assessment and care in developing versus developed countries.[12,15]

As for the impact of socio-behavioral factors on cognitive function in Alzheimer's disease (AD) in systematic review and meta-analysis of observational studies, Williams et al<sup>[16]</sup> in 2010 determined that depressive disorders and unmarried status with less social support increased risk for AD, whereas higher levels of education and physical activity decreased risk for AD. They also found that depressive disorders increased risk of cognitive decline while physical activity decreased risk of cognitive decline, whereas higher levels of education, social network, or social support systems were not associated with risk of cognitive decline.<sup>[16]</sup> Baumgart et al<sup>[17]</sup> in 2015 concluded presence of depressive history increased risk of cognitive decline, whereas years of formal education and physical activity decreased risk of cognitive decline and dementia. Livingston et al<sup>[18]</sup> in 2017 identified sociobehavioral risk factors for dementia in late life, including depression, physical inactivity, and social isolation. By far, risk factors for cognitive decline in patients with AD regarding sociobehavioral factors under different cultural backgrounds are still inconclusive due to inadequate evidence and heterogeneity of studies.[16,17,18]

In our study, a uniformed data set (UDS) was administered regarding AD, in association with the applications of service composition and Internet of Medical Things. Service composition is a technology capable of combining a collection of existing services where many smaller services are coordinated together to form a larger one.<sup>[19]</sup> The Internet of Medical Things is a building block for modern health care having enormously stringent resource constraints; thus, lightweight health data security and privacy are crucial requirements.<sup>[20]</sup> Sociobehavioral factors have impacts on dementia in different nations and cultures, so by practicing relevant socioeconomic support behaviors, these might contribute to lessening the negative impact of dementia and preserving cognition in different country populations.<sup>[21]</sup> Our study focused on the cross-national difference in AD patients between Taiwan and Korea, and extended this to the issue of cognitive preservation in association with sociobehavioral factors with a 2-year follow-up.

# 2. Methods

#### 2.1. Countries

The study was conducted in Taiwan and Korea at different times. The study was conducted from June 30, 2011, to December 31, 2012, in Taiwan by Yuan-Han Yang at Kaohsiung Medical University Hospital and his colleagues at other medical centers in Taiwan. The study was then extended to Korea, mainly Seoul Special City, from January 1, 2013, to June 30, 2014, to recruit AD patients by Sang-Yun Kim.<sup>[12,13,15]</sup> It took 18 months to recruit the participants in each country.

#### 2.2. Participants

All of the participants received a comprehensive medical evaluation, including clinical history, physical and neurologic examinations, brain-computed tomography or magnetic resonance imaging, and blood chemistry examinations to exclude other possible causes for the current cognitive status. For all the recruited participants, the diagnosis of AD was based on the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDSADRDA) criteria,<sup>[14]</sup> and the Diagnostic and Statistical Manual of Mental Disorder 4th edition (DSM-IV) criteria.<sup>[22]</sup> Patients with other conditions possibly contributing to the diagnosis of AD were excluded.

#### 2.3. Ethics

All of the procedures were approved by the respective Institutional Review Boards or Ethic Committees from each country involved. All of the participants or their legal representatives provided written informed consent. Each of the patients was administered the examinations by a neuropsychologist and an experienced physician based on information from a knowledgeable source, usually a spouse or an adult child.

