# **Original Article**

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# The Effects of Social Activities and Living Arrangements on Cognitive Functions in Middle-aged and Elderly Adults: A Panel Study Using the 2006-2018 Korean Longitudinal Study of Aging

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**Objectives:** Previous studies have shown that participation in social activities (SA) can prevent cognitive decline (CD) and that living arrangements (LA) can affect cognitive function. This study aimed to evaluate the effects of SA and LA on CD, as well as their interactions, using longitudinal data.

**Methods:** Data were used from the 2006-2018 Korean Longitudinal Study for Aging, which followed 10 254 adults older than 45 years over a 12-year period. CD was defined as a  $\geq$ 4-point score decrease in the Mini-Mental Status Exam over 2 years. We developed an extended Cox proportional hazards model for time-dependent covariates to estimate the hazard ratio (HR) of CD in 4 groups: (1) socially active and living with others, (2) socially active and living alone, (3) socially inactive and living with others (SILO), and (4) socially inactive and living alone (SILA). The model was stratified by gender and adjusted for important confounders.

**Results:** The HR of CD was significantly higher in the SILO group in men (HR,1.36; 95% confidence interval [CI], 1.08 to 1.78) and in the SILA group in women (HR, 1.72; 95% CI, 1.08 to 2.75). However, the interaction term for gender was not significant.

**Conclusions:** Among socially inactive elderly adults, the HR of CD was elevated in men who lived with others and in women who lived alone, although the interaction term for gender was not significant. Socially inactive men who live with others and socially inactive women who live alone are particularly encouraged to participate in SA to prevent CD.

Key words: Dementia, Cognitive decline, Mini-Mental State Examination, Social activities, Living arrangements

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# **INTRODUCTION**

Dementia causes cognitive decline (CD) and behavioral problems and is a growing public health issue in an aging society. The prevalence of dementia increases worldwide with age, (e.g., 24% of people in their 70s and up to 40% of those >90 years) [1]. The prevalence of dementia in Korea is estimated to be 9.2% in those  $\geq$ 65 years, and the age-specific prevalence of dementia doubles with each 5.8-year age in-

crease [2]. In Korea, the burden of disease due to dementia is 5117 per 100 000 in the elderly population ( $\geq$ 65 years old), which accounted for 4.5% of the total burden of disease in 2008 [3]. Alzheimer disease comprises 70% of cases of dementia, followed by vascular dementia [4]. Brain tissue damage in Alzheimer disease or vascular dementia is irreversible, and most drugs have been unsuccessful in reversing brain tissue damage [5]. Thus, prevention and screening for dementia are important at the current stage of drug development [6].

Risk factors of dementia include lifestyle, environmental factors, comorbidities, and genetic factors [7]. In addition, active involvement in physical and mental activities is known to lower the risk of dementia [8]. Participation in social activities (SA) is widely known as a protective factor against CD in the elderly. A Japanese study following 13 984 adults for 9.4 years showed that community group activities and employment lowered the risk of dementia [9]. A Korean study using data from the 2006-2012 Korean Longitudinal Study for Aging (KLoSA) suggested that participation in religious activities, social gatherings, school/hometown alumni groups, or grand family associations was effective in maintaining cognitive functions in adults older than 45 years [5]. Previous studies have also reported that social networks had a role in preventing dementia [10,11], and that social isolation might increase the risk of Alzheimer disease [12]. A systematic review of 10 cross-sectional or longitudinal studies showed that increased loneliness was associated with lower cognitive function [13]. Living arrangements (LA) could also influence cognitive functions in the elderly; elderly adults living in more complex family types are more protected from CD than elderly adults living in simple family types or living alone [8]. In Korea, the number of elderly adults living alone has increased from 1.27 million in 2016 to 1.58 million in 2020, increasing by 25% over 4 years [14]. According to the Korea Employment Information System, elderly adults who live alone showed lower cognitive function than elderly adults living with family members [15].

