

Research article

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**Influence of social support on cognitive function in the elderly**Shu-Chuan Jennifer Yeh \*<sup>1,2</sup> and Yea-Ying Liu<sup>1,3</sup>

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**Abstract**

**Background:** Social support is important in daily activities of the elderly. This study tests the hypothesis that there is an association between social support and cognitive function among the elderly in a community setting.

**Methods:** Face-to-face interviews were conducted in a cross-sectional stratified random sample of 4,993 elderly ( $\geq 65$  years) city residents. Using multiple regression analysis, we investigated the influence of social support on cognitive function.

**Results:** 12% were over 80 years old. 53.28% were men. 67.14% were married. Higher Short Portable Mental Status Questionnaire (SPMSQ) scores (higher score means better cognitive function) were associated with strong social support, as measured by marital status and perceived positive support from friends. Lower cognitive function was associated with older and with female respondents. Only instrumental activities of daily living (IADL) were statistically and negatively related to SPMSQ. Lower functional status was associated with lower cognitive function. Elders with grade school educations had lower SPMSQ scores than did elders with high school educations.

**Conclusions:** In Taiwan, higher cognitive function in community-living elderly was associated with increased social support. Life-style management should provide social activities for the elderly to promote a better quality of life.

**Background**

Social support is important in daily activities for the elderly living in community settings, and several studies have provided evidence of an association between social support and cognitive function. A socially engaging lifestyle is correlated with higher cognition scores in both community and nursing home settings [1,2]. Because social activities provide the challenge of effective communication and participation in complex interpersonal exchanges, social support has been thought to inhibit cognitive decline in the elderly [3].

A longitudinal study from Bassuk & colleagues (1999) found that elderly persons who had no social ties were at increased risk for cognitive decline, compared with those who had five or six social ties [4]. Using frequency of contact with friends and colleagues as an indicator for social support, Boult & colleagues found that social support was associated with a reduced risk of developing disability up to 4 years later [5]. Research has also shown that social role involvement and personal control were factors not only in slowing age-related decline in physical health, but also in reducing levels of ADL disability [6]. In a prospective cohort study that followed 1,203 non-demented aged

75 and over for 3 years, Fratiglioni and colleagues (2000) found that a social network reduced the incidence of dementia [7].

Except for Fratiglioni et al.'s study, research regarding the cognitive status of the elderly and social support generally has been limited by sample size and by the absence of adjustment for potential confounders, such as education or health status. Because respondents were usually self-referred, selection bias in data collection has also been present.

The concept of social support has been difficult to measure. Several studies have used proxy indicators such as occupational status to make inferences about the effect of social activities on cognition [8,9]. Some have treated prior favorable socioeconomic status as synonymous with social activity in old age [10,11], while others have used composite activity scales as proxies for social engagement [1,4].

Loneliness has also been used to predict mental status, including depression [12]. However, loneliness is subjective and not synonymous with objective social isolation. A person may live alone with few social contacts and not feel lonely. In contrast, an individual surrounded by others may report a long-standing sense of loneliness. With respect to the elderly, a discrepancy between the social network and the need for social contact may cause loneliness [13–16]. Social contacts and perceived social support from family members, friends and acquaintances are important for fulfillment of different social needs. Although one study indicated that ADL functions were associated with emotional and social loneliness [17], it did not examine the relationship between loneliness and cognitive function.

We examine the effect of social support on cognitive function in a large sample selected to represent a cross-section of the elderly population in Taiwan. By controlling for individual characteristics such as age, gender and health status, we investigated the association between social support and cognitive function in the elderly.

## Methods

### **Study sample**

In October 2000, we used stratified random sampling to collect data from all 11 districts in Kaohsiung City, southern Taiwan. An equal interval method randomly selected respondents from each district. Lists of residents  $\geq 65$  years old were obtained from Resident Registries, which contain the names, addresses, sex and ages of all city residents. The study was approved by the Research Ethics Committee of the Health Department of Kaohsiung City.

All elderly residents  $\geq 65$  years old living in the Kaohsiung area were included unless they were vegetative, stuporous, semi-comatose, suffering from dementia or other serious psychiatric diseases or had a serious spinal cord injury. Individuals with an unknown address or proxy respondents were excluded from final analysis.