#### 2.4. Evaluation of sociobehavioral factors

National Institute on Aging in United States convened a Clinical Task Force, composed of clinical leaders from Alzheimer's Disease Centers, to develop a uniform set of assessment procedures to characterize individuals with mild AD and mild cognitive impairment (MCI) compared with nondemented aging. The UDS<sup>[23]</sup> defines a common set of clinical observations to be collected longitudinally on ADC participants in accordance with standard methods. Data obtained with the UDS are submitted to the National Alzheimer's Coordinating Center and represent a unique and valuable source of data to support and stimulate collaborative research. In our study, we used the UDS as a tool to evaluate the demographic factors and related sociobehavioral factors. The UDS containing several individual forms, Form A-D, was originally designed to provide clinical and cognitive data from persons with AD dementia and cognitively healthy control individuals in the United States to support collaborative research initiatives.<sup>[23]</sup> In our study, Form A (A1-A5) was administered to collect the basic demographic characteristics of AD patients and their informants to outline the current status of AD and its related issues in Taiwan and Korea. The A1 component was the patient's demographic data, including information on sex, race, ethnicity, and marital status. The A2 component was the informant's demographic data, including the relationship with the patient and the number and frequency of visits made by the informant to the patient. Form A3 was the patient's family history related to dementia or AD, with a focus on the illness as experienced by the patient's first-degree relatives. Forms A4 and A5 were the patient's medications and health history, respectively.

#### 2.5. Evaluation of cognitive preservation

For all of the recruited participants of AD, the corresponding evaluations, including the Traditional Chinese version Mini-Mental Status Examination (MMSE),<sup>[24]</sup> Clinical Dementia Rating (CDR),<sup>[25]</sup> and CDR scale Sum of Boxes (CDR-SB),<sup>[25]</sup> were collected at the recruited time and for 2 continuous years. Patients were excluded if not fulfilling the 2-year follow-up. The MMSE is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. MMSE contains 8 categories, namely orientation to time (5 points), orientation to place (5 points), registration (3 points), attention and calculation (5 points), recall (3 points), language (2 points), repetition (1 point), and complex commands (6 points). MMSE is the summation of the scores of 8 categories. The higher scores of MMSE indicate better cognitive function. The CDR Dementia Staging Instrument in 1 aspect is a 5-point scale used to characterize 6 domains of cognitive and functional performance applicable to AD and related dementias, namely memory, orientation, judgment, and problem solving, community affairs, home and hobbies, and personal care. Each domain has a 5-point scale as follows, 0 = normal; 0.5 = very mild dementia; 1 = milddementia; 2 =moderate dementia; 3 = severe dementia. The summation of scores of each domain is calculated as CDR-SB. CDR Scoring Algorithm was developed to interpret the scores of each domain to the total CDR, where higher scores of CDR-SB and CDR indicate worse cognitive function. The necessary information to make each rating is obtained through a semistructured interview of the patient and a reliable informant or collateral source, such as family members or caregivers, referred to as the CDR Assessment Protocol.

The change of MMSE scores in 1-year follow-up (1Y $\Delta$ MMSE) means the difference of MMSE scores between the second year and the first year (baseline). The definitions are the same as the 2-year follow-up and the change of CDR-SB scores ( $\Delta$ CDR-SB). Cognitive preservation is defined as  $\Delta$ MMSE more than or equal to zero or  $\Delta$ CDR-SB less than or equal to zero. In brief, the

definition for cognitive preservation and cognitive decline are summarized as follows:

1YΔMMSE= (MMSE-2nd year) – (MMSE-1st year) 2YΔMMSE= (MMSE-3rd year) – (MMSE-1st year) ΔMMSE≥0, cognitive preservation ΔMMSE < 0, cognitive decline 1YΔCDR-SB= (CDR-SB -2nd year) – (CDR-SB -1st year) 2YΔCDR-SB= (CDR-SB -3rd year) – (CDR-SB -1st year) ΔCDR-SB≦0, cognitive preservation ΔCDR-SB≥0, cognitive decline

#### 2.6. Statistical analysis

Descriptive statistical analyses were conducted for all continuous variables by mean (standard deviation) and categorical variables by numbers (percentage). We elucidated the demographic characteristics, including age (grouped as <75 years of age and  $\geq 75$  years of age), gender and dementia severity by MMSE, CDR (grouped as 0.5, 1.2, and 3), and CDR-SB, as well as sociobehavioral factors, including education duration (grouped as <6 years and  $\geq 6$  years), living status, marital status, and level of independence. The difference of each factor for cognitive preservation in 1-year and 2-year follow-up were then compared, then the independent factors for cognitive preservation by stepwise regression analysis were identified and presented with adjusted odds ratio and 95% confidence intervals. All statistical tests were 2-tailed, and a P value of .05 was considered to show significance with 95% confidence interval. The data analysis was performed using SPSS (version 12.0.1 for Windows; SPSS Inc., Chicago, IL).

