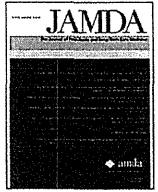


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## Original Study

## Eating Alone as Social Disengagement is Strongly Associated With Depressive Symptoms in Japanese Community-Dwelling Older Adults



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## A B S T R A C T

**Keywords:**  
Eating alone  
depressive symptoms  
social engagement

**Objectives:** Depression in later life poses a grave challenge for the aging countries. The reported key risk factors include social disengagement, but the lack of social companionship during mealtimes, namely eating alone, has not been examined extensively, especially in relation to living arrangement. Past studies on changes along geriatric trajectories in the association between social engagement and depression also remain inadequate. This study aims to examine the association between social engagement and depressive symptoms with a particular focus on eating alone and how the association changes along the aging and mental frailty trajectories.

**Design:** A cross-sectional study.

**Setting:** Kashiwa-city, Chiba-prefecture in Japan.

**Participants:** A total of 1856 community-dwelling older adults.

**Measurements:** The 15-item Geriatric Depression Scale was used to measure depressive symptoms. The indicators used to assess social engagement included eating alone, living arrangement, reciprocity of social support, social participation, social stressors and social ties.

**Results:** Social engagement was significantly associated with depressive symptoms. Those who live with their families yet eat alone were found to be at particular risk (odds ratio = 5.02, 95% confidence interval 2.5–9.9 for young-old; odds ratio = 2.41, 95% confidence interval 1.2–4.8 for old-old). Younger and less mentally frail populations showed stronger associations.

**Conclusions:** Eating alone was a key risk factor for depressive symptoms in community-dwelling older adults. The living arrangement in which they eat alone is important in identifying those with the greatest risk. Mental health management for older adults requires comprehensive assessment of their social relations that takes into account their companionship during mealtimes. Social preventive measures need to involve early interventions in order to augment their effectiveness against mental frailty.

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The problem of depression in later life has become a pressing global concern, as the population aging continues worldwide.<sup>1</sup> It undermines well-being and quality of life while adding to healthcare costs, with potential consequences on a wide range of health outcomes.<sup>2</sup> The problem poses a grave socioeconomic burden on aging countries, not least in Japan where the unprecedented level of aging threatens to undermine its social security system.<sup>3</sup> The prevalence of

depression among community-dwelling older adults varies enormously and has been reported to be as high as 35%.<sup>4</sup>

The key reported predictors of depressive symptoms include female gender, cognitive and functional impairments, medical disorders, low level of education, and social disengagement.<sup>1,5–10</sup> Social engagement is an “umbrella concept for the various components of an individual’s social behavior and social structure”<sup>11</sup> and its different aspects have consistently been found to predict mortality, disease outcomes, disability, cognitive decline as well as depressive symptoms.<sup>12–16</sup> While the conceptualization of social engagement lacks a strong consensus,<sup>17</sup> this should not be viewed as a weakness but as an invitation to explore its unexamined aspects in a search for the most relevant screening questions to identify older adults at risk.<sup>11</sup> This study, thus, aims to examine new concepts and ideas that remain under-explored, especially in relation to depression.

One such aspect is the social behavior during mealtimes. Commensality (ie, the act of eating with others) provides opportunities for social interactions and exchange of information and support by facilitating participation in shared social activities of mealtimes.<sup>18</sup> Eating alone deprives older adults such valuable social opportunities. Eating alone has been studied in relation to dietary intake, but research in relation to depression and wider health outcomes remains limited.<sup>19</sup> To our knowledge, none has examined its association with depression in combination with other components of social engagement nor investigated it in relation to the living arrangement. Living alone is often cited as a key risk factor for older adults, as does the Ministry of Health, Labor and Welfare, Japan, but eating alone is rarely discussed. A shared living arrangement may result in increased opportunities for commensality, but does not guarantee it,<sup>18,19</sup> requiring independent considerations.

Furthermore, past studies have not adequately examined how the association between social engagement and depression changes along geriatric trajectories such as aging and frailty. Frailty is not only a physical but a multidimensional concept,<sup>20</sup> and mental frailty, one important dimension, may manifest as depressive states. The role of social engagement vis-à-vis depression is expected to change as older adults age or become more mentally frail, influencing the effectiveness of social intervention measures.

The purpose of the present study is 2-fold. The first objective is to examine whether social engagement is associated with depressive symptoms with a particular focus on eating alone and its relation to the living arrangement. Second, effects of geriatric trajectories, namely aging and mental frailty trajectory on the above association, are examined in order to better identify the most effective social intervention sites for depressive symptoms.

## Methods

### Study Design

The study was cross-sectional.

### Setting and Participants

This study was based on data from 1856 randomly selected community-dwelling older adults (independent or those requiring support), aged 65–94, who participated in the first year health assessment of a 3-year cohort study between 2012 and 2014 in Kashiwa city, Japan. A total of 2044 persons participated in the assessment and 188 persons were excluded due to missing items of data.

## Measurements

### Depressive symptoms

The 15-item Geriatric Depression Scale (GDS) was used. Scores of  $\geq 6$  were defined as “depressive symptoms,”<sup>21</sup> 6–9 as “mild depression,” and  $\geq 10$  as “severe depression.”<sup>4</sup>

### Social engagement

Seven components were assessed: (1) living arrangement; (2) eating arrangement; (3) reciprocal social support; (4) social participation; (5) social stressors; (6) social ties with family; and (7) social ties with friends. The following questions were asked regarding each item: (1) Do you live with your family: yes or no? (No = living alone); (2) Do you eat your meals with anyone else, at least once a day: yes or no? (No = eating alone); (3) Do you give advice and a helping hand to your family or friends: yes or no? (No = low reciprocal social support); (4) Are you going out less frequently compared to last year: yes or no? (The Kihon Check List, Ministry of Health, Labor and Welfare) (No = fewer frequency of going out); and (5) Did you experience any major changes in life in the past year, such as moving home, retirement, loss of relatives, financial troubles, troubles in the relationships with people: yes or no? (Yes = major change in life). For (6) and (7), the abbreviated Lubben Social Network Scale-6 and its Family and Friends subscales<sup>22,23</sup> were used. Living arrangement and eating arrangement were crossed to construct 4 dummy variables: “living and eating alone,” “living alone yet eating with others,” “living with others yet eating alone,” and “living and eating with others” (reference).

### Sociodemographic variables

Age and the years of education were included in the analysis as continuous variables. Health literacy was measured by 5 items developed for Japanese persons.<sup>24</sup> Information on economic status was obtained as income ranking based on long-term care insurance premiums. Logistic regression was performed with the income ranking and depressive symptoms as the independent and dependent variables, respectively. The odds ratios were plotted to observe changes in the trend and those with less than 1.4 million Japanese Yen per person were categorized as the “low income” group.

### Medical histories

Medical histories of hypertension, osteoporosis, cerebrovascular diseases, diabetes, heart diseases, and malignant neoplasm were obtained through medical interviews by nurses.

### Number of medications

The total number of oral medications was recorded as a continuous variable, as polypharmacy is known to be associated with increased depressive symptoms.<sup>25</sup>

### Physical health and functions

Instrumental activities of daily living (IADL) was measured using the Tokyo Metropolitan Institute of Gerontology index of competence.<sup>26</sup> Mobility was assessed by Life-Space Assessment,<sup>27,28</sup> measured with the Elderly-Status Assessment Set.<sup>29,30</sup> The highest level of life-spaces (level 5) was used. To assess usual and maximum gait speeds, participants were instructed to walk over an 11-m course and the time spent in the middle 5 m was recorded.<sup>31</sup>

### Cognitive function

The Mini-Mental State Examination was used, and its score was included in the analysis as a continuous variable.

### Oral health and functions

The Japanese version of the General Oral Health Assessment Index (GOHAI)<sup>32,33</sup> was used to measure the oral health-related quality of