However, it is not clear how participation in SA and LA interact with each other to affect cognitive function in the elderly. For example, the effect of not participating in SA on CD might be exacerbated by living alone. Thus, the hypothesis was made that not participating in SA would increase the risk of CD, and that living alone would negatively compound this effect. Although most studies analyzing the effects of participation in SA on CD had longitudinal designs [5,16,17], they used linear mixed models [5,16] or simple logistic models [17]. Studies regarding LA often used cross-sectional designs [15]. Thus, the possibility of reverse causation could not be excluded in these studies. This study used survival analysis, in which individuals who showed signs of CD were excluded at each wave, to help overcome the problem of reverse causation.

#### **METHODS**

#### **Study Participants**

Data were used from the 2006-2018 KLoSA, an ongoing study that recruited 10 254 panel participants older than 45 years in 2006, who were followed up every year to study various aspects of aging in Korea. Skilled personnel interviewed study participants using computer data entry. In even-numbered years, the study collected information about the various aspects of aging including demographics, family relationships, health, occupation, employment, income, and assets, and the study covered specific topics in depth in odd-numbered years. The data from even-numbered years were included in 7 waves from 2006 to 2018.

Study participants whose Mini-Mental Status Exam (MMSE) scores were  $\leq$  23 (n=2449) were excluded at the baseline, and only the participants who showed within-normal-range cognitive functions as measured by the MMSE were included. Individuals with missing MMSE values were further excluded (n=237), resulting in 7568 participants as the baseline. After follow-up from 6 waves (from wave 2 to wave 7), 4622 participants were left in wave 7, and the average follow-up rate was 92.5% (Supplemental Material 1).

#### **Variables of Interest**

Included in SA were: participation in religious activities, social gatherings, sports/cultural/leisure clubs, college programs for elderly adults, school/hometown alumni groups, grand family associations, volunteer activities, political party activities, civil organizations, or interest groups. If an individual participated in at least 1 of the above activities, he or she was considered *socially active*. If a study participant replied that he or she did not participate in any SA, including the activities listed above, then he or she was considered *socially inactive*. LA was defined by the type of family with whom a participant lived; if the participant lived with family members or any other persons, he or she was defined as *living with others*. Otherwise, participants were defined as *living alone*. Both SA and LA were

considered as variables with time-varying effects, as they changed over the follow-up period.

CD was defined by a decrease in the MMSE score of  $\geq 4$ points in the course of a 2-year period. The MMSE is a screening tool widely used in primary healthcare settings to evaluate cognitive functions in individuals with suspected CD. It is composed of 7 categories with 11 questions or tasks and evaluates cognition for time, place, and person; memory of 3 objects; attention; calculation; recall of the 3 objects; and verbal and visual capacities [18]. An MMSE score  $\leq$  17 indicates dementia, and an MMSE score of 18-23 indicates mild cognitive impairment. The MMSE is the most widely used tool for dementia screening [19]. However, the screening result is affected by the age, gender, and education level of the examinee. Moreover, in a panel study, the MMSE score is a time-varying variable as participants age over the follow-up period. Thus, a variable that could represent the change in cognitive functions over time was more desirable. Jongstra et al. [20] reported that the odds ratio of developing dementia was 3.55 (95% confidence interval [CI], 2.51 to 5.00) for elderly populations in primary care who showed a  $\geq$  2 point decline in the MMSE score over 2 years. However, according to the study by Hensel et al. [21], changes in the range of 2-4 points over 1.5 years were necessary to conclude that an individual experienced a true change (90% confidence) in MMSE results. Thus, we defined CD as a  $\geq$ 4 point decrease in the MMSE score over 2 years to identify individuals showing substantial changes in MMSE scores.