# 3. Results

#### 3.1. Demographic characteristics

In total, 503 AD patients from Taiwan and 77 AD patients in Korea were recruited to participate in the study. The demographic characteristics of the participants and informants are shown in Figure 1 (supplementary Table 1, http://links.lww.com/ MD/E24). The mean age was  $77.6 \pm 7.8$  years in Taiwan and  $77.2 \pm 5.7$  years in Korea. As for the gender distribution in AD, females were consistently predominant in both Taiwan (69.4%) and Korea (75.3%). There was no significant difference in age and gender between the 2 countries. The levels of education in Taiwan were significantly higher than Korea  $(7.4 \pm 5.3 \text{ vs } 5.5 \pm$ 4.6 years, P = .003). As for social-behavioral factors, Korea had significantly higher proportions in living alone (24.7% vs 9.0%, P < .001) and independence than did Taiwan (80.5% vs 66.7%, P = .008). There was no difference in marital status between the 2 countries. As for informants, there was no difference between the 2 countries, except for living together, which showed a higher proportion of living together of informants and AD patients in Taiwan than in Korea (74.0% vs 54.5%, P<.001).

#### 3.2. Baseline and follow-up cognitive function

The baseline dementia severity and follow-up cognitive function by CDR, CDR-SB, and MMSE between the 2 countries is illustrated in Figure 2 (supplementary Table 2, http://links.lww. com/MD/E24). The baseline dementia severity and follow-up cognitive function in CDR in the recruited participants revealed difference between the 2 countries. The proportion of CDR 0.5 in baseline was higher in Korea (35.0% vs 18.7%), whereas the



Figure 1. Demographic characteristics of the participants and informants in Taiwan and Korea. \*P<.05, statistically significant.





proportion of CDR 1 in baseline was higher in Taiwan (56.6% vs 33.8%). During the follow-up, the proportion of CDR2 and CDR3 increased in both countries, indicating the progressive disease course of dementia. The overall mean MMSE measures in baseline and follow-up in our study were not significantly different between the 2 countries. The overall CDR-SB in baseline showed no difference, whereas Korea had higher dementia severity scoring by CDR-SB in the follow-up than did Taiwan (for 1-year follow-up,  $7.9 \pm 4.3$  vs  $6.6 \pm 3.2$ , P = .002, for 2-year follow-up,  $9.3 \pm 4.7$  vs  $7.3 \pm 3.6$ , P < .001).

# 3.3. Association of global status and follow-up cognitive change

Association of global status and follow-up cognitive change by MMSE in participants in Taiwan and Korea is shown in Figure 3 (supplementary Table 3, http://links.lww.com/MD/E24). It shows that independence was associated with higher cognitive preservation in 2-year follow-up (72.8% vs 63.4%, P=.035), while lower levels of education and baseline dementia severity in CDR were associated with higher cognitive decline in 2-year follow-up in the Taiwanese population. In the Korean population, only living alone was the factor associated with cognitive



Figure 3. Association of global status and follow-up cognitive change by MMSE in participants in Taiwan (n = 503) and Korea (n = 77).  $\Delta$ MMSE = change of MMSE scores in follow-up; CDR = Clinical Dementia Rating; MMSE = Mini-Mental State Examination. \*P < .05, statistically significant.



Figure 4. Association of global status and follow-up cognitive change by CDR-SB in participants in Taiwan (n=498) and Korea (n=77).  $\Delta$ CDR-SB=change of CDR-SB scores in follow-up; CDR=Clinical Dementia Rating; CDR-SB=CDR scale Sum of Boxes. \*P<.05, statistically significant.

preservation in 2-year follow-up (39.3% vs 16.3%, P=.025). Association of global status and follow-up cognitive change by CDR-SB in participants in Taiwan and Korea is shown in Figure 4 (supplementary Table 4, http://links.lww.com/MD/ E24). It shows that younger age, higher levels of education, and independence were associated with cognitive preservation in 2year follow-up in the Taiwanese population. The role of independence was also noted in 1-year follow-up in Taiwan. In the Korean population, there was no factor associated with cognitive preservation in CDR-SB. The progressive disease course was not correlated with gender in both Taiwan and Korea in our study.