**Table 1**  
Geriatric Characteristics of Normal (Nondepressed) and Depressed Study Participants\* (n = 1856)

Variables	Young-Old (65–74 Years Old)			Old-Old (≥75 Years Old)		
	Normal (n = 1033)	Depressive Symptoms (n = 168)	P Value	Normal (n = 551)	Depressive Symptoms (n = 104)	P Value
	Mean ± SD or n (%)			Mean ± SD or n (%)		
<b>Sociodemographic variables</b>						
Sex (male)	519 (50.2)	71 (42.3)	.055	282 (51.2)	56 (53.8)	.618
Age	69.6 ± 2.7	69.6 ± 2.6	.969	79.0 ± 3.7	79.4 ± 4.0	.294
Education (years)	13.0 ± 2.5	12.6 ± 2.6	.089	12.4 ± 3.1	11.7 ± 3.3	.056
Health literacy	4.03 ± 0.61	3.71 ± 0.67	<.001	4.07 ± 0.60	3.64 ± 0.70	<.001
Low income	598 (57.9)	126 (75.0)	<.001	293 (53.2)	62 (59.6)	.227
<b>Social engagement</b>						
Living alone	77 (7.5)	20 (11.9)	.050	84 (15.2)	15 (14.4)	.830
Eating alone	91 (8.8)	42 (25.0)	<.001	104 (18.9)	34 (32.7)	.002
Living and eating with others	929 (89.9)	124 (73.8)	<.001	428 (77.7)	68 (65.4)	.007
Living and eating alone	64 (6.2)	18 (10.7)	.031	65 (11.8)	13 (12.5)	.839
Living alone yet eating with others	13 (1.3)	2 (1.2)	1.000	19 (3.4)	2 (1.9)	.555
Living with others yet eating alone	27 (2.6)	24 (14.3)	<.001	39 (7.1)	21 (20.2)	<.001
Low reciprocal social support	45 (4.4)	29 (17.3)	<.001	34 (6.2)	18 (17.3)	<.001
Fewer frequency of going out	127 (12.3)	65 (38.7)	<.001	107 (19.4)	47 (45.2)	<.001
Major change in life	225 (21.8)	62 (36.9)	<.001	85 (15.4)	28 (26.9)	.004
Social ties with family	8.33 ± 3.1	6.58 ± 3.1	<.001	8.21 ± 3.2	6.91 ± 3.0	<.001
Social ties with friends	8.43 ± 3.5	6.23 ± 3.4	<.001	8.43 ± 3.6	6.30 ± 3.4	<.001
<b>Medical histories</b>						
Hypertension	388 (37.6)	78 (46.4)	.029	270 (49.0)	69 (66.3)	.001
Cerebrovascular diseases	36 (3.5)	16 (9.5)	<.001	47 (8.5)	13 (12.5)	.198
Diabetes	116 (11.2)	17 (10.1)	.671	68 (12.3)	14 (13.5)	.752
Osteoporosis	77 (7.5)	21 (12.5)	.027	79 (14.3)	23 (22.1)	.045
Heart diseases	151 (14.6)	28 (16.7)	.489	111 (20.1)	32 (30.8)	.016
Malignant neoplasm	152 (14.7)	16 (9.5)	.072	92 (16.7)	23 (22.1)	.183
Number of medications	2.21 ± 2.5	2.85 ± 2.9	.008	3.80 ± 3.3	5.72 ± 3.9	<.001
<b>Physical health and functions</b>						
IADL	4.90 ± 0.36	4.77 ± 0.63	.013	4.85 ± 0.50	4.61 ± 0.89	.007
Mobility	25.8 ± 9.8	21.1 ± 10	<.001	24.1 ± 9.9	20.9 ± 11	.003
Cognitive function: MMSE	28.5 ± 1.7	28.0 ± 1.9	.002	28.0 ± 1.9	27.3 ± 2.3	.006
Oral health and functions: GOHAI	55.8 ± 5.4	51.3 ± 7.1	<.001	54.5 ± 6.3	49.5 ± 8.9	<.001
<b>Nutritional and dietary status</b>						
BMI (kg/m <sup>2</sup> )	23.0 ± 2.9	22.6 ± 3.0	.071	22.7 ± 3.1	22.6 ± 3.0	.625
Food variety	3.63 ± 2.0	3.04 ± 1.9	<.001	4.23 ± 2.1	3.72 ± 2.1	.021
MNA-SF	12.7 ± 1.3	12.1 ± 1.8	<.001	12.4 ± 1.5	11.8 ± 1.8	.004

BMI, body mass index; MMSE, Mini-Mental State Examination; SD, standard deviation.

\* $\chi^2$  test or Fisher exact test was used for categorical variables and nonpaired *t*-test was used for continuous variables.

life. Numbers of remaining teeth were counted by dental hygienists. Occlusal force was assessed by Dental Prescale (Fujifilm, Shizuoka-prefecture, Japan).

#### Nutritional and dietary status

BMI was calculated by dividing the weight by the square of height. Food variety score was calculated from a 10-item questionnaire.<sup>34</sup> Nutritional status was assessed by Mini-Nutrition Assessment-Short Form (MNA-SF), with scores  $\leq 11$  indicating possible malnutrition.<sup>35</sup>

#### Statistical Analysis

Binomial multiple logistic regression analysis was performed with depressive symptoms as the dependent variable, stratified by the age groups (65–74 years old indicating “young-old” and  $\geq 75$  years old indicating “old-old”). Multinomial multiple logistic regression analysis was performed with different degrees of depressive states (“mild depression” and “severe depression”) as the outcome. The characteristics of the 4 groups by eating and living arrangement were also compared, to explore the reasons behind their differing associations with depressive symptoms. For continuous variables only, multiple comparison test (Dunnnett T3) was used to test whether there were significant differences between “living with others yet eating alone” and “living and eating with others.” IBM SPSS statistics v 22 for Windows (IBM Japan, Tokyo, Japan) was

used to perform statistical analysis. *P* value of  $<.05$  was considered to indicate statistical significance.

#### Ethical Considerations

The study was approved by the Ethics Committee of the University of Tokyo. Data received for analysis had the participants' names substituted with ID numbers, and confidential information was excluded to ensure protection of personal information.

## Results

#### Sample Characteristics

Of the total 1856 participants (928 male and 928 female, mean age was  $72.9 \pm 5.5$  years), 1201 (64.7%) were young-old whereas 655 (35.3%) were old-old. Furthermore, 14.7% showed depressive symptoms (14.0% of young-old and 15.9% of old-old, 15.6% of women and 13.7% of men); 10.6% were living alone (8.1% of young-old and 15.1% of old-old, 15.4% of women and 5.7% of men); 14.6% were eating alone (11.1% of young-old and 21.1% of old-old, 17.9% of women and 11.3% of men); and 6.0% were eating alone despite living with family members (4.2% of young-old and 9.2% of old-old, 5.2% of women and 6.8% of men).

**Table 2**  
Association Between Depressive Symptoms and Risk Factors by Binomial Multiple Logistic Regression

Variables	Young-Old (65–74 Years Old) (n = 1201)			
	Model 1		Model 2	
	OR (95% CI)	P Value	OR (95% CI)	P Value
<b>Social engagement</b>				
Living and eating with others (ref)	–		–	
Living and eating alone	1.94 (1.1–3.6)	.034	1.53 (0.79–2.9)	.204
Living alone yet eating with others	1.59 (0.32–7.9)	.569	1.14 (0.19–6.8)	.885
Living with others yet eating alone	6.33 (3.3–12)	<.001	5.02 (2.5–9.9)	<.001
Low reciprocal social support	2.57 (1.5–4.6)	.001	2.41 (1.3–4.5)	.006
Fewer frequency of going out	3.79 (2.6–5.6)	<.001	2.57 (1.7–3.9)	<.001
Major change in life	1.78 (1.2–2.6)	.004	1.72 (1.1–2.6)	.009
Social ties with family	0.901 (0.84–0.96)	.002	0.905 (0.84–0.97)	.005
Social ties with friends	0.911 (0.86–0.96)	.001	0.940 (0.88–1.0)	.049
<b>Sociodemographic variables</b>				
Sex (male)			1.29 (0.77–2.2)	.334
Health literacy			0.691 (0.52–0.93)	.013
Low income			1.77 (1.0–3.0)	.038
<b>Medical histories</b>				
Hypertension			1.17 (0.75–1.8)	.486
Cerebrovascular diseases			1.99 (0.89–4.4)	.094
Osteoporosis			1.38 (0.74–2.6)	.308
Number of medications			1.03 (0.96–1.1)	.402
<b>Physical health and functions</b>				
IADL			0.824 (0.54–1.3)	.369
Mobility			0.973 (0.96–0.99)	.007
Cognitive function: MMSE			1.04 (0.92–1.2)	.521
Oral health and functions: GOHAI			0.944 (0.92–0.97)	<.001
<b>Nutritional and dietary status</b>				
Food variety			0.929 (0.84–1.0)	.163
MNA-SF			0.870 (0.76–0.99)	.038
Variables	Old-Old (≥75 Years Old) (n = 655)			
	Model 1		Model 2	
	OR (95% CI)	P Value	OR (95% CI)	P Value
<b>Social engagement</b>				
Living and eating with others (ref)	–		–	
Living and eating alone	1.01 (0.51–2.0)	.968	1.06 (0.48–2.4)	.889
Living alone yet eating with others	0.753 (0.17–3.4)	.712	0.979 (0.19–5.0)	.980
Living with others yet eating alone	2.45 (1.3–4.7)	.006	2.41 (1.2–4.8)	.014
Low reciprocal social support	1.91 (0.95–3.9)	.071	1.04 (0.48–2.3)	.917
Fewer frequency of going out	2.97 (1.9–4.7)	<.001	2.09 (1.2–3.6)	.008
Major change in life	1.98 (1.2–3.4)	.012	2.18 (1.2–3.9)	.009
Social ties with family	0.981 (0.90–1.1)	.651	0.972 (0.89–1.1)	.548
Social ties with friends	0.880 (0.82–0.94)	<.001	0.895 (0.83–0.97)	.006
<b>Sociodemographic variables</b>				
Sex (male)			1.56 (0.88–2.8)	.126
Health literacy			0.499 (0.34–0.74)	<.001
<b>Medical histories</b>				
Hypertension			1.46 (0.83–2.6)	.185
Osteoporosis			1.27 (0.63–2.5)	.505
Heart diseases			1.21 (0.68–2.1)	.525
Number of medications			1.10 (1.0–1.2)	.010
<b>Physical health and functions</b>				
IADL			0.842 (0.59–1.2)	.340
Mobility			1.00 (0.98–1.0)	.990
Cognitive function: MMSE			0.919 (0.82–1.0)	.160
Oral health and functions: GOHAI			0.935 (0.90–0.97)	<.001
<b>Nutritional and dietary status</b>				
Food variety			0.982 (0.87–1.1)	.770
MNA-SF			0.929 (0.79–1.1)	.365

CI, confidence interval; MMSE, Mini-Mental State Examination; OR, odds ratio.

