学位論文

Association of changes in behavioral activities on mental and physical health among age-specific Japanese older adults: a cohort study

(特定年齢の日本人高齢者における行動活動の変化と心身の健康との関連性：コホート研究)

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Contents

List of publications and presentations

Publications:

(1) Shan, Y., Zhao, W., Hao, W., Kimura, T., Ukawa, S., Ohira, H., Takashi, K., Kenji, W., Masahiko, A. and Tamakoshi, A. (2022). Changes in behavioral activities and transition of depressive symptoms among younger-old community-dwelling adults during 6 years: An age-specific prospective cohort study. International Journal of Geriatric Psychiatry, 37(8).

(2) Shan, Y., Zhao, W., Hao, W., Kimura, T., Ukawa, S., Ohira, H., Takashi, K., Kenji, W., Masahiko, A. and Tamakoshi, A. (2023). Changes in social activities and the occurrence and persistence of depressive symptoms: Do type and combination of social activities make a difference?. Archives of Gerontology and Geriatrics, 104, 104800.

Presentations:

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Summary

Background and purpose: People worldwide are living longer. The proportion of people aged 60 and over will increase from 12.8% in 2020 to 21.6% in 2050 worldwide. Japan has one of the highest levels of ageing rate in the world. The proportion of Japanese people over 65 years is expected to increase to 37.7% in 2050 from 28.8% in 2021. Ageing populations are vulnerable to develop common conditions, such as depression and disability. The prevalence of depressive disorder in older adults increased with age both worldwide and Japan. Life expectancy (LE) and healthy life expectancy (HALE) increased with years, but the increase in HALE has not kept pace with the growth in LE. The reason may be caused by the number of increased years lived with disability (YLDs). Therefore, as depression and disability in older adults become an increasing significant component of disease burden and health expenditure, it is essential to take measures to protect them from depressive disorders and prolong their disability-free survival times. Lack of behavioral activities (social, physical activities) is a common risk factor for depressive disorders and functional disability among older adults. However, as people age, behavioral activities are more likely to be changed due to changes in social and physical environments. Changes in behavioral activities in older adults may extend in a positive direction (increase or maintain in a higher level), or flourish in an adverse direction (decrease or maintain in a lower level).

Given this, the present study assumes that positive change in behavioral activities in older adults can be an effective strategy to prevent the development or improve the prognosis of depressive symptoms and disability. Therefore, I hypothesized that

1. Changes in behavioral activities are associated with the temporal evolution of depressive symptoms. Among three type of behavioral activities, changes in social activities may substantially affect depressive symptoms.

2. In the association between changes in social activities and depressive symptoms, the effect of types and combinations of social activities on the onset/persistence of

depressive symptoms are different.

3. Among depressed older adults, higher levels of social activities can protect them from disability. Thus, an increased or continued regular frequency of social activities is expected to postpone the incident functional disability and prolong the disability-free survival time among depressed older adults.

Subjects and Methods: Study participants aged 64/65 between 1996 to 2005 were selected from the New Integrated Suburban Seniority Investigation (NISSIN) project, an ongoing, age-specific cohort study. Behavioral activities (social activities, daily walking, and exercise habits) were measured by self-reported questions. Social activities were assessed by a set of questions in social-related, learning, and personal activities; daily walking by one question on daily walking time; and exercise habits by one question on weekly exercise frequency. Changes in behavioral activities were classified into continued low frequency (CLF), continued regular frequency (CRF), increased frequency (IF), and decreased frequency (DF). Depressive symptoms were assessed using the 15-item Geriatric Depression Scale, a score ≥ 6 is indicative of depressive symptoms. Functional disability was defined according to Japan's Long-term Care Insurance System (LTCI). There are seven levels of LTCI certification, support levels 1-2 and care levels 1-5. Mild disability was defined as people need support levels 1-2 and care level 1; severe disability was defined as people need care levels 2-5. Risk ratios, hazard ratios, 25^{th} percentile differences and their 95% confidence intervals were calculated by modified Poisson regression models, cox proportional hazard models, and Laplace regression models, respectively.

Results:

1. In the association between changes in behavioral activities and depressive symptoms, participants without depressive symptoms at baseline and engaged in all three behavioral activities at a CRF, social activities and daily walking at an IF, and a greater variety of behavioral activities at CRF were less likely to have depressive symptoms onset at follow-up. Although this negative association also showed among

participants with depressive symptoms at baseline, there is no significant difference.