#### 3.4. Factors for cognitive preservation

Table 1 reveals the result of follow-up cognitive preservation by MMSE and CDR-SB in Taiwan and Korea using step-wise regression analysis. By MMSE, the lower level of education and less severity of dementia were independent factors for cognitive preservation in Taiwan. By CDR-SB, the higher levels of education (adjusted OR=1.594, 95% CI=1.049–2.421, P=.029) and independence (adjusted OR=1.657, 95% CI=1.109–2.477, P=.014) were independent factors for cognitive preservation in 2-year follow-up in Taiwan. The role of levels of education in cognitive preservation was discrepant by MMSE and CDR-SB in Taiwan. By MMSE, living alone was the only

# Table 1

Stepwise regression analysis for follow-up cognitive preservation by MMSE and CDR-SB in participants in Taiwan and Korea.

	Adjusted OR	95% CI	Р
Taiwan (n $=$ 503)			
1YAMMSE			
CDR 0.5 ref			
CDR 1	0.346	0.208-0.575	<.001
CDR 2	0.515	0.289-0.916	.024*
Living alone	1.747	0.914-3.340	.091
2YAMMSE			
Education ≥6	0.516	0.340-0.781	.002*
CDR 0.5 ref			
CDR 1	0.320	0.195-0.527	<.001
CDR 2	0.267	0.148-0.482	<.001
CDR 3	0.634	0.037-10.899	.754
$1Y\Delta CDR-SB$			
Gender, Female	0.709	0.474-1.059	.093
Independence	1.596	1.089-2.340	.017*
$2Y\Delta CDR-SB$			
Education≥6	1.594	1.049-2.421	.029*
Independence	1.657	1.109-2.477	.014*
Korea $(n = 77)$			
$1Y\Delta MMSE$	NA	NA	NA
$2Y\Delta MMSE$			
Living Alone	3.316	1.135-9.687	.028 <sup>*</sup>
$1Y\Delta CDR-SB$			
Education $\geq 6$	0.352	0.133-0.933	.036*
CDR 0.5 ref			
CDR 1	0.891	0.284-2.793	.843
CDR 2	1.890	0.557-6.409	.307
$2Y\Delta CDR-SB$			
CDR 0.5 ref			
CDR 1	1.556	0.454-5.330	.482
CDR 2	3.500	0.991-12.35	.052

95% Cl=95% confidence intervals, CDR=Clinical Dementia Rating, CDR-SB=CDR scale Sum of Boxes, MMSE=Mini-Mental State Examination, OR=odds ratio,  $\Delta$ CDR-SB=change of CDR-SB scores in follow-up,  $\Delta$ MMSE=change of MMSE scores in follow-up.

" P<.05, statistically significant.

factor for cognitive preservation (adjusted OR=3.316, 95% CI=1.135-9.687, P=.028) in 2-year follow-up in Korea. By CDR-SB, lower level of education was associated with cognitive preservation in 1-year follow-up in Korea.

#### 4. Discussion

We report on the cross-national difference of sociobehavioral factors for cognitive preservation in AD between Taiwan and Korean populations in a uniform manner. It demonstrated that cognitive preservation was associated with independence in the Taiwanese population, whereas cognitive preservation was related to living alone in the Korean population.

For age, there was no difference between participants in both country samples. For gender, females were predominant among both country patients (69.4% in Taiwan and 75.3% in Korea). This reflected the fact that AD was predominant in females, which is consistent with previous studies.<sup>[26–28]</sup> Sociobehavioral factors, including levels of education, living situation, and level of independence, as well as baseline CDR staging were different between the 2 countries, and this might be due to the existing selection bias in recruiting the participants of AD and the limited case numbers in Korea.