Model 1: social engagement.

Model 2: social engagement, sociodemographic variables, medical histories, number of medications, physical health and functions, cognitive function, oral health and functions, and nutritional and dietary status.

### Social Engagement and Depressive Symptoms by Age Groups

Table 1 shows the comparison of the geriatric characteristics between normal and depressed participants for young-old and old-old, respectively. Based on this result, logistic regression was performed to identify the key risk factors for depressive symptoms (Table 2). The variables independently associated with depressive symptoms for

both age-groups were “living with others yet eating alone,” social participation (fewer frequency of going out), social stressors (major change in life), and social ties of friends, health literacy, and GOHAI. Those unique to young-old were low reciprocal social support, social ties with family, low income, mobility, and MNA-SF scores. Risk factor unique to old-old was the number of medications.

**Table 3**  
Geriatric Characteristics of Normal, Mildly Depressed and Severely Depressed Participants\* (n = 1856)

Variables	Normal (n = 1584)	Mild Depression (n = 193)	Severe Depression (n = 79)	P Value
	Mean ± SD or n (%)			
<b>Sociodemographic variables</b>				
Sex (male)	801 (50.6)	84 (43.5)	43 (54.4)	.601
Age	72.8 ± 5.4	72.7 ± 5.6	74.8 ± 6.0	.201
Education (years)	12.8 ± 2.7	12.3 ± 2.9	12.2 ± 3.1	.007
Health literacy	4.04 ± 0.61	3.75 ± 0.67	3.52 ± 0.70	<.001
Low income	891 (56.3)	137 (71.0)	51 (64.6)	.001
<b>Social engagement</b>				
Living alone	161 (10.2)	19 (9.8)	16 (20.3)	.031
Eating alone	195 (12.3)	47 (24.4)	29 (36.7)	<.001
Living and eating with others (ref)	1357 (85.7)	146 (75.6)	46 (58.2)	<.001
Living and eating alone	129 (8.1)	19 (9.8)	12 (15.2)	.031
Living alone yet eating with others	32 (2.0)	0 (0.0)	4 (5.1)	.681
Living with others yet eating alone	66 (4.2)	28 (14.5)	17 (21.5)	<.001
Low reciprocal social support	79 (5.0)	30 (15.5)	17 (21.5)	<.001
Fewer frequency of going out	234 (14.8)	75 (38.9)	37 (46.8)	<.001
Major change in life	310 (19.6)	66 (34.2)	24 (30.4)	<.001
Social ties with family	8.29 ± 3.1	6.82 ± 3.1	6.42 ± 3.0	<.001
Social ties with friends	8.43 ± 3.5	6.42 ± 3.4	5.86 ± 3.4	<.001
<b>Medical histories</b>				
Hypertension	658 (41.5)	107 (55.4)	40 (50.6)	.001
Cerebrovascular diseases	83 (5.2)	17 (8.8)	12 (15.2)	<.001
Diabetes	184 (11.6)	23 (11.9)	8 (10.1)	.805
Osteoporosis	156 (9.8)	31 (16.1)	13 (16.5)	.003
Heart diseases	262 (16.5)	43 (22.3)	17 (21.5)	.043
Malignant neoplasm	244 (15.4)	27 (14.0)	12 (15.2)	.739
Number of medications	2.77 ± 2.9	3.84 ± 3.4	4.20 ± 3.9	<.001
<b>Physical health and functions</b>				
IADL	4.88 ± 0.42	4.73 ± 0.70	4.66 ± 0.83	<.001
Mobility	25.2 ± 9.8	21.0 ± 10	20.9 ± 11	<.001
Cognitive function: MMSE	28.3 ± 1.8	27.7 ± 2.0	27.7 ± 2.2	<.001
Oral health and functions: GOHAI	55.4 ± 5.8	51.1 ± 7.4	49.2 ± 8.7	<.001
<b>Nutritional and dietary status</b>				
BMI (kg/m <sup>2</sup> )	22.9 ± 3.0	22.7 ± 3.1	22.3 ± 2.9	.163
Food variety	3.84 ± 2.0	3.34 ± 2.0	3.20 ± 2.1	<.001
MNA-SF	12.6 ± 1.4	12.1 ± 1.7	11.7 ± 1.9	<.001

BMI, body mass index; MMSE, Mini-Mental State Examination; SD, standard deviation.

\*Cochran-Armitage trend test was used for categorical variables and Jonckheere-Terpstra trend test was used for continuous variables.

### Social Engagement and Different Degrees of Depression

Table 3 shows the comparison of the geriatric characteristics between “normal,” “mildly depressed” and “severely depressed” participants. Based on this result, multinomial logistic regression was performed, as shown in Table 4. The variables independently associated with both degrees of depression were eating alone, social participation (fewer frequency of going out), social ties with friends, health literacy, the number of medications, and GOHAI. Those unique for “mild depression” were living alone; they had low reciprocal social support, social stressors (major change in life), social ties with family, age, low income, and mobility. Risk factors unique for “severe depression” were male gender, history of cerebrovascular diseases, and MNA-SF scores.

### Living Arrangement and Eating Arrangement

To examine further the role of eating alone and its potential risk factors, living arrangement and eating arrangement were crossed and the physical, mental, oral, cognitive, nutritional and dietary as well as social characteristics of the 4 resultant groups [living and eating alone (n = 160), living alone yet eating with others (n = 36), living with others yet eating alone (n = 111), living and eating with others (n = 1549)] were compared. The results are shown in Table 5.

The participants “living with others yet eating alone” had the poorest scores of social ties with family and friends, years of education, health literacy, physical health and functions (normal and

maximum gait speeds, IADL and mobility), cognitive function, oral health and functions (GOHAI, number of remaining teeth, and occlusal force), and nutritional and dietary status (MNA-SF and food variety).

Furthermore, greater proportion of those who “live with others yet eat alone” live with their children, children-in-law, and grandchildren, compared with those who “live and eat with others,” most of whom live with their spouse.

### Discussion

The main aim of the present study was to examine the association between social engagement and depressive symptoms in community-dwelling Japanese older adults, with a particular focus on eating alone and on the changes in the association along geriatric trajectories of aging and mental frailty.

The study was carried out on a population sample of Japanese older adults, of whom 14.7% showed depressive symptoms (GDS ≥6). This is on the lower end compared with previous studies that used the same GDS cut-off point, in which the prevalence ranged between 14% and 40%.<sup>4</sup>

The results highlighted a significant association between depressive symptoms and social engagement variables such as social ties, eating alone, social participation, social stressors and reciprocity of social support. Of particular interest was eating alone, which to our knowledge has not been assessed before in combination with different components of social engagement and in relation to the

**Table 4**  
Association Between Mild and Severe Depression and Their Risk Factors by Multinomial Multiple Logistic Regression (n = 1856)

Variables	Mild Depression (n = 193)		Severe Depression (n = 79)	
	OR 95%CI	P Value	OR 95%CI	P Value
Social engagement				
Living alone	0.374 (0.19–0.74)	.005	0.777 (0.33–1.8)	.566
Eating alone	2.96 (1.8–5.0)	<.001	3.33 (1.6–6.8)	.001
Low reciprocal social support	1.73 (1.0–2.9)	.045	1.66 (0.80–3.4)	.172
Fewer frequency of going out	2.21 (1.5–3.2)	<.001	2.79 (1.6–4.8)	<.001
Major change in life	1.78 (1.2–2.6)	.002	1.63 (0.93–2.9)	.091
Social ties with family	0.940 (0.88–1.0)	.046	0.935 (0.85–1.0)	.162
Social ties with friends	0.929 (0.88–0.98)	.007	0.895 (0.82–0.97)	.009
Sociodemographic variables				
Sex (male)	1.27 (0.78–2.1)	.335	2.46 (1.2–5.0)	.013
Age	0.950 (0.92–0.98)	.005	0.998 (0.95–1.0)	.943
Education (years)	1.05 (0.98–1.1)	.190	1.03 (0.93–1.1)	.582
Health literacy	0.670 (0.52–0.87)	.003	0.440 (0.31–0.63)	<.001
Low income	1.72 (1.1–2.8)	.024	1.65 (0.84–3.3)	.145
Medical histories				
Hypertension	0.743 (0.51–1.1)	.118	1.14 (0.64–2.0)	.655
Cerebrovascular diseases	1.38 (0.74–2.6)	.312	2.36 (1.1–5.2)	.033
Osteoporosis	0.712 (0.43–1.2)	.184	0.839 (0.39–1.8)	.652
Heart diseases	1.00 (0.65–1.5)	.994	1.28 (0.67–2.5)	.461
Number of medications	1.08 (1.0–1.1)	.017	1.10 (1.0–1.2)	.027
Physical health and functions				
IADL	0.834 (0.63–1.1)	.215	0.862 (0.59–1.3)	.446
Mobility	0.983 (0.97–1.0)	.044	0.988 (0.96–1.0)	.327
Cognitive function: MMSE	0.927 (0.85–1.0)	.103	0.994 (0.87–1.1)	.930
Oral health and functions: GOHAI	0.943 (0.92–0.97)	<.001	0.928 (0.90–0.96)	<.001
Nutritional and dietary status				
Food variety	0.959 (0.88–1.0)	.344	0.960 (0.84–1.1)	.531
MNA-SF	0.936 (0.84–1.0)	.251	0.839 (0.72–0.98)	.029