Covariates included: gender, age groups (45-54, 55-64, 65-74, 75-84, and  $\geq$  85 years), education level (elementary school attendance/graduates, middle school attendance/graduates, high school attendance/graduates, college attendance/graduates, and graduate school attendance/graduates), annual house-hold income levels (quintile: <6 810 000, 6 810 000-17 999 999, 18 000 000-29 999 999, 30 000 000-49 999 999,  $\geq$  50 000 000 Korean won [KRW]/y)(1000 KRW is equivalent to 0.85 USD), tobacco smoking (currently smoking or not), alcohol consumption (currently drinking or not), the number of comorbidities (diabetes, cancer, lung diseases, liver diseases, heart diseases, cerebrovascular diseases, neuropsychiatric diseases, and arthritis), and depression (had depressive mood for longer than 2 weeks in the past year or took an anti-depressant).

#### **Statistical Analysis**

In wave 1, comparisons were made of the following variables: presence of CD, MMSE scores, gender, age groups, education

levels, annual household incomes, smoking, alcohol consumption, the number of comorbidities, and the presence of depression by combining SA and LA. This was done by creating 4 groups: (1) those participating in at least 1 type of social activity and living with at least 1 or more persons; socially active, living with others (SALO), (2) socially active, living alone (SALA), (3) not participating in any SA and living with others; socially inactive, living with others (SILO), and (4) socially inactive, living alone (SILA).

Kaplan-Meier (K-M) plots were generated in wave 1 to compare the proportions without CD, maintaining MMSE scores >17 and MMSE scores >23, according to participation in SA and LA, using the 4 groups (SALO, SALA, SILO, SILA).

Once a participant experienced an initial event of CD, then the participant was censored and excluded from further analysis. SA, LA, and combinations of SA and LA varied throughout the waves; thus, the extended Cox proportional hazards model for time-dependent covariates (TDC) was used to estimate the hazard ratio (HR) of CD by SA, LA, and the combination of SA and LA. All the Cox models were based on the extended Cox model for TDC throughout this study. The model was adjusted for gender, age groups, education levels, annual household income, smoking, alcohol consumption, the number of comorbidities, and the presence of depression as defined earlier. The same analysis was repeated by stratifying the population into men and women. The significance of differences between men and women was expressed as a p-value of the interaction term for gender. We analyzed the HR of CD, scores  $\leq$  17, and scores of 18-23 on the MMSE by participation in SA, LA, and the combination of SA and LA, adjusting for the same covariates and stratified for gender.

Stratified HRs were also estimated for age groups and education levels; age groups were divided into young (<65 years old) and old ( $\geq$ 65 years old), and education levels were divided into low (middle school graduate or lower) and high (high school attendance or higher). Interaction terms for the age groups (young vs. old) and education levels (high vs. low) were considered when testing for the significance of any differences in HR of CD according to age group or education level. For sensitivity analysis, we defined *socially active* as being involved in SA more than once a month, and then analyzed the data using the Cox model, stratified by gender.

The 'survival' R package (https://cran.r-project.org/) was used to analyze extended Cox models for TDC, and 'survminer' (https:// cran.r-project.org/) was used to create K-M plots. We consid-