The MMSE and CDR-SB in the recruited AD participants for the cognitive function evaluation in continuous follow-up for 2 years revealed progressive disease course in AD, with the MMSE scores being grossly proportional to the CDR-SB in the 2 countries. As far as the role of levels of education is concerned, it revealed inconsistent effect in cognitive preservation by MMSE and CDR-SB in the Taiwan population and by CDR-SB in that of Korea, so the role of levels of education in cognitive preservation remains inconclusive. Williams et al<sup>[16]</sup> concluded that higher levels of education decreased the risk of AD and had no association with cognitive decline in the literature review. Baumgart et al<sup>[17]</sup> identified years of formal education decreased the risk of dementia and cognitive function with a strong level of evidence.<sup>[29,30]</sup> Furthermore, the discrepancies of role of levels of education in our study might result from MMSE being influenced by cultural background, education, and age<sup>[31-33]</sup> therefore, the comparison of the impact of education duration in cognitive preservation by CDR-SB and MMSE could be disproportional in our study.

As for marital status, it is important for the clinical course of dementia, as it affects the survival condition of patients with dementia.<sup>[34]</sup> Previous studies found that AD patients will become institutionalized more rapidly if the caregiver is not the spouse.<sup>[35]</sup> In our study, we found that only 55.1% of AD participants in Taiwan and 51.9% of the AD participants in Korea were currently married. These findings emphasize the burden for both countries in caring for AD patients due to marital status. Sommerlad et al<sup>[36]</sup> conducted a systematic review and meta-analysis of observational studies, concluding being married is associated with a reduced risk of dementia than lifelong single people or being widowed, and this is underdiagnosed in routine clinical practice. Social isolation was identified as a risk factor for dementia by Livingston et al<sup>[18]</sup>; therefore, social isolation due to unmarried status might contribute to the development of dementia.<sup>[37]</sup> Sjöberg et al<sup>[38]</sup> concluded marital status and living situation both had the potential to buffer the detrimental effects of low mood on dementia onset.

Despite this, there appears to be no direct evidence so far pointing out marital status in association with cognitive decline in AD.<sup>[16,17]</sup> Nevertheless, education, physical health, and enhancing social engagement as modifiable risk factors should be highlighted for dementia prevention in unmarried people. Overall, marital status showed no association with cognitive preservation in 2-year follow-up in our study. Further studies are needed to clarify the correlation.

Our finding identified independence was associated with cognitive preservation for AD participants in Taiwan, whereas living alone was associated with cognitive preservation for AD participants in Korea. The level of independence could reflect the disease severity and capacity of physical activity. In our study, a high majority of patients (66.7% in Taiwan and 80.5% in Korea) were independent, and a smaller part of them (13% in Taiwan and 13% in Korea) needed assistance for complex activities. It could be explained partly by most of our recruited AD participants being classified as mild to moderate stages (for CDR 1 and CDR 2, 80.9% in Taiwan and 59.8% in Korea). Most of our participants were hospital-based, so that participants at a severe stage would be less likely to be recruited in our study. The higher level of independence reflected less severity of dementia and higher capacity of physical activity.<sup>[36]</sup> The exercise and physical activity had beneficial effects on depression symptoms, and lessened the impact of depression on cognitive decline and AD. Thus, the finding of independence in association with cognitive preservation is predictable for AD participants in Taiwan in the study. Similar findings were determined for living status, where the family home was the most popular residence type for AD participants in Taiwan (91.0%), including living with a spouse or partner, with friends, relatives, or children, with a group, or at a nursing home with a caregiver. On the contrary, 24.7% of AD participants in Korea had residence type as living alone. Sjöberg et al<sup>[39]</sup> concluded marital status and living situation have the potential to buffer the detrimental effects of low mood on dementia onset, whereas our study showed living alone was associated with cognitive preservation for AD patients in Korea population. Living alone, on the contrary, might represent adequate available physical activities and capability of self-caring.