CI, confidence interval; MMSE, Mini-Mental State Examination; OR, odds ratio.

living arrangement. “Living with others yet eating alone” was a significant predictor of depression for both age groups, with odds ratio reaching as high as 5 times for the young-old. This suggests that eating alone acts as stronger risk factor than living alone, and that the living arrangement in which older adults eat alone can act as a critical determinant of depressive risks. Meals are an important location of socialization whereby older adults enjoy intimate interactions, and when shared with others, they can provide valuable opportunities for companionship and social support.<sup>18</sup> A lack of communication during meals may result in feelings of loneliness and depressed moods.<sup>19</sup>

Table 5 suggests that those who eat alone despite living with their families tend to be the most socially withdrawn, with least awareness of their health conditions and the poorest physical, oral, and cognitive functions as well as nutritional status. The fact that they do not share a single meal with their families despite living together suggests that they have distant relationships with them. Compared with those who eat with others, a greater proportion of those who eat alone live with their children, children-in-law or grandchildren, and less with their spouse. This suggests that they may be eating alone because they lead different life styles, suffer from emotional distance, concerns that they will add burdens on their families if they eat together, or from uncomfortable relationships with family members such as children-in-law. This is supported by the fact that they have the weakest social ties with family. This may result in lower interest in their health shown by their families, as well as in lower self-interest. The fact that they show the lowest health literacy also supports this hypothesis. They also exhibit the lowest mobility and social ties with friends, suggesting that they are the most socially isolated not only at home but also outside. The fact that their gait speeds and IADL are the lowest imply that their poor physical functions play a role in limiting their social activities. GOHAI scores, number of remaining teeth and occlusal force are lowest in this group, indicating the possibility that they eat alone because they eat too slowly, require different menus, or because they have concerns about their oral appearance. The poor oral functions and nutritional/dietary status (low food variety and

MNA-SF scores) may also be another manifestation of the lack of interest in their health shown by their families as well as by themselves.

In any case, the sentiments or perceptions that lead them to eat alone despite living with their families are likely to be negative in nature and may be internally conceived by the older adults themselves, or externally imposed by families living together or the wider society. The functional decline, which may be a cause as well as a result from eating alone, may also contribute to the depressive outcomes.

Stratification by age groups and multinomial regression analysis by different severities of depression revealed that fewer variables of social engagement were associated with depressive outcomes as the population ages or becomes more mentally frail. This suggests that social engagement is a more powerful predictor of mental health at earlier points along geriatric trajectories, and, thus, that effective social preventive measures require early interventions. Lower down the geriatric trajectories, social factors fall in their relative importance and the role of health and functional factors increase. This is suggested by the fact that the number of medications becomes a significant predictor for old-old, and the history of cerebrovascular diseases and MNA-SF scores become significant for severe depression.

Outside the domain of social engagement, the independent risk factors for depressive symptoms in both age groups included GOHAI and health literacy, supporting the findings of previous studies.<sup>36–38</sup> Uniquely for young-old, mobility, MNA-SF, and income were associated. For old-old only, the number of medications remained a predictor of depressive symptoms.

This study elucidates that reducing the risk of depression requires much more than medical care and that preventive measures need to be introduced early on in the geriatric trajectories, before frailty sets in. The present study shows that social factors such as eating alone pose substantial risk for mental health. Comprehensive assessment that covers a wide range of health-related domains including physical health, oral functions, nutritional, and dietary status as well as social relations will be necessary to identify those at risk effectively.

**Table 5**  
Characteristics by Living and Eating Arrangement (n = 1856)

Variables	Living and Eating Alone (n = 160)	Living Alone Yet Eating With Others (n = 36)	Living with Others Yet Eating Alone (n = 111)	Living and Eating With Others (n = 1549)	P Value*
	Mean ± SD or n (%)				
<b>Social engagement</b>					
Live with spouse	—	—	61 (55.0)	1393 (89.9)	<.001
Live with children	—	—	74 (66.7)	627 (40.5)	<.001
Live with children-in-law	—	—	21 (18.9)	117 (7.6)	<.001
Live with grand-children	—	—	29 (26.1)	171 (11.0)	<.001
Social ties with family	7.24 ± 3.4	8.83 ± 3.5	7.19 ± 3.2	8.19 ± 3.1	<.001*
Social ties with friends	8.08 ± 3.4	8.86 ± 2.9	6.86 ± 4.0	8.19 ± 3.6	.003*
<b>Sociodemographic variables</b>					
Sex (male)	42 (26.3)	11 (30.6)	63 (56.8)	812 (52.4)	<.001
Age	74.6 ± 6.0	75.4 ± 5.2	75.3 ± 5.7	72.5 ± 5.3	<.001*
Education (years)	11.9 ± 2.7	12.0 ± 2.7	11.8 ± 3.2	12.9 ± 2.7	<.001*
Health literacy	3.87 ± 0.71	4.13 ± 0.71	3.86 ± 0.66	4.01 ± 0.62	.015
Number of medications	3.50 ± 3.5	4.17 ± 4.3	3.76 ± 3.7	2.79 ± 2.9	.004
<b>Physical health and functions</b>					
Usual gait speed (m/s)	1.43 ± 0.25	1.44 ± 0.26	1.41 ± 0.27	1.48 ± 0.25	.026
Max gait speed (m/s)	2.05 ± 0.38	2.03 ± 0.46	2.01 ± 0.36	2.17 ± 0.39	<.001*
IADL	4.94 ± 0.30	4.94 ± 0.23	4.69 ± 0.84	4.86 ± 0.46	.007
Mobility	23.9 ± 10	27.3 ± 11	21.0 ± 11	24.9 ± 9.9	<.001*
<b>Mental health</b>					
GDS	3.18 ± 3.4	2.86 ± 3.2	4.83 ± 4.1	2.39 ± 2.7	<.001*
Depressive symptoms: GDS ≥6	31 (19.4)	4 (11.1)	45 (40.5)	192 (12.4)	<.001
Severe depression: GDS ≥10	12 (7.5)	4 (11.1)	17 (15.3)	46 (3.0)	<.001
Cognitive function: MMSE	28.3 ± 1.8	28.0 ± 1.6	27.8 ± 1.9	28.2 ± 1.8	.029
<b>Oral health and functions</b>					
GOHAI	53.8 ± 7.3	53.3 ± 7.8	53.1 ± 6.6	54.9 ± 6.2	<.001*
Number of remaining teeth	20.5 ± 8.0	19.2 ± 8.4	17.8 ± 9.7	21.0 ± 8.3	.003*
Occlusal force (N)	496 ± 333	522 ± 365	478 ± 345	585 ± 361	<.001*
<b>Nutritional and dietary status</b>					
BMI (kg/m <sup>2</sup> )	22.3 ± 3.3	24.3 ± 3.6	22.8 ± 3.3	22.9 ± 2.9	.002
Food variety	3.74 ± 2.0	3.89 ± 2.0	3.26 ± 2.1	3.79 ± 2.0	.037
MNA-SF	12.2 ± 1.6	12.4 ± 1.6	12.1 ± 1.7	12.5 ± 1.4	.007

Those continuous variables that showed significant difference between "living with others yet eating alone" and "living and eating with others" in the multiple comparison test (Dunnnett T3) are highlighted with "".

\*Kruskal-Wallis test for continuous variables and  $\chi^2$  test for categorical variables.

The limitations of our study are mainly 4-fold. First, the cross-sectional nature of the study prevents it from making any conclusive comments about the causality between independent variables and the outcome. Second, data on household income were not available, and instead, individual income was used. Given that the older adults in the present study grew up in a period when it was rare for women to work after marriage, household income would have been a better indicator of the economic environment for women. Third, depressive symptoms were measured using self-administered GDS questionnaire rather than diagnosis by physicians. Fourth, the participants inevitably comprised those who had greater degrees of interest in health and lower barriers to participation in the study. This may have skewed the nature of participants, to those who were more socially active and interested in health, missing out those who were most socially disengaged.

## Conclusions

For community-dwelling Japanese older adults, depressive symptoms were significantly associated with social engagement, with greater associations in younger and less mentally frail populations. Eating alone was identified as a key risk factor for depressive symptoms, and those who live with their families yet eat their meals alone were at highest risk. Mental health management for older adults, therefore, requires comprehensive assessment of their social relations, taking into account their companionship during mealtimes. Social preventive measures need to involve early interventions in order to augment their effectiveness against mental frailty.

Given that depression can lay the ground for further frailty and

various detrimental health outcomes, further study with a longitudinal design, with more detailed data collection on social predictors of depression, may play a pivotal role in identifying possible intervention opportunities to prevent not only mental but also physical frailties.