Of 106,697 persons listed, a total of 6,367 questionnaires were sent out and from these 4,993 face-to-face interviews were completed successfully by trained registered nurses. The interviewers' training involved both a general introduction to survey interviewing and fieldwork techniques and procedures, and a review of the specific aspects of the study for which interviewers were responsible. Inter-rater reliability was measured by intraclass correlation coefficient (ICC) during the training stage. Correlation among raters was 0.827.

82 subjects were represented by proxy interviews with a close acquaintance or family member. Proxy respondents were not asked about self-perceived memory and were removed from the final analysis. Forty-six elders with serious psychiatric diseases were excluded. Forty-two elders died prior to the interview, and 742 were never contacted due to a change in residence or an unknown address. Four respondents were diagnosed with dementia during the study period. Seventy-six refused to participate. Over half of the data was missing for 386 respondents. These subjects were excluded from the final analysis. Final study sample contained 4,989 respondents with aged  $\geq 65$  years.

Around 12 percent of the elderly were over 80 years old, 53.28% were men, 67.14% were married, and 18.9% had at least a high school education. These percentages were representative of the overall elderly population in Kaohsiung [18]. Although distributions of gender ( $\chi^2 = 3.43$ ,  $p = .148$ ) and education ( $\chi^2 = 5.955$ ,  $p = .062$ ) in our study were similar to those of the entire elderly population in Taiwan, marital status ( $\chi^2 = 48.432$ ,  $p < .05$ ) and age (t-value = 15.26,  $p < .05$ ) were not.

## Measures

### **Dependent variable**

The dependent variable was cognitive status measured by the 10-item Short Portable Mental Status Questionnaire (SPMSQ). The SPMSQ was developed by Pfeiffer to assess mental status of the elderly. We chose SPMSQ to measure cognitive status because its brevity permitted assessment without taxing the endurance and capabilities of the least cognitively fit. Although public health nurses were pre-trained for conducting interviews, their formal neurologic training was not evaluated. However, Welch & West (1999) found that SPMSQ could be accurately applied by persons without formal neurologic training [19]. For all of

these reasons, we chose SPMSQ, even though MMSE has better sensitivity and specificity [20]. MMSE scores are also more easily affected by education, intelligence, age, CVA and social class.

The validity of SPMSQ in a Taiwanese population and in patients with organic brain syndrome has been established [21–24]. SPMSQ can assess the total range of performance from intact functioning despite severe impairment. Respondents were asked the questions and not allowed access to information or objects that might stimulate their memories. This test included 10 questions dealing with orientation, personal history, remote memory and calculations. Correct answers received 1 point each. A summary score was constructed by summing the 10 items, yielding a range from 0 to 10. Internal consistency of SPMSQ scale for this study was 0.98.

Missing items from cognitive tests are generally informative in the measurement of cognitive performance [25], and a "don't know" response is generally considered incorrect [11,26]. In this study, missing values in the SPMSQ were always considered incorrect answers.

#### *Independent variables*

Four measures of social support that reflected objective and subjective dimensions were examined. Marital status, measured by one dichotomous variable (married *vs.* non-married) was chosen because a spouse can be an important source of emotional and tangible support [27]. Perceived positive support from friends was measured by asking the respondent whether he had a good friend with whom to talk. Living alone was measured by one categorical variable (yes *vs.* no). Loneliness was measured by asking respondents to rank this feeling on a 3-point scale: 1 = strong, 2 = some and 3 = little.

#### *Control variables*

Social support might be related to SPMSQ because of its association with other factors known to be involved in the aging process. To reduce the possibility of spurious associations, we selected a set of control variables that have been empirically evaluated with respect to social relationships and SPMSQ [28–30].

#### *Socio-economic status*

Five socio-demographic variables were used. Age was the difference between date of birth and date of interview. Gender was defined as a dummy variable, with male coded as 0 and female as 1. Religion was categorized into 4 dummy variables: Traditional, Christian, Catholic and other, with Buddhist as the reference group. Occupation was classified into 5 dummy variables: blue collar, farmer, professional-administrator, retired and housewife, with white collar as the reference group. Education was catego-

rized into 2 dummy variables: grade school or below and college or above, with high school as the reference.