#### Table 1. Summary statistics for study variables<sup>1</sup>

Variables		Socially active, living with others	Socially active, living alone	Socially inactive, living with others	Socially inactive, living alone
No. of participants	Wave 1	5475	306	1627	160
	Wave 2	4861	337	960	143
	Wave 3	4249	321	1003	139
	Wave 4	4115	345	889	156
	Wave 5	3820	418	754	162
	Wave 6	3479	422	835	198
	Wave 7	3301	438	681	202
MMSE score	Wave 1	28.0±1.8	27.2±2.0	27.9±2.0	$27.2 \pm 2.0$
	Wave 2	27.3±2.9	26.5±3.0	25.6±4.4	$24.8 \pm 4.4$
	Wave 3	27.3±3.2	25.8±4.2	25.0±4.8	$24.4 \pm 5.2$
	Wave 4	27.4±3.1	26.0±4.3	24.9±5.1	$24.2 \pm 5.2$
	Wave 5	$27.2 \pm 3.4$	25.4±4.7	$23.9 \pm 6.0$	$23.1 \pm 6.1$
	Wave 6	$27.2 \pm 3.4$	25.6±4.1	23.7±5.8	$23.6 \pm 5.3$
	Wave 7	$26.9 \pm 3.8$	$25.4 \pm 4.7$	22.8±6.7	$22.5 \pm 6.3$
Cognitive decline <sup>2</sup>	Wave 2	644 (13.2)	51 (15.0)	209 (21.8)	43 (30.1)
	Wave 3	393 (9.2)	52 (16.2)	188 (18.7)	32 (23.0)
	Wave 4	376 (9.1)	42 (12.2)	137 (15.4)	22 (14.1)
	Wave 5	465 (12.2)	77 (18.4)	161 (21.4)	35 (21.6)
	Wave 6	344 (9.9)	54 (12.8)	159 (19.0)	28 (14.1)
	Wave 7	365 (11.1)	66 (15.1)	176 (25.8)	49 (24.3)
Gender	Men	2784 (50.8)	63 (20.6)	817 (50.2)	50 (31.3)
	Women	2691 (49.2)	243 (79.4)	810 (49.8)	110 (68.8)
Age (y)	45-54	2420 (44.2)	55 (18.0)	565 (34.7)	25 (15.6)
	55-64	1694 (30.9)	85 (27.8)	482 (29.6)	44 (27.5)
	65-74	1079 (19.7)	123 (40.2)	438 (26.9)	67 (41.9)
	75-84	268 (4.89)	39 (12.7)	131 (8.1)	21 (13.1)
	≥85	14 (0.3)	4 (1.3)	11 (0.7)	3 (1.9)
Education levels	Elementary school	1500 (27.5)	175 (57.2)	700 (43.1)	101 (63.1)
	, Middle school	1107 (20.3)	51 (16.7)	326 (20.1)	27 (16.9)
	High school	1961 (36.0)	58 (19.0)	453 (27.9)	23 (14.4)
	College or more	880 (16.2)	22 (7.2)	146 (9.0)	9 (5.6)
Annual household income (10 <sup>4</sup> KRW)	Q1 (<1000)	1652 (31.6)	167 (66.0)	737 (47.4)	111 (86.7)
	Q2 (1000-2100)	1121 (21.4)	54 (21.3)	385 (24.7)	11 (8.6)
	Q3 (2101-3619)	1355 (25.9)	22 (8.7)	258 (16.6)	4 (3.1)
	04 (≥3620)	1103 (21.1)	10 (4.0)	176 (11.3)	2 (1.6)
Smoking	Yes	1735 (31.7)	57 (18.6)	583 (35.8)	47 (29.4)
	No	3740 (68.3)	249 (81.4)	1044 (64.2)	113 (70.6)
Alcohol consumption	Yes	2423 (44.3)	90 (29.4)	643 (39.5)	50 (31.3)
	No	3052 (55.7)	216 (70.6)	984 (60.5)	110 (68.8)
No. of comorbidities	0	3309 (60.4)	117 (38.2)	918 (56.4)	62 (38.8)
	1	1470 (26.8)	112 (36.6)	420 (25.8)	60 (37.5)
	2	513 (9.5)	47 (15.4)	200 (12.3)	22 (13.8)
	≥3	183 (3.3)	30 (9.8)	89 (5.5)	16 (10.0)
Depression	Yes	5057 (92.4)	258 (84.3)	1444 (88.8)	118 (73.8)
· F · = = = = = = = = = = = = = = = = =	No	418 (7.6)	48 (15.7)	183 (11.3)	42 (26.3)

Values are presented as mean  $\pm$  standard deviation or number (%).

MMSE, Mini-Mental Status Exam; KRW, Korean won.