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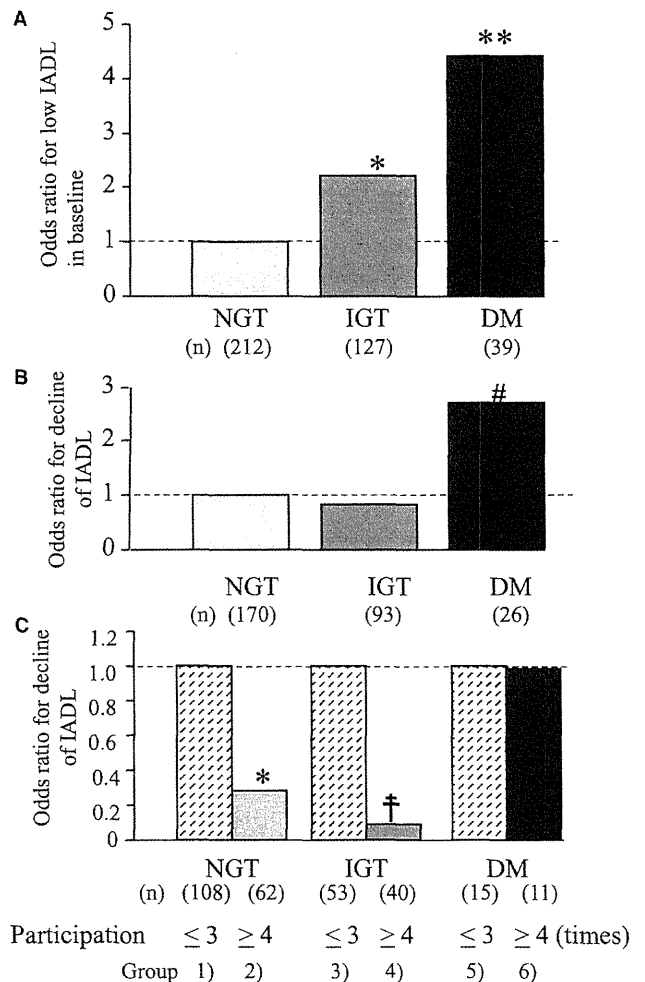
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### EFFECT OF EARLY DIAGNOSIS AND LIFESTYLE MODIFICATION ON FUNCTIONAL ACTIVITIES IN COMMUNITY-DWELLING ELDERLY ADULTS WITH GLUCOSE INTOLERANCE: 5-YEAR LONGITUDINAL STUDY

*To the Editor:* Older people with diabetes mellitus frequently have functional impairment,<sup>1–4</sup> but there are few reports of the protective effects of longitudinal interventions on functional decline in older people newly diagnosed according to an oral glucose tolerance test (OGTT).<sup>5</sup> The association between glucose intolerance and decline in instrumental activities of daily living (IADL) was examined to verify the hypothesis that annual education on lifestyle modification can help prevent IADL decline in people with glucose intolerance in a 5-year longitudinal study.

Community-dwelling people aged 60 and older were screened using an OGTT (World Health Organization criteria) for the first time in 2006 in Tosa, Japan<sup>5</sup> (N = 378; 212 with normal glucose tolerance (NGT), 127 with impaired glucose tolerance (IGT), 39 with diabetes mellitus (DM)). The prevalence at baseline of disability in IADLs ( $\leq 4$  of five of the IADL items in the Tokyo Metropolitan Institute of Gerontology index),<sup>6,7</sup> was 9.0% for NGT, 15.7% for IGT, and 30.8% for DM ( $P < .001$ , chi-square test). DM (odds ratio (OR) = 4.42, 95% confidence interval (CI) = 1.62–12.08,  $P = .004$ ) and IGT (OR = 2.23, 95% CI = 1.03–4.82,  $P = .04$ ) were associated with IADL disability as assessed using multiple logistic regression after adjusting for dependent basic activities of living (ADL) (OR = 5.12, 95% CI = 1.99–13.18,  $P < .001$ ),<sup>8</sup> age, sex, depression,<sup>9</sup> body mass index (BMI), and falling (Figure 1A).

Of the 289 participants who were independent in IADLs (score of 5) at baseline, who could be followed up during the 5-year study, the incidence of IADL disability was 15.6% for NGT, 11.8% for IGT, and 23.1% for DM groups. DM (OR = 2.70, 95% CI = 0.87–8.39 vs NGT,  $P = .09$ ) was mildly associated with decline in IADL ability, but IGT was not, as indicated by multiple logistic regression after adjusting for dependence in ADLs (OR = 3.01, 95% CI = 1.03–8.82,



**Figure 1.** (A) Cross-sectional association between glucose intolerance and instrumental activity of daily living (IADL) disability at baseline (N = 378).  $P < .05$ , \*\*0.01 using multiple logistic regression. (B) Longitudinal association between glucose intolerance and IADL decline over 5 years (n = 289). # $P < .10$  using multiple logistic regression. (C) Protective effect of participation of follow-up on IADL decline over 5 years in impaired glucose tolerance (IGT) and normal glucose tolerance (NGT) groups (n = 289). \* $P < .05$  (NGT), † $P < .05$  (IGT) using multiple logistic regression. DM = diabetes mellitus.

$P = .04$ ), depression (OR = 2.77, 95% CI = 0.94–8.15,  $P = .06$ ), age, sex, falling, and BMI (Figure 1B).

All subjects were invited to participate in the five annual glucose intolerance and geriatric functional analyses and education about lifestyle modification during the 5-year study period.<sup>5,10</sup> To analyze the preventive effect of follow-up participation of participants with NGT, IGT and DM on IADL decline, all subjects were assigned to one of two groups: more participation ( $\geq 4$ ) or less participation ( $\leq 3$ ).

- 1 NGT with less participation (n = 108, 16.7% with IADL decline).
- 2 NGT with more participation (n = 62, 14.5% with IADL decline).

- 3 IGT with less participation (n = 53, 15.1% with IADL decline).
- 4 IGT with more participation (n = 40, 7.5% with IADL decline).
- 5 DM with less participation (n = 15, 15.1% with IADL decline).
- 6 DM with more participation (n = 11, 36.4% with IADL decline).

In each NGT, IGT, and DM group, the odds of more participation compared with less participation were calculated for IADL decline during the 5 years (Figure 1C). In NGT and IGT, more participation had a protective effect on IADL decline (group 2 vs 1: OR = 0.28, 95% CI = 0.09–0.86,  $P = .03$ ; group 4 vs 3: OR = 0.093, 95% CI = 0.011–0.780) vs group 3,  $P = .03$ ) after adjustment for age, sex, ADL dependence, and depression. With DM, there was no significant difference between the groups with less and more participation.

At baseline, no subject was taking anti-DM medication, but during the following 5-year study period, 11 in the DM or IGT group started taking anti-DM medication. The results showed no difference in the incidence of IADL disability between those taking and not taking medication. In the analysis of subjects not taking anti-DM medication during the study, the significant protective effect on IADL decline in the group with more participation was preserved in IGT group.

Despite the strong association between DM and IGT and IADL disability at baseline, IADL decline during the 5-year study period was mildly associated with DM but not with IGT. Lifestyle modifications were associated with less IADL decline in people with IGT in annual follow-up visits. Improvement in DM indicators was made using nonpharmaceutical intervention through lifestyle modification in the community.<sup>5</sup> Diligent dieting and exercise in the groups with more participation might have preserved IADLs during the 5-year period.

In conclusion, early diagnosis and annual follow-up using nonpharmaceutical interventions for lifestyle modification in elderly adults with glucose intolerance may be effective in the longitudinal preservation of functional abilities.

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## HIGH PREVALENCE OF UNDIAGNOSED EYE DISEASES IN INDIVIDUALS WITH DEMENTIA

*To the Editor:* With the world's population aging, dementia and eye diseases pose a growing burden.<sup>1,2</sup> However, persons with dementia may be less likely to complain of visual symptoms and report early impairment in vision, and thus, many vision-threatening eye diseases may be underdiagnosed and undertreated. Data are limited regarding the prevalence of eye diseases in individuals with dementia and the proportion of these eye diseases that are underdiagnosed. Some studies suggest that individuals with underdiagnosed or undertreated visual problems are more likely to develop cognitive decline.<sup>3</sup> Such data will not only allow better understanding of the needs of individuals with dementia but also improve the design of effective eye disease screening programs in these individuals. The current study explored the use of a simple retinal photograph to detect four major age-related eye diseases in a cohort of individuals with dementia and the prevalence of these diseases that are undiagnosed.

## METHODS

Individuals diagnosed with dementia aged 60 and older were consecutively recruited from July 2009 to December

2012 from three tertiary hospitals in Singapore. All underwent clinical, neurological, and neuropsychiatric assessments. Dementia was diagnosed based on *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) criteria,<sup>4</sup> and the severity was assessed using the Clinical Dementia Rating (CDR).<sup>5</sup> Digital retinal photographs were taken using a standard retinal camera, after pupil dilation using tropicamide 1% and phenylephrine hydrochloride 2.5%. Two retinal fundus photographs of each eye were obtained, centered at the optic disc and at the fovea. Ophthalmologists and trained graders assessed the photographs for the presence of eye pathology. Of the major age-related eye diseases studied, qualified graders assessed age-related macular degeneration (AMD) and diabetic retinopathy (DR) using standard grading systems,<sup>6,7</sup> and an ophthalmologist reviewed the photographs to identify glaucoma (defined as having optic disc features of glaucoma) and cataracts (defined based on media opacity).<sup>8</sup>

An interviewer-administered questionnaire was used to ascertain past history of AMD, DR, or previous laser photocoagulation treatment, cataracts, or glaucoma from participants or caregivers. Undiagnosed eye disease was defined in participants who were not aware that they had the eye diseases but with eye pathology identified from retinal photographs.

## RESULTS

Two hundred sixty-eight individuals with dementia were recruited, 264 of whom had gradable retinal photographs. Of these, 239 (90.5%) had at least one eye disease, 160 of whom (66.9%) had previously undiagnosed conditions. Figure 1 shows the frequency of undiagnosed and diagnosed age-related eye diseases in the cohort with dementia. AMD was the most frequent eye condition that was undiagnosed (90.1%), followed by DR (77.6%) and glaucoma (75.7%), whereas cataract had a much lower frequency as an undiagnosed eye condition (18.4%), even though it was the most prevalent eye disease in the dementia cohort.