#### *Functional status*

Physical health status might affect social networks and social support, particularly if the interviewee considered disease, disability and self-rated health stressful [31]. Functional status was the ability to perform activities of daily living (ADL) and instrumental activities of daily living (IADL). Katz index of ADL was used to assess personal self-maintenance (bathing, dressing, toileting, transferring, continence and feeding) on a four-point scale: 0 = independent, 1 = semi-independent on devices (needs assistance by using devices), 2 = semi-independent on persons (needs assistance from persons) and 3 = totally dependent. Total score was produced by summing the scored items, yielding a range from 0 to 18. Internal consistency was  $\alpha = 0.95$ .

IADL are complex tasks such as traveling, shopping, preparing meals, doing housework and handling personal finances [32]. Unlike ADL, which is largely concerned with basic bodily maintenance, IADL deals with the execution of more complicated tasks that have a broad impact in linking social competency and independent living [33,34]. Therefore, IADL might be more useful than ADL in detecting disabilities in an elderly population [32]. Lower functional status has been assumed to limit opportunities for social contact by reducing interactions with family and friends outside the home [35] and by limiting social activities [36].

The self-reported functional status measure asked respondents if they were able to perform each IADL on their own: preparing meals, shopping, taking medicine, traveling out of walking distance, managing money or using the telephone. We used a three-point scale to measure the above six items: 0 = independent, 1 = semi-independent on devices (needs assistance by using devices), 2 = semi-independent on persons (needs assistance from persons) and 3 = totally dependent. Total score was produced by summing the scored items, yielding a range of 0 to 18. Internal consistency was  $\alpha = 0.91$ .

#### *Reported health conditions*

An interrelation among health condition variables (Parkinson's disease, heart disease, hypertension, chronic lung diseases, diabetes and stroke) and psychometric tests, such as SPMSQ, has been suggested. However, research regarding this interrelation has yielded inconclusive results [37–39]. We included several health conditions as dummy variables (1 = yes and 0 = no): hypertension, diabetes, vision, hearing, cancer and depression. We did not include dementia as a health condition because of its strong

**Table I: Description of sample response rates**

No. of questionnaires sent out	6367
No. interviews completed and suitable for analysis	4993 (78%)
Interviews not completed or excluded from analysis because of:	
Death	42
Not contactable (e.g. change of address)	742
Refusal	76
Excluded because of dementia	4
Excluded because of other serious psychiatric disease	46
Proxy interview only	82
Too many missing items on interview	386
Total interviews not completed or used in analysis	1378 (22%)

association with the dependent variable and because of its exclusion from the final analysis.

#### Analytic plan

Descriptive analyses were conducted to understand the study sample. Differences in SPMSQ were examined with respect to demographic variables. We also investigated the association between SPMSQ scores and all two-level demographic and health-related variables by using chi-square test. For multiple groups of demographic variables, one-way analysis of variances (ANOVA) was used to detect any differences in variance among groups. Once differences were confirmed, post-hoc analysis (Scheffe's test) was applied to evaluate specific group differences.

Multiple regression was used to regress SPMSQ scores on independent variables (social support) and all covariates to find significant indicators (used  $\alpha$  level at 0.05 and 0.01). Initial analyses included age, gender, religion, occupation and health-condition variables (e.g., diabetes and hypertension) as covariates to determine the relationship between individual characteristics, functional status, social support and SPMSQ. All analyses used SAS 8e statistical software.

#### Results

Table 1 describes the response rates of the study sample. We sent out 6,367 questionnaires. 4,993 interviews were valid, and 1,378 were invalid. Response rate was 78%.

Summary statistics for the study variables are displayed in Table 2. Mean age of participants was 73 years  $\pm$  5.49. Most subjects were married, perceived positive support from friends and felt lonely. 56% were Buddhists (56%). 33.93% were housewives. Around 20% were professional administrators. About 32 percent had hypertension and 0.6% had cancer. Average ADL and IADL scores (range 0–18) were 0.35 and 0.95, respectively. Mean SPMSQ score was 9.36 ( $\pm$  1.41), range 0–10.

SPMSQ scores were used to measure cognitive function (Table 3). Cognitive function in females was lower than in males. Unmarried elders had lower cognitive function than did married elders. Elderly who perceived positive support from friends had higher SPMSQ scores than those without such a perception. Most covariates showed differences in SPMSQ scores except for the following: living alone, diabetes, Parkinson's disease, depression, hearing and dental problems. Correlations between SPMSQ scores and 3 continuous variables (ADL, IADL and age) were statistically significant.