2. In the association between changes in social activities and depressive symptoms, participants with CRF or IF of all types of social activities, and with a combination of multiple social activities maintaining the same frequency or increase the number of regular frequency activities were less likely to develop depressive symptoms. This association did not show statistical significance in the persistence of depressive symptoms among participants with depressive symptoms at baseline.

3. Among depressed older adults, an IF of learning activities not only reduced the risk of developing mild disability and prolonged their disability-free survival time. A CRF of learning activities also showed a reduced risk of developing severe disability and a prolonged disability-free survival time. Still, this association was not significant after controlling all the confounding factors.

Discussion:

1. Participating in behavioral activities that people get positive personal interaction broadens older individuals' social lives, increases their confidence, self-efficacy, and self-esteem, and then brings protective effects on depression. Daily walking for recreational purposes, rather than utilitarian purposes, was strongly associated with a reduction in the risk of developing depression. The maintenance, rather than increase, of exercise could protect older adults from depression. As exercise-related improvements to the capacity for vascular hippocampal plasticity that exert antidepressant effects decreased with age, which may not be entirely beneficial for preventing depressive symptoms among older adults.

2. The effect size of the negative relation between CRF or IF of social activities and depressive symptoms varied across different types of social activities, which confirmed that a higher level of perceived emotional support could protect people from depressive symptoms, whereas a lower level is associated with the presence or development of depressive symptoms. There are cumulative and compensatory effects among different types of social activities influencing depressive symptoms, which

means a gain in certain activities may compensate for losses in other activities.

3. Increased learning activities help depressed older adults get benefits for their cognitive function and then protect them from disability. However, for people with much severe disability, it seems that only maintaining higher frequency of learning activity would reduce the risk of disability. Future studies still need to demonstrate this association, because the lower prevalence of severe disability in my study may cause underestimation.

Conclusions:

1. Consistent and regular participation in one or more behavioral activities was negatively associated with the onset of depressive symptoms.

2. In different types of social activities, personal activities were more manifest in preventing depressive symptoms, regardless of depressive status at baseline. Also, an engagement in a combination of all three social activities was negatively associated with the onset of depressive symptoms.

3. Among depressed older adults, an increased frequency of learning activities could significantly reduce the risk of mild disability and prolong their disability-free survival time.

In conclusion, older adults should make positive behavioral changes to protect them from future disease onset or improve the prognosis of the disease.

List of Abbreviations

ANOVA	Analysis of variance
BMI	Body mass index
CI	Confidence interval
CLF	Continued low frequency
CRF	Continued regular frequency
CVD	Cardiovascular disease
DF	Decreased frequency
GDS	15-item Geriatric Depression Scale
HALE	Healthy life expectancy
HRs	Hazard ratios
IF	Increased frequency
LE	Life expectancy
LTCI	Long-term care insurance system
NISSIN	New Integrated Suburban Seniority Investigation Project
PDs	Percentile differences
RRs	Risk ratios
YLDs	Years lived with disability

Introduction

People worldwide are living longer. By 2030, one in six people worldwide will be aged 60 or over. The proportion of people aged 60 and over will increase from 1 billion (12.8% of total population) in 2020 to 1.4 billion (16.5% of total population) in 2030. By 2050, the number of people aged 60 years and above will double (2.1 billion, 21.6%) (World Health Organization, 2022b). Japan has one of the highest levels of ageing rate in the world. In 2021, the population aged 65 and over in Japan reached 36.21 million, accounting for 28.8% of the total population. The ageing rate was expected to increase to 37.7 in 2050 (National Institute of Population and Social Security Research, 2022).

Ageing populations are vulnerable to develop common conditions, such as hearing loss, cataracts and refractive errors, back and neck pain and osteoarthritis, chronic obstructive pulmonary disease, diabetes, depression, dementia and disability (World Health Organization, 2022a).

Over 100 million older adults aged 65-89 with mental disorders globally, and 3 million in Japan. Among the major mental disorders, depressive disorders had the highest prevalence, about 39.0% globally and 31.0% in Japan (Institute for Health Metrics and Evaluation, 2019a). In addition, over 16% of community-dwelling older adults may experience an episode of clinically relevant depressive symptoms (Fernandez-Rodrigues et al., 2022). Moreover, depressive symptoms in older adults are associated with various health problems, such as decreased physical, social, and cognitive function, increased risk of morbidity and suicide (Penninx, 2017; Buigues et al., 2015; Demakakos et al., 2010; Blazer, 2003), and a high financial burden (Vyas and Okereke, 2020). In Japan, the prevalence of depressive symptoms in older adults increases with age (Institute for Health Metrics and Evaluation, 2019c). Among all people with mood disorders (e.g., manic depression and depression), the percentage of the average length of hospitalization for older adults aged 65 years and over has increased from 55% in 2017 to 60% in 2021 (Ministry of Health Labour and Welfare,

2022). This trend is raising concern for causing a huge burden not only for depressed patients but also for their families and the medical and social resources. With the rapid ageing of its population, Japan needs to take measures for potential interventions for depressive disorder among community-dwelling older adults.