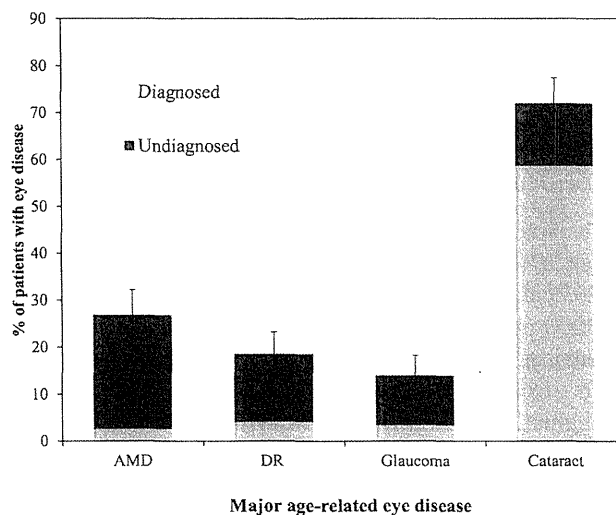


Figure 1. Frequency of undiagnosed and diagnosed age-related eye diseases (age-related macular degeneration (AMD), diabetic retinopathy (DR), glaucoma, and cataract) in the cohort with dementia.

ORIGINAL RESEARCH

## Oxidized Low Density Lipoprotein Among the Elderly in Qinghai-Tibet Plateau

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**Objective.**—Several environmental factors including hypoxia have been reported to contribute to oxidative stress in individuals living in the highlands. However, little is known about the role of oxidized low-density lipoprotein (ox-LDL) among community-dwelling elderly in the Qinghai-Tibet plateau.

**Methods.**—The study population comprised 168 community-dwelling elderly subjects aged 60 years or older (male to female ratio, 70:98; mean age, 65.8 years) living in Haiyan County, located 3000 to 3200 m above sea level, 30 km northwest of Xining, Qinghai. The subjects were volunteers who joined a Comprehensive Geriatric Assessment. Plasma ox-LDL was measured in 168 community-dwelling elderly subjects aged 60 years or older (23 Tibetans and 145 Hans) with a monoclonal antibody-based enzyme-linked immunosorbent assay.

**Results.**—Mean ox-LDL level was higher among Tibetan elderly than Han elderly (Tibetan,  $79.0 \pm 29.6$  U/L; Han,  $62.8 \pm 23.5$  U/L;  $P = .003$ ). Tibetan ethnicity was significantly associated with ox-LDL levels after adjusting for LDL cholesterol levels. In addition, high ox-LDL levels ( $\geq 70$  U/L) were significantly associated with a homeostasis model assessment insulin resistance index of at least 1.6 (odds ratio [OR], 2.82; 95% confidence interval [95% CI], 1.11 to 7.15;  $P = .029$ ) and ankle brachial pressure index of less than 1.0 (OR, 4.85; 95% CI, 1.14 to 10.00;  $P = .028$ ), after adjusting for age, sex, and ethnicity.

**Conclusions.**—Our findings support the hypothesis that ox-LDL levels are higher among Tibetan elderly highlanders compared with those among Han elderly. As ox-LDL levels can affect insulin resistance and arteriosclerosis, further research is needed to determine how oxidative stress influences the health situation among elderly individuals at high altitudes.

*Key words:* Oxidative stress, Ox-LDL, High altitude, Elderly people, Tibetan, Han

### Introduction

Inspired oxygen pressure decreases with altitude. Compared with values at sea level, this pressure is roughly 89% at an altitude of 1000 m, 79% at 2000 m, 69% at 3000 m, 60% at 4000 m, and 52% at 5000 m.<sup>1</sup> Several environmental factors including hypoxia may contribute to oxidative stress in individuals living in the highlands.<sup>2,3</sup> In general, ultraviolet radiation increases

by approximately 4% per 300 m because of decreases in clouds, dust, and water vapour.<sup>4</sup> In addition, as much as 75% of ultraviolet radiation can be reflected back by snow.<sup>4</sup> Low temperature stress contributes significantly to oxidative stress, and temperature decreases with increasing altitude at a rate of approximately 6.5°C per 1000 m.<sup>4,5</sup> Lower dietary intake of antioxidants such as fruits and vegetables could also result in higher levels of oxidative stress.<sup>6–8</sup> Oxidative stress is widely recognized as being associated with various disorders including atherosclerosis, diabetes mellitus, hypertension, and hypercholesterolemia, to name a few.<sup>9–13</sup> Many studies have pointed out the advantageous points of the Tibetan

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adaptation to high altitude. However, our previous study, which measured serum hydroperoxides with the Diacron reactive oxygen metabolites test (d-ROMs; Diacron, Parma, Italy), showed the Tibetan elderly had higher levels of reactive oxygen metabolites (ROM) than the Han elderly.<sup>14</sup> The present study aimed to investigate oxidized low-density lipoprotein (ox-LDL) level as a reliable measure of oxidative stress and its association with other cardiovascular and metabolic variables among community-dwelling elderly individuals living at high altitudes.<sup>15-19</sup>

## Materials and methods

### SUBJECTS

Our study population comprised 168 community-dwelling elderly subjects aged 60 years or older (male/female ratio, 70:98; mean age, 65.8 years) living in Haiyan County (Qinghai, China). Haiyan County is located 3000 to 3200 m above sea level, 30 km northwest of Xining, which is the capital of Qinghai province in China. Our subjects were elderly volunteers who joined our medical and geriatric examination camp. The survey for community-dwelling elderly living in Haiyan County was conducted in August 2008.

### OX-LDL LEVELS

In February 2009, concentrations of ox-LDL in cryopreserved plasma samples at Affiliated Hospital of Qinghai University, China, were measured by a competitive enzyme-linked immunosorbent assay (ELISA) kit using a specific murine monoclonal antibody, mAb-4E6 (Mercodia, Uppsala, Sweden). The results were interpreted in accordance with the manufacturer's instructions. The mAb-4E6 is directed against a conformational epitope in the apolipoprotein B-100 (apoB-100) moiety of low-density lipoprotein (LDL) that is generated as a consequence of the substitution of at least 60 lysine residues of apoB-100 with aldehydes. The substituting aldehydes can be produced by peroxidation of LDL lipids, which generates ox-LDL. The results were interpreted in accordance with the manufacturer's instructions.

### Comprehensive Geriatric Assessments

Blood pressure was measured twice with the subject in a sitting position using an autosphygmomanometer (HEM 757, Omron, Japan). Hypertension was defined as 140 mm Hg or greater for systolic pressure, 90 mm Hg or greater for diastolic pressure, or if the subject was taking antihypertensive medication. Blood chemical tests were conducted twice, at fasting and 2 hours after drinking 75 g of glucose, among subjects who provided informed

consent. Diabetes mellitus and impaired glucose tolerance were defined according to World Health Organization criteria. Specifically, diabetes mellitus was defined as a fasting blood sugar (FBS) of 126 mg/dL or greater or 2-hour oral glucose tolerance test (OGTT) of 200 mg/dL or greater, or if the subject was taking diabetes medication, and impaired glucose tolerance was defined as an FBS from 110 mg/dL to 126 mg/dL or an OGTT from 140 to 200 mg/dL. Insulin resistance was assessed using the homeostasis model assessment insulin resistance index (HOMA-R) and was calculated as fasting plasma glucose  $\times$  fasting serum insulin / 405.<sup>20</sup> Blood chemical analyses were conducted in the central laboratory of Qinghai University Hospital. Ankle brachial pressure index (ABI) and the cardio ankle vascular index (CAVI) were measured using a VaSera instrument (Fukuda Denshi, Tokyo, Japan). Carotid plaques were examined by carotid ultrasound. Plaques were defined as focal structures that encroached into the arterial lumen at least 0.5 mm, comprised 50% of the surrounding intima-media thickness value, or that for which the thickness was 1.5 mm from the media-adventitia interface to the intima-lumen interface.

### ETHICAL APPROVAL

These surveys were approved by the Ethics Committee of the Research Institute for Humanity and Nature (2007-02) and Medical Institute of Qinghai University. Written informed consent was obtained from each subject.

### STATISTICAL ANALYSIS

Data were analyzed with SPSS 15.0 for Windows (IBM Corp, Armonk, NY). Baseline data are presented as mean  $\pm$  SE or percentages. Stepwise multiple regression analyses (to  $P < .05$ ) were used to assess associations between ox-LDL and other variables. Standardized  $\beta$  coefficients were used, as they allow for a direct comparison of the strength of associations between ox-LDL and other variables. Any factors significant in the univariate model were used in the multivariate analysis, and a probability value of less than 0.05 was considered statistically significant. Logistic regression analysis (to  $P < .05$ ) was used to assess associations between ox-LDL and geriatric variables. The logistic regression analysis incorporated covariates of age, sex, and ethnicity.