Regression results showed that higher SPMSQ scores were clearly associated with two groups: married elders ( $\beta = 0.13, p = 0.005$ ) and those who perceived positive support from friends ( $\beta = 0.11, p = 0.005$ ). Older ( $\beta = -0.03, p < .0001$ ) or female ( $\beta = -0.38, p < .0001$ ) respondents were more likely to have cognition problems as indicated by lower SPMSQ scores. Cognitive function of respondents who had a grade school education was lower in comparison with those who had a high school education ( $\beta = -0.22, p < .001$ ). Compared with white-collar workers, both farmers and blue-collar workers were negatively associated with SPMSQ scores ( $\beta = -0.61, p < .0001; \beta = -0.19, p = .016$ , respectively). IADL ( $\beta = -0.14, p < .0001$ ) was statistically and negatively related to SPMSQ. The association of ADL with cognitive function was not statistically significant. Two reported health conditions, depression ( $\beta = -0.79, p = 0.031$ ) and vision problems ( $\beta = -0.19, p = 0.017$ ), were associated with lower cognitive function (lower SPMSQ score). Other factors were not statistically significant. Overall model fit statistic (adjusted R<sup>2</sup>) was 0.2019 ( $F = 40.33; p < .0001$ ). Table 4 lists results for the full regression model.

#### Discussion

Our study examined primary data collected on an elderly population in Kaohsiung, Taiwan. The relationship between social support and cognitive function indicated that two out of the four measures of social support, mari-

**Table 2: Descriptive analyses for Kaohsiung elderly (n = 4,993)**

Variable	Frequency (%)	Mean (Std Dev)
Female <sup>+</sup>	2,330 (46.67)	
Education <sup>++</sup>		
Grade School or below (1)	4,037 (81.10)	
High School (2)	576 (11.57)	
College or above (3)	365 (7.33)	
Married <sup>+</sup>	3,345 (67.14)	
Perceives positive support <sup>+</sup>		
Yes	3,350 (71.92)	
No	1,308 (28.08)	
Feels lonely <sup>++</sup>		
Strong	2,844 (59.27)	
Some	1,708 (35.60)	
Little	246 (5.13)	
Lives alone		
Yes	427 (8.79)	
No	4,431 (91.21)	
Religion <sup>++</sup>		
Buddhist (1)	2,796 (56.0)	
Traditional (2)	1,111 (22.25)	
Christian (3)	247 (4.95)	
Catholic (4)	73 (1.46)	
Other (5)	651 (13.04)	
Occupation <sup>++</sup>		
White collar (1)	495 (9.91)	
Blue collar (2)	873 (17.48)	
Farmer (3)	267 (5.35)	
Prof-Admin (4)	998 (19.99)	
Retired (5)	610 (12.22)	
Housewife (6)	1,644 (33.93)	
Comorbidities <sup>+</sup>		
CVA	169 (3.38)	
Hypertension	1,592 (31.88)	
Cancer	28 (0.56)	
DM	391 (7.83)	
CHD	283 (5.67)	
Parkinson's	12 (0.24)	
Vision problem	308 (6.0)	
Hearing problem	56 (1.1)	
Dental problem	87 (1.7)	
ADL		0.35 (1.94)
IADL		0.95 (2.98)
Age		72.72 (5.49)
SPMSQ		9.36 (1.41)

Higher ADL or IADL scores indicate more functional dependency.

tal status and perceived positive support from friends, were statistically significant. These findings support our hypothesis that social support is an indicator of cognitive function in community-dwelling older adults. We suggest that interventions or activities that enhance social support would improve cognitive functions in the elderly.

Living alone and loneliness were not significantly associated with the SPMSQ scores. Our result regarding living

alone is similar to another study that used ADLs, IADLs, cognition and nursing home utilization as outcome indicators to investigate whether living alone influenced these outcomes [40]. It was determined that patients living alone after hospitalization were less likely to improve in physical function; however, no relationship with cognitive function was found.

Research on the association between loneliness and cognitive function is limited. Our results indicate that loneliness did not have a statistically significant influence on cognitive function. However, post-hoc analyses using Scheffe's method (Table 3) revealed that elders who felt very alone had higher SPMSQ scores than those who felt less lonely. Studies have indicated that there is a negative relationship between loneliness and social support [17,41,42]. Therefore, we believe that although loneliness can be associated with social support, it cannot predict all perspectives of mental status, including cognitive function.