<sup>1</sup>Percentage of MMSE categories at wave 6 according to variables at wave 1. <sup>2</sup>Number of participants who experienced a decline in MMSE score of  $\geq$  4 points over the last 2 years.

ered *p*-values <0.05 to indicate statistical significance. SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R software version 3.2.1 (https://cran.r-project.org/) were used for statistical analyses.

#### **Ethics Statement**

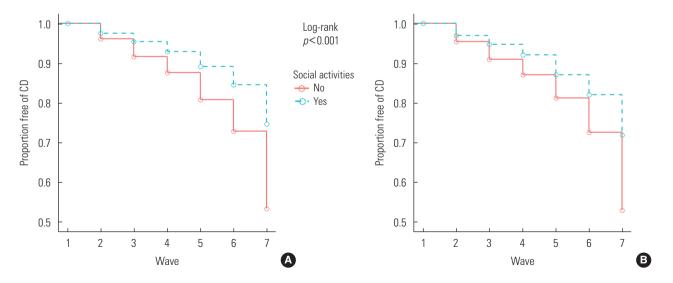
KLoSA data are deidentified and publicly available; thus, ethical review was not required.

#### RESULTS

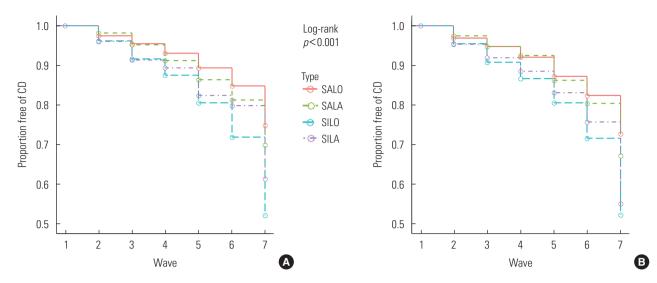
The general characteristics of study participants were analyzed using the SA and LA combinations as described in the Methods section (Table 1). The number of participants increased in the living alone groups (SALA and SILA) from 306 in wave 1 to 438 in wave 7. The individuals in the SALO group showed the highest MMSE scores throughout the study period from 2006 to 2018, followed by the SALA, SILO, and SILA groups. The proportion of participants who experienced CD was lowest in the SALO group, followed by the SALA, SILO, and SILA groups. The proportions of women were greater in the SALA and SILA groups than in the SALO and SILO groups. The proportion of participants with low education levels was found to be greater in the groups living alone (SALA and SILA) than in the groups living with others (SALO and SILO).

MMSE scores were relatively high in individuals who participated in SA compared to those who did not (Supplemental Material 2). K-M plots showed that the proportion of individuals without CD was greater in both men and women who were socially active (Figure 1), but not significantly different according to LA (Supplemental Material 3). In Figure 2, the proportion of individuals without CD was highest in the SALO group, followed by the SALA, SILA, and SALO groups for both men and women. The extended Cox proportional hazards model for TDC showed that the HR of CD was higher in individuals not participating in SA (Table 2). When stratified by gender, the HR was higher in the socially inactive groups for both men (HR, 1.33; 95% Cl, 1.06 to 1.66) and women (HR, 1.23; 95% Cl, 0.99 to 1.55), but it was significant only in men. The interaction term for gender was not significant. The HR of scoring <17 or 18-23 on the MMSE was elevated in the socially inactive groups for both men and women (Supplemental Material 4). The HR of CD was higher in the SILO group (HR, 1.24; 95% CI, 1.05 to 1.47) and the SILA group (HR, 1.59; 95% CI, 1.09 to 2.34) (Table 3). When stratified by gender, the HR was significantly higher in the SILO group for men only (HR, 1.36; 95% CI, 1.08 to 1.72), while the HR was significantly higher in the SILA group for women only (HR, 1.72; 95% CI, 1.08 to 2.75). However, the interaction term for gender was not significant. The risk of scoring  $\leq$  17 or 18-23 on the MMSE was higher in the SILO group for both men and women (Supplemental Material 5).