## Results

### COMPARISON OF TIBETAN AND HAN ELDERLY HIGHLANDERS

Our elderly study population consisted of 23 Tibetans and 145 Hans. Table 1 compares basic characteristics of Tibetan and Han elderly highlanders in Haiyan County

**Table 1.** Comparison of basic characteristics between Tibetan and Han elderly highlanders

Characteristic	Tibetan (n = 23) <sup>a</sup>	Han (n = 145) <sup>a</sup>	P value <sup>b</sup>
Age (years)	65.7 (65.0–66.6)	65.8 (63.9–67.5)	.919
Sex (female)	11 (47.8)	87 (60.0)	.363
Current smoker (no, yes, unknown)	12 (52.2), 3 (13.0), 8 (34.8)	87 (60.0), 23 (15.9), 35 (24.1)	.552
Vegetables intake more than 5 times a week (no, yes, unknown)	4 (17.4), 11 (47.8), 8 (34.8)	31 (21.4), 80 (55.2), 34 (23.4)	.504
Fruits intake at least once a week (no, yes, unknown)	5 (21.7), 10 (43.5), 8 (34.8)	55 (37.9), 53 (36.6), 37 (25.5)	.309
Meat intake more than 2 times a week (no, yes, unknown)	3 (13.0), 12 (52.2), 8 (34.8)	56 (38.6), 54 (37.2), 35 (24.1)	.058
Eggs intake at least once a week (no, yes, unknown)	3 (13.0), 11 (47.8), 9 (39.1)	48 (33.1), 57 (39.3), 40 (27.6)	.143
Dairy products intake at least once a week (no, yes, unknown)	4 (17.4), 11 (47.8), 8 (34.8)	66 (45.5), 45 (31.0), 34 (23.4)	.039
Work or gardening more than 5 times a week (no, yes, unknown)	5 (21.7), 10 (43.5), 8 (34.8)	42 (29.0), 68 (46.9), 35 (24.1)	.522

<sup>a</sup> Data are given as the number (percentage) or as mean (95% confidence interval).

<sup>b</sup> P values were calculated using Student's *t* test or  $\chi^2$  test.

(Qinghai province). Mean age and sex ratios did not differ significantly, but dairy product intake was higher among Tibetans. Table 2 compares cardiovascular and

metabolic variables of the 2 ethnic groups. No significant difference was found in mean systolic blood pressure, oxygen saturation, hemoglobin concentration, fasting

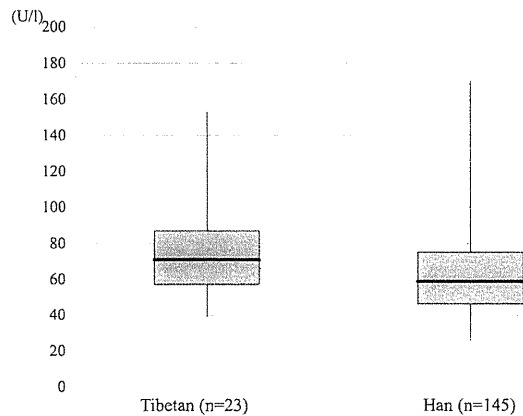
**Table 2.** Comparison of cardiovascular and metabolic items between Tibetan and Han elderly highlanders

Item	Tibetan (n = 23) <sup>a</sup>	Han (n = 145) <sup>a</sup>	P value <sup>b</sup>
Systolic blood pressure (mm Hg)	130.4 (119.5–141.4)	139.0 (134.8–143.3)	.130
Diastolic blood pressure (mm Hg)	78.8 (73.7–84.0)	85.3 (83.0–87.6)	.034
Hypertension	11 (47.8)	76 (52.4)	.657
SpO <sub>2</sub> (%)	90.1 (88.6–91.6)	89.9 (89.1–90.6)	.799
Hemoglobin (g/dL)	15.8 (15.0–16.7)	16.1 (15.7–16.5)	.679
Fasting blood sugar (mg/dL)	92.6 (76.1–109.1)	84.5 (80.0–89.0)	.216
IFG, IGT, or diabetes	4 (17.4)	22 (15.2)	.758
HOMA-R	1.08 (0.66–1.50)	1.14 (0.97–1.30)	.799
HOMA-R $\geq$ 1.6	1 (4.3)	23 (15.9)	.197
Triglyceride (mg/dL)	63.2 (45.1–81.3)	61.4 (57.2–65.6)	.836
HDL cholesterol (mg/dL)	53.6 (46.8–60.3)	48.2 (46.3–50.1)	.054
LDL cholesterol (mg/dL)	175.9 (157.5–194.3)	137.9 (131.9–143.9)	<.001
Dyslipidemia	18 (78.3)	80 (55.2)	.006
ox-LDL (U/L)	79.0 (65.9–92.1)	62.8 (58.9–66.6)	.003
ox-LDL $\geq$ 70 U/L	14 (39.1)	42 (29.0)	.004
Carotid plaque	10 (43.5)	37 (25.5)	.132
CAVI	9.3 (8.7–9.9)	9.3 (9.0–9.6)	.895
CAVI $\geq$ 9.0	13 (56.5)	74 (51.0)	1.000
ABI	1.06 (0.99–1.13)	1.10 (1.08–1.13)	.162
ABI < 1.0	2 (8.7)	14 (9.7)	1.000

SpO<sub>2</sub>, oxygen saturation of hemoglobin; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; HOMA-R, homeostasis model assessment insulin resistance index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ox-LDL, oxidized low-density lipoprotein; CAVI, cardio ankle vascular index; ABI, ankle brachial pressure index.

<sup>a</sup> Data are given as the number (percentage) or as mean (95% confidence interval).

<sup>b</sup> P values were calculated using Student's *t* test or  $\chi^2$  test.



**Figure.** Level of oxidized low-density lipoprotein (LDL) in Tibetan and Han elderly highlanders. The thick horizontal lines represent medians, boxes represent interquartile ranges, and whiskers represent extreme values. The oxidized LDL levels differed significantly between Tibetan and Han after adjustment for LDL levels ( $P = .025$ ).

blood glucose, HOMA-R, triglycerides, high-density lipoprotein (HDL) cholesterol, CAVI, and ABI levels between Tibetan and Han individuals. Mean diastolic blood pressure was lower in Tibetan elderly than in Han elderly, whereas LDL cholesterol was higher in Tibetan elderly than in Han elderly. The ox-LDL levels differed significantly between Tibetan and Han after adjustment for LDL levels ( $P = .025$ ; Figure). The prevalence of dyslipidemia and ox-LDL of 70 U/L or greater was significantly higher in Tibetan elderly than in Han elderly.

### OX-LDL LEVELS, ASSOCIATED FACTORS, AND PROBLEMS

The univariate analysis demonstrated that being Tibetan, LDL cholesterol levels, and frequency of vegetable intake and meat intake were associated with ox-LDL levels. The stepwise multiple regression analysis found that being Tibetan and LDL cholesterol levels were independent predictors of increasing ox-LDL levels (Table 3).

High ox-LDL levels ( $\geq 70$  U/L) were significantly associated with prevalence of dyslipidemia, HOMA-R of 1.6 or greater, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), diabetes, carotid plaque, and ABI of less than 1.0 in Han elderly highlanders by  $\chi^2$  test (Table 4). High ox-LDL levels ( $\geq 70$  U/L) were significantly associated not only with dyslipidemia but also with HOMA-R of 1.6 or greater, IFG, IGT, or diabetes, after adjusting for age, sex, and ethnicity by logistic regression analysis (Table 5). The cutoff level for ox-LDL was defined as the cutoff at the 70th percentile.

### Discussion

The present study showed that Tibetan elderly highlanders had higher ox-LDL levels than Han elderly highlanders. High ox-LDL levels were significantly associated with high HOMA-R ( $\geq 1.6$ ) and low ABI ( $< 1.0$ ) levels, and are associated with insulin resistance

**Table 3.** Factors associated with levels of oxidized low-density lipoprotein by regression analysis

Factor	Univariate analysis		Multivariate analysis <sup>a</sup>	
	Standardized coefficient $\beta$	P value	Standardized coefficient $\beta$	P value
Age (years)	.024	.758		
Female (vs male)	-.029	.705		
Tibetan (vs Han)	.225	.003	.267	.004
Systolic blood pressure (mm Hg)	-.092	.239		
Diastolic blood pressure (mm Hg)	-.146	.063		
SpO <sub>2</sub> (%)	.082	.314		
Hemoglobin (g/dL)	-.101	.212		
Fasting blood sugar (mg/dL)	.02	.804		
HDL cholesterol (mg/dL)	.064	.427		
LDL cholesterol (mg/dL)	.394	<.001	.206	.029
Current smoker	-.051	.569		
Vegetables intake more than 5 times a week	-.19	.034	-.076	.388
Fruits intake at least once a week	.122	.178		
Meat intake more than 2 times a week	.266	.003	.126	.163
Eggs intake at least once a week	.136	.140		
Dairy products intake at least once a week	.027	.761		
Work or gardening more than 5 times a week	.082	.364		

SpO<sub>2</sub>, oxygen saturation of hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

<sup>a</sup> Multiple regression analysis was used. Multivariate model considered factors with  $P < .05$  in the univariate analysis.