Cognitive function was correlated with functional status in ways consistent with available knowledge. Because physical function may confound the association of social support and cognitive status, we controlled for ADL and IADL in the model. We found that functional status, particularly IADL, may have substantial impact on cognitive function (with partial R-square = 0.14, F-value = 699.48, p-value < .0001).

In summary, this study used data from a representative elderly community sample of substantial size in Taiwan. Respondents were not self-referred, thereby reducing referral bias. Our results confirm the findings of two earlier studies that found a positive association between social support and cognitive function [1,3]. In our study, marriage and perceived positive support from friends were significantly and positively associated with cognitive function. Loneliness and living alone were not significantly associated with cognitive function.

### Limitations

This and other similar studies are limited because the SPMSQ score (the only cognitive measure available for this analysis) may provide only attenuated information on memory and does not optimally detect mild cognitive deficits [29]. Some respondents who seemed cognitively intact may have been suffering from early-stage dementia [4]. Perhaps a more sophisticated neuropsychological test would be better measure for evaluating the relationship between cognition function and social support.

Although our study has a substantial representative sample, it is not a longitudinal study. Variables measured at a single point in time tend to be related more than those

**Table 3: Descriptive analyses for Kaohsiung elderly (n = 4,993)**

Variable	Mean (Std Dev)	t-value [F-value]	p-value	Scheffe's
Gender <sup>+</sup> : Female	9.07(1.63)			
Male	9.60(1.12)			
Education <sup>++</sup> : Grade School or below (1)	9.26(1.47)	[60.55]	< .0001	
High School (2)	9.80(0.76)			
College or above (3)	9.81(0.89)			
Marital Status <sup>+</sup> : Married	9.52(1.18)	-10.13	< .0001	
Unmarried	9.04(1.70)			
<b>Perceives positive support<sup>+</sup>: Yes</b>	9.46(1.24)	-4.60	< .0001	
No	9.23(1.56)			
Lives alone <sup>+</sup> :				
Yes	9.39(1.37)	-0.45	0.66	
No	9.36(1.39)			
Feels lonely <sup>+</sup>				
Strong (1)	9.49(1.25)	[33.16]	< .0001	1>2
Some (2)	9.32(1.36)			1>3
Little (3)	8.81(1.95)			2>3
Religion <sup>++</sup>				
Buddhist (1)	9.32(2.04)	[7.94]	< .0001	5>1
Traditional (2)	9.27(1.35)			5>2
Christian (3)	9.58(0.95)			
Catholic (4)	9.49(1.45)			
Other (5)	9.63(1.02)			
Occupation <sup>++</sup>				
White collar (1)	9.82(0.66)	[41.59]	< .0001	1>4; 1>2
Blue collar (2)	9.41(1.39)			1>6; 1>3
Farmer (3)	8.73(1.92)			4>6; 4>3
Prof-Admin (4)	9.56(1.14)			5>6; 5>3
Retired (5)	9.55(1.17)			2>6; 2>3
Housewife (6)	9.10(1.58)			6>3
Reported Health Conditions <sup>+</sup>				
Stroke: Yes	8.66(2.26)	4.12	< .0001	
No	9.38(1.36)			
Hypertension: Yes	9.44(1.23)	-3.03	< .0001	
No	9.32(1.49)			
Cancer: Yes	9.82(0.39)	-6.09	< .0001	
No	9.36(1.41)			
Diabetes: Yes	9.37(1.31)	-0.14	0.89	
No	9.36(1.42)			
Heart Disease: Yes	9.52(1.24)	-2.21	0.03	
No	9.35(1.42)			
Parkinson's: Yes	8.00(2.56)	1.84	0.09	
No	9.36(1.40)			
Depression: Yes	8.17(2.04)	2.03	0.07	
No	9.36(1.41)			
Vision problem: Yes	9.10(1.79)	2.62	0.01	
No	9.38(1.38)			
Hearing problem: Yes	9.55(1.41)	-1.26	0.21	
No	9.36(1.06)			
Dental problem: Yes	9.35(1.49)	0.07	0.94	
No	9.36(1.41)			
ADL <sup>+++</sup>	-0.27		< .0001	
IADL <sup>+++</sup>	-0.38		< .0001	
Age <sup>+++</sup>	-0.20		< .0001	

1. Higher ADL or IADL scores indicate more functional dependence. 2. <sup>+</sup>t-statistic used to compare mean SPMSQ scores in 2 groups defined by dichotomous covariates. 3. <sup>++</sup>ANOVA used to test the differences in variance of SPMSQ scores among multiple groups. 4. <sup>+++</sup>Correlation analysis was used. 5. Statistical significance is being assessed at the 0.05 levels.