To some extent, it promoted cognitive preservation in the longterm follow-up in our study. Although living alone might lead to some kind of social isolation and depression, the cultural and economic effects should be considered to evaluate their effects in cognitive function. The study in Korea showed that living alone was susceptible to cognitive impairment and depression, influenced by factors, including the number of daily meals, social contact, and self-perceived health status.<sup>[40]</sup> If ongoing community interest and support was practiced, these were helpful in lessening the negative impact of living alone. Another study in Korea with participants mainly recruited from Seoul Special City concluded that economic resources were more important than health and social ties for alleviating the negative impact of living alone on the development of depressive symptoms in older widows.<sup>[41]</sup> With adequate socioeconomic support, it is explainable that living alone is associated with cognitive preservation for AD patients in Korea.

In our study, we evaluated the cognitive function using MMSE, CDR, and CDR-SB. MMSE has both validity and reliability for the diagnosis and longitudinal assessment of AD. The advantages for the MMSE include requiring no specialized equipment, short administration period, and ease of use,<sup>[42]</sup> while the limitations include being affected by demographic factors such as age, education, and cultural background; besides, MMSE lacks adequate sensitivity to discriminate MCI and mild AD from normal individuals.<sup>[43]</sup> CDR is credited with being able to discern very mild impairments, provides early and accurate diagnosis of dementia, and appears to be a reliable and valid tool for assessing and staging dementia, which is essential to proper clinical care of AD.<sup>[44]</sup> The disadvantages of CDR include taking a large amount of time, reliance on subjective assessment, and inability to capture changes over time.<sup>[45]</sup> The CDR-SB is extended from the CDR score for dementia staging, and owing to the increased range of values, the CDR-SB offers several advantages over the CDR score, including increased utility in accurately staging AD patients and tracking changes within and between stages of dementia severity. CDR-SB did not analyze other forms of mild dementia syndromes such as frontotemporal dementia or Parkinson disease, and although CDR-SB can discriminate between patients with very early AD and those with MCI, it is impossible to use CDR due to the nature of the scale.<sup>[46]</sup>

Our study has several strengths in providing useful information for cognitive preservation in AD patients. First, this is the first cross-national study to report the sociobehavioral factors for cognitive preservation between 2 countries with similar current social developments with continuous 2- year follow-up. Second, we used the UDS, which can connect and collaborate with Western society so that the data could be compared, and it would be helpful in upcoming dementia care in enhancing cognitive preservation for AD patients.<sup>[23]</sup>

Although our finding is encouraging, it has some limitations. First, sampling selection bias is present in the study and it is difficult to perform a randomized sampling study to register AD patients in both countries. Besides, there was a great difference in the numbers of participants (503 participants in Taiwan and 77 participants in Korea), which may have led to results bias. Second, not all of the recruited subjects were randomized to represent the typical dementia profiles in 2 countries. Country or society-specific characteristics of caregivers or informants in relation to disease severity could be related to many other socioeconomic statuses, which could be examined in another comprehensively randomized sampling study. Besides, medical services are affordable to people in higher socioeconomic societies and thus have an influence in cognitive preservation. Third, we only focused on the sociobehavioral factors, and did not address possible risk factors for cognitive decline and AD for analysis such as Apolipoprotein E gene with allele £4 genotyping (APOEɛ4), traumatic brain injuries, lifestyle, depression, medication history, and family history.<sup>[16,17]</sup> Besides, vascular risk factors possibly resulting in vascular dementia such as diabetes, hypertension, or previous stroke events were not presented in our study.<sup>[47]</sup> If possible, more large-scale studies using UDS to provide more updated information with multi-country involvement should be encouraged to explore the prevention of cognitive decline for AD in the Asian area.

# 5. Conclusion

Our study demonstrated that cognitive preservation was associated with independence in the Taiwanese population, whereas cognitive preservation was related to living alone in the Korean population. The levels of education showed inconsistency in cognitive preservation in both countries. By practicing relevant socioeconomic support systems, this might contribute in lessening the negative impact of dementia and preserving population cognition in different countries.

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## Author contributions

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