**Table 4.** Relations of high oxidized LDL ( $\geq 70$  U/L) to cardiovascular and metabolic problems in Tibetan and Han elderly highlanders

Variable	Tibetan (n = 23) <sup>a</sup>			Han (n = 145) <sup>a</sup>		
	ox-LDL < 70 U/L (n = 9)	ox-LDL $\geq$ 70 U/L (n = 14)	P value <sup>b</sup>	ox-LDL < 70 U/L (n = 103)	ox-LDL $\geq$ 70 U/L (n = 42)	P value <sup>b</sup>
Hypertension	2 (22.2)	9 (64.3)	.089	56 (54.4)	20 (47.6)	.578
Dyslipidemia	6 (66.7)	12 (85.7)	1.000	49 (47.6)	31 (73.8)	.001
HOMA-R $\geq$ 1.6	0 (0.0)	1 (7.1)	1.000	12 (11.7)	11 (26.2)	.043
IFG, IGT, or diabetes	1 (11.1)	3 (21.4)	1.000	11 (10.7)	11 (26.2)	.038
Carotid plaque	2 (22.2)	8 (57.1)	.070	31 (30.1)	6 (14.3)	.048
CAVI $\geq$ 9.0	4 (44.4)	9 (64.3)	.203	53 (51.5)	21 (50.0)	1.000
ABI < 1.0	1 (11.1)	1 (7.1)	1.000	6 (5.8)	8 (19.0)	.024

ox-LDL, oxidized low-density lipoprotein; HOMA-R, homeostasis model assessment insulin resistance index; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; CAVI, cardio ankle vascular index; ABI, ankle brachial pressure index.

<sup>a</sup> Data are given as the number (percentage).

<sup>b</sup> P values were calculated using  $\chi^2$  test.

and arteriosclerosis. Although the precise pathophysiologic mechanisms have not been established, we speculate that differences in lifestyles and evolutionary genetic backgrounds between Tibetans and Hans affected ox-LDL levels. Factors known to affect ox-LDL include living in hypoxic environments, ultraviolet light, smoking habits, vegetable or fruit intake, and coldness.<sup>6</sup> In addition, one that we find particularly interesting is the effect of the natural selection of endothelial Per-Arnt-Sim domain protein 1 (*EPAS1*).<sup>21</sup>

Several ways by which Tibetans have adapted to high altitudes have been reported as advantageous. For example, Tibetans tend to have lower hemoglobin (Hb).<sup>22,23</sup> A mild increase in Hb is advantageous for oxygen transport to tissues, but too much Hb increases the risk of morbidities from pulmonary hypertension, stroke, and intrauterine

growth restriction.<sup>24</sup> A study of individuals in the Andes found that ideal Hb concentrations are actually not so high.<sup>25</sup> Compared with Andeans, Tibetans have been reported to have higher ventilation volume at rest, lower pulmonary vasoconstriction under low oxygen, fewer low-birth-weight babies, and lower Hb.<sup>26,27</sup> One other way that Tibetans adapt to high altitude hypoxic environments is increased nitric oxide (NO) production.<sup>28-30</sup> Tibetans has been reported to have higher forearm blood flow and higher plasma nitrite levels compared with residents at sea level in the United States.<sup>30</sup> Higher blood flow and circulating NO products can offset high altitude hypoxia, and serve as a type of adaptation to hypoxia.<sup>30</sup> However, nitroxides are known to have dual activities as prooxidants and antioxidants.<sup>31</sup> Increased reactive oxygen species (ROS) reduce the amount of bioactive NO by chemical inactivation to form toxic peroxynitrite. In turn, peroxynitrite can uncouple endothelial NO synthase to become a dysfunctional superoxide-generating enzyme that contributes to vascular oxidative stress.<sup>32</sup>

Our study found that Tibetan elderly highlanders have higher ox-LDL levels compared with those of Han elderly highlanders, but pathophysiological mechanisms in convincing detail remain to be identified. Several interesting reports have been published with regard to natural selection of *EPAS1*, egl nine homolog 1 (*EGLN1*), and peroxisome proliferator-activated receptor alpha (*PPARA*), identified as being involved in the adaptational process to hypoxia that has occurred in Tibetans over generations.<sup>21,33,34</sup> They are highly involved in gene regulation with regard to angiogenesis and metabolism of carbohydrates and fat. One study found that after exposure to hypoxic conditions, heterozygous *EPAS1*-deficient mice were protected against

**Table 5.** Relations of high oxidized low-density lipoprotein ( $\geq 70$  U/L) to cardiovascular and metabolic problems

Variable	Odds ratio <sup>a</sup>	95% confidence interval	P value
Hypertension	1.01	0.52-1.98	.978
Dyslipidemia	4.97	2.00-12.35	.001
HOMA-R $\geq$ 1.6	2.82	1.11-7.15	.029
IFG, IGT, or diabetes	2.68	1.08-6.64	.034
Carotid plaque	0.56	0.24-1.31	.180
CAVI $\geq$ 9.0	1.05	0.48-2.30	.901
ABI < 1.0	4.85	1.14-10.00	.028

HOMA-R, homeostasis model assessment insulin resistance index; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; CAVI, cardio ankle vascular index; ABI, ankle brachial pressure index.

<sup>a</sup> Logistic regression analysis (to  $P < .05$ ) was used. Covariates considered were age, sex, and ethnicity.

pulmonary hypertension and right ventricular hypertrophy.<sup>35</sup> Yet another study found that in such mice, oxidative stress was increased.<sup>36</sup> Indeed, as mentioned above, compared with Andeans, Tibetans have lower pulmonary hypertension under low oxygen. According to the results of the present study, Tibetan elderly individuals had higher levels of ox-LDL, an indicator of oxidative stress, relative to their Han counterparts. In Yushu County located at 3700 m above sea level, we detected increased weight, hypertension, and impaired glucose tolerance in relatively high prevalence among the Tibetan elderly.<sup>37</sup> We should be more concerned about the relationships among hypoxia, selected genes, oxidative stress, and metabolic problems. Although the data remain somewhat inconclusive, it is certainly possible that selected genes of Tibetans may partially contribute to the levels of ox-LDL.<sup>21,30,35,36,38,39</sup> It should be noted that advantages under certain conditions may become disadvantageous from different aspects.

#### LIMITATIONS

This cross-sectional study may suggest an association between ox-LDL levels and cardiovascular and metabolic indicators, but a cause-and-effect relationship cannot be concluded here. This study focused only on ox-LDL levels as an indicator of oxidative stress, but multilateral methods were needed to examine the consequences of ROS generation, which can be detected by formation of biomolecules altered by oxidation, including DNA, lipids, and proteins. To determine ethnicity, we used identification cards that included a description of ethnicity, but were unable to determine the precise duration for which an individual and his or her ancestors had resided at high altitude. The population-genetic mixture between Tibetans and Hans could not be determined by our data. The single-county location limits the generalizability. In addition, the study has a small and unequal sample size. The statistical power to detect the difference of ox-LDL between Tibetan and Han was approximately 0.83.

#### Conclusions

Our findings support the hypothesis that ox-LDL levels are higher among Tibetan elderly highlanders relative to those among Han elderly. As ox-LDL levels can affect insulin resistance and arteriosclerosis, further research is needed to determine how oxidative stress occurs among elderly individuals at high altitudes.

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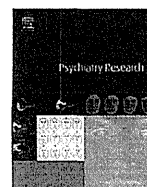
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## Postcard intervention for depression in community-dwelling older adults: A randomised controlled trial

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### ABSTRACT

Depression in older adults erodes their health, quality of life and the economy. Existing interventions are not feasible for broad application at the community. Postcard intervention only requires a few resources, and previous studies have shown its effectiveness for patients following drug overdose, self-harm and hospitalisation for major depression. The purpose of the present study is to evaluate the effectiveness of a postcard intervention. Participants were community-dwelling individuals, aged 65 or older, who eat meals alone and with the score of 4 or higher on the 15-item Geriatric Depression Scale (GDS-15). We enrolled 184 eligible participants, with 93 in the intervention and 91 in the control arm. Postcards were sent to participants once a month for eight months. Primary outcome was the GDS-15 score at post-intervention. Secondary outcomes were quality of life and activities of daily living. There was no significant difference in primary and secondary outcomes between completers of the intervention and the control arm. However, most of the participants who received intervention thought the intervention was effective. The postcard intervention for depression in community-dwelling elderly people in Japan is neither feasible nor effective. However, the descriptive results suggest that the intervention may be effective given different parameters.

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### 1. Introduction

The United Nations reports that nearly all the countries of the world face population aging (United Nations, 2013). Currently in Japan, one out of four people is over 65 years old, and it is estimated that one out of three people will be over 65 years old in twenty years' time (Statistics Bureau in Japan, 2014). Future problems related to the aging population will be even more serious than the present situation.

Depression is one of the most serious problems in elderly people. It erodes their health and quality of life (QOL) and imposes huge economic costs on the society. The mortality rate of people with depression is 1.8 times greater than that of non-depressed subjects, due to suicide, unhealthy habits, and medical illnesses (Cuijpers and Schoevers, 2004). QOL of elderly people with

depression is lower than those with many other chronic diseases (Unutzer, 2009). Depression deteriorates elderly patients' well-being, perceived physical functioning, bodily pain, and general health perceptions (Saarijärvi et al., 2002). It is reported that the additional medical cost per one depressed older adult is USD 686 for 1 year and USD 5271 for 4 years (Unutzer et al., 1997). Depressed older adults use more outpatient resources than those without depression, including frequent appointments and laboratory and radiographic tests. They also have more nonspecific medical complaints, and this is associated with increased total ambulatory care costs (Luber et al., 2001).

Furthermore, the prevalence of depression in elderly people is high, with poor prognosis. A review of community prevalence of depression in later life reported that the proportion of individuals reporting depressive symptoms is 2.8–35% (Beekman et al., 1999). A 6-year follow-up study showed that 76% of elderly patients with depressive disorder follow either an unfavourable fluctuating or a severe chronic course of depression, and only 23% of patients experience full remission (Beekman et al., 2002).

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