The HR of CD in socially inactive participants was significantly higher among those  $\geq$ 65 years (Supplemental Material 6) and those with low education levels (middle school graduates or lower), but not in participants <65 years or those with



**Figure 1.** Kaplan-Meier plot of the proportion of individuals showing cognitive decline (CD) over 7 waves (12 years) in socially active (A) and inactive (B) individuals.



**Figure 2.** Kaplan-Meier plot of the proportion of individuals showing cognitive decline (CD) over 7 waves (12 years) in men (A) and women (B). SALO, socially active and living with others; SALA, socially active and living alone; SILO, socially inactive and living alone.

Factors	Total	<i>p</i> -value	Men	<i>p</i> -value	Women	<i>p</i> -value	Gender interaction ( <i>p</i> -value )
Socially active	1.00 (reference)		1.00 (reference)		1.00 (reference)		
Social inactive	1.28 (1.10, 1.51)	0.002	1.33 (1.06, 1.66)	0.014	1.23 (0.99, 1.55)	0.067	0.518
Living with others	1.00 (reference)		1.00 (reference)		1.00 (reference)		
Living alone	1.05 (0.82, 1.34)	0.677	1.27 (0.77, 2.09)	0.343	0.98 (0.72, 1.33)	0.885	0.373

Values are presented as hazard ratio (95% confidence interval).

<sup>1</sup>Definition of cognitive decline: Mini-Mental Status Exam score decrease of  $\geq$ 4 points over 2 years.

<sup>2</sup>Adjusted for gender, age group, education levels, annual household income, smoking, alcohol consumption, comorbidity, depression.

#### Table 3. Hazard ratios and 95% confidence intervals of cognitive decline<sup>1</sup> by social activities and living arrangements<sup>2</sup>

Factors	Total	<i>p</i> -value	Men	<i>p</i> -value	Women	<i>p</i> -value	Gender interaction ( <i>p</i> -value )
Socially active, living with others	1.00 (reference)		1.00 (reference)		1.00 (reference)		
Socially active, living alone	0.94 (0.70, 1.28)	0.712	1.27 (0.77, 2.09)	0.343	0.79 (0.54, 1.17)	0.242	0.128
Socially inactive, living with others	1.24 (1.05, 1.47)	0.013	1.36 (1.08, 1.72)	0.010	1.21 (0.88, 1.44)	0.364	0.233
Socially inactive, living alone	1.59 (1.09, 2.34)	0.017	1.20 (0.61, 2.39)	0.595	1.72 (1.08, 2.75)	0.023	0.616

Values are presented as hazard ratio (95% confidence interval).

Significance level: *p*-value < 0.016 by the Bonferroni correction.

<sup>1</sup>Definition of cognitive decline: Mini-Mental Status Exam score decrease  $\geq$  4 over 2 years.

<sup>2</sup>Adjusted for gender, age group, education levels, annual household income, smoking, alcohol consumption, comorbidity, depression.

high education levels. The HR of CD was elevated in both the SILO and SILA groups for participants  $\geq$  65 years and those with low education levels (Supplemental Material 7). A sensitivity analysis showed that defining SA as participation in SA more than once a month did not change the overall results (Supplemental Material 8).

#### DISCUSSION

CD was investigated using data from the KLoSA study over 12 years of follow-up considering the subjects' participation in SA and their LA (i.e., living with others or alone). Not participating in SA showed a greater risk of CD overall. Among socially inactive elderly adults, the HR of CD was highest in men who lived with others and in women who lived alone.

The starting hypothesis was that the SILA group would experience CD faster than other groups; interestingly, not only SILA, but also SILO was associated with an increased risk of CD. Furthermore, the increase in the HR of CD was significant only in the SILO group for men and in the SILA group for women, although the gender difference was not significant. In other words, among socially inactive elderly adults, men tended to have a greater risk of CD when living with others, while women tended to have a greater risk of CD when living alone.