**Table 4: Multiple regression of SPMSQ scores, social support and characteristics**

Variable	Coefficients (s.e.)	T value	P-value
Intercept	12.30(0.29)	42.97	< .0001
Social Support			
Married	0.13(0.04)	2.81	0.005
Perceives positive support	0.11(0.04)	2.79	0.005
Feels lonely	-0.03(0.03)	-1.09	0.276
Lives alone	0.09(0.07)	1.25	0.210
Age	-0.03(0.00)	-9.40	< .0001
Female vs. male	-0.38(0.06)	-6.57	< .0001
Education			
Grade School vs. High School	-0.22(0.05)	-4.37	< .0001
College vs. High School	-0.05(0.09)	-0.58	0.564
Religion			
Christian vs. Buddhist	0.16(0.08)	2.01	0.078
Catholic vs. Buddhist	0.04(0.15)	0.26	0.793
Occupation			
Farmer vs. white collar	-0.61(0.10)	-5.88	< .0001
Blue collar vs. white collar	-0.18(0.07)	-2.40	0.016
Prof-Admin vs. white collar	-0.08(0.07)	-1.19	0.233
Housewife vs. white collar	-0.09(0.09)	-1.12	0.264
Retirement vs. white collar	-0.11(0.08)	-1.37	0.172
ADL	-0.01(0.01)	-0.56	0.578
IADL	-0.14(0.01)	-15.35	< .0001
Reported Health Conditions			
CVA	-0.02(0.11)	-0.21	0.835
Hypertension	0.07(0.04)	1.56	0.118
DM	0.02(0.07)	0.26	0.796
CHD	0.11(0.08)	1.30	0.195
Cancer	0.40(0.26)	1.56	0.118
Parkinson's	-0.52(0.35)	-1.49	0.136
Depression	-0.79(0.37)	-2.14	0.031
Vision problem	-0.24(0.08)	-3.16	0.017
Hearing problem	0.23(0.19)	1.21	0.227
Dental problem	0.16(0.15)	1.06	0.287
Adjusted R-square	0.2019		
F-value	40.33		< .0001

s.e. = standard error

measured at different points. Cross-sectional studies cannot establish the direction of an association (cause and effect) [44,45]. Therefore, future research needs to test the causality between social support and cognition function in the elderly by using longitudinal design.

Mean ADL and IADL scores tended to be lower, which meant most of the elders were more independent. Since we lacked the information on ADL and IADL status for the total elderly population in Taiwan, we could not determine whether any difference in functional status existed between our study sample and national data.

We used specifically defined indicators (marital status, living alone, loneliness or perceived positive support from friends) to make inferences about the effects of social sup-

port on cognition. Although we did not examine in detail the nature of the social interactions, two of our simple measures showed significant associations with cognitive function. Social interactions require varying levels of cognitive effort. An earlier study found that active behaviors represented more robust associations with cognition than did passive behaviors [43]. Future research may employ different social-activity constructs to examine these issues.

Perceived positive support from friends have been used proxies for social support in USA [46]; however, it has not been validated in Taiwan elderly population. In addition, a 3-point scale for loneliness may not be discriminatory enough to measure loneliness. For future study, the revised UCLA loneliness scale may be a better choice. This scale contains 20 questions, each with a 4-point Likert-

type answer ranging from never to often. Although this questionnaire was not specifically designed for use with the elderly, its reliability and validity have been reported to have a Cronbach's alpha of 0.96. Factor analysis has indicated that it measures emotional as well as social loneliness. Thus, validation of the suitability of applying the revised UCLA loneliness scale in Taiwan's elderly population is a subject worthy of future research.

## Authors' Contributions

SCY participated in the design of the study, carried out the study, performed the statistical analysis and drafted the manuscript. YYL participated in the design of the study and literature review.

## Competing interests

None declared

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