Life expectancy (LE) globally increased by more than six years, from 66.8 years in 2000 to 73.4 years in 2019. Healthy life expectancy (HALE) also increased by more than five years, from 58.3 years in 2000 to 63.7 years in 2019. However, the increase in HALE has not kept pace with the growth in LE. The reason may be the declining mortality rather than the reduction in the number of years lived with disability (YLDs) (**Figure 1**) (World Helath Organization, 2019).

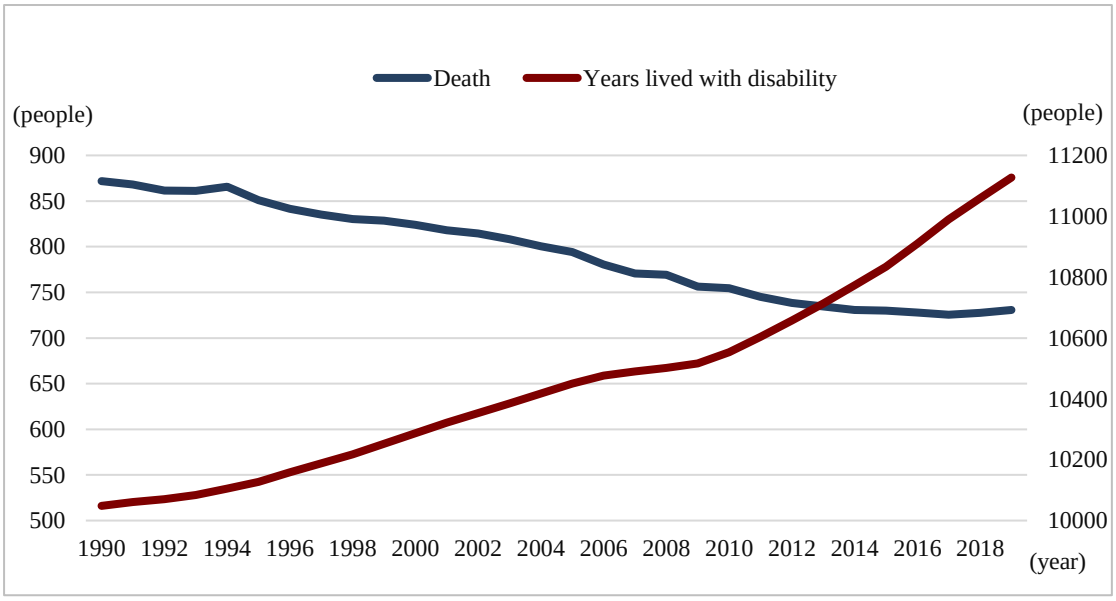

Figure 1 Rate of death and years lived with disability among all age population globally in 1990-2019, per 100k

(Data source: Global Burden of Disease Study 2019 (GBD 2019) Results, Global Burden of Disease Collaborative Network.)

As of 2020, LE of Japanese was 81.56 years for men and 87.71 years for women, and it is expected to be increasing in the future (Japan Cabinet Office, 2019). Although the HALE of Japanese, shown in Figure 2, also increased by years, the discrepancy between LE and HALE may also cause by increased YLDs. In addition, it is reported

that the number of Japanese aged 65 and over with disability increased 1.4 times, from 3.54 million in 1990 to 8.61 million in 2019 (Institute for Health Metrics and Evaluation, 2019b). To address the demands of middle-aged and older persons with disabilities, the Japanese government introduced the Long-term care insurance (LTCI) system in 2000 (Yamada and Arai, 2020). However, the number of people who require long-term care has increased by 3.4 times from 1.49 million in 2000 to 5.07 million in 2021, LTCI expenditure increased from JPY 3.6 trillion in 2000 to JPY 11.1 trillion in 2020 (Ministry of Health Labor and Welfare, 2021). As disability become an increasingly significant component of disease burden and health expenditure, it is essential to take measures to help Japanese older adults to postpone the incident functional disability and prolong the disability-free survival times.