Despite an assumption that elderly adults living alone are at a disadvantage when it comes to cognitive stimulation, previous studies have shown that living alone is not associated with poor cognitive function [22,23]. The study by Evans et al. [22] reported that elderly adults living alone are not at greater risk of poor cognitive function, either at baseline or after follow-up for two years. Living alone may actually stimulate cognitive functions, in that people who live alone are responsible for managing their own lives, using skills such as paying bills, shopping, and maintenance, which require cognitive input [22,24]. People who live alone and are not able to manage themselves independently usually move into a care home. These people, living with others, are likely to be less responsible for household tasks and play relatively passive roles [22,25]. For women, however, the risk of CD was elevated in the SILA group rather than in the SILO group. This could be due to the fact that the proportion of women was greater in the SILA group (68.8%) than in the SILO group (49.8%), and individuals in the SILA group tended to be older than those in the SILO group (Table 1). Another possibility is that, among socially inactive individuals, elderly men are more likely to be cared for by their family members and less active when living with others, whereas elderly women are more likely to care for their spouse and family [26], and thus may be more active when living with others. The risk of CD according to SA and LA appears to be different between men and women, probably because of differing gender roles. Therefore, further studies are warranted to analyze the effects of gender roles on CD.

The major strength of this study is that it followed the study participants over the course of 12 years. Dementia progresses over a long period of time; for example, Alzheimer disease can take 10 years to 15 years for cognitive symptoms to become apparent as beta-amyloid aggregation progresses in brain tissue [27]. Another strength of this study is that it used survival analysis to estimate the effects of SA and LA on CD, so that individuals who present signs of CD can be excluded, thereby mitigating the risk of reverse causation. This study also investigated the interaction between participation in SA and type of LA, and offers useful insights for developing specific policies or strategies. For example, elderly men living with others and elderly women living alone, in particular, should be encouraged to participate in SA. Additionally, this study showed that adults  $\geq$  65 years and the elderly with low educational levels were more susceptible to CD; thus, these groups should receive particular attention in CD prevention policies.

This study has several limitations. First, although SA included religious activities, social gatherings, sports/cultural/leisure clubs, and college programs for the elderly, the effects of specific types of SA on CD were not studied in detail. Second, this study did not fully account for the frequency of SA. Although the sensitivity analysis showed that defining SA as participation in SA more than once a month did not change the overall results (Supplemental Material 8), the differential effects of SA frequency were still probable, though not examined in this study. Third, although this study used survival analysis, the possibility of reverse causation cannot be excluded completely, as the participants were followed up biennially and important events in the intervening period may not have been captured. For example, a participant could have developed symptoms of CD before he or she was evaluated and determined to have CD. In such a case, families might have protected them from outside activities or the participants might have isolated themselves from SA. However, this type of situation is limited within a 2-year period, and as individuals are censored immediately after determination of CD, the effect of reverse causation is considered to be minimized. In this study, by using KLoSA data from 2006 to 2018, it was shown that middle-aged and elderly adults who did not participate in SA had a greater risk of CD. Among individuals who did not participate in any SA, individuals living with others showed a greater risk of CD in men, and those living alone showed a greater risk of CD in women. This suggests that socially inactive men living with others and socially inactive women living alone would particularly benefit from participation in SA.

### SUPPLEMENTAL MATERIALS

Supplemental materials are available at https://doi.org/10. 3961/jpmph.20.384.

# **CONFLICT OF INTEREST**

The authors have no conflicts of interest associated with the material presented in this paper.

## **FUNDING**

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# **AUTHOR CONTRIBUTIONS**

Conceptualization: YJC, YKD. Data curation: YJC, Formal analysis: YJC, Funding acquisition: None. Writing – original draft: YJC, YKD. Writing – review and editing: YJC, YKD, YCH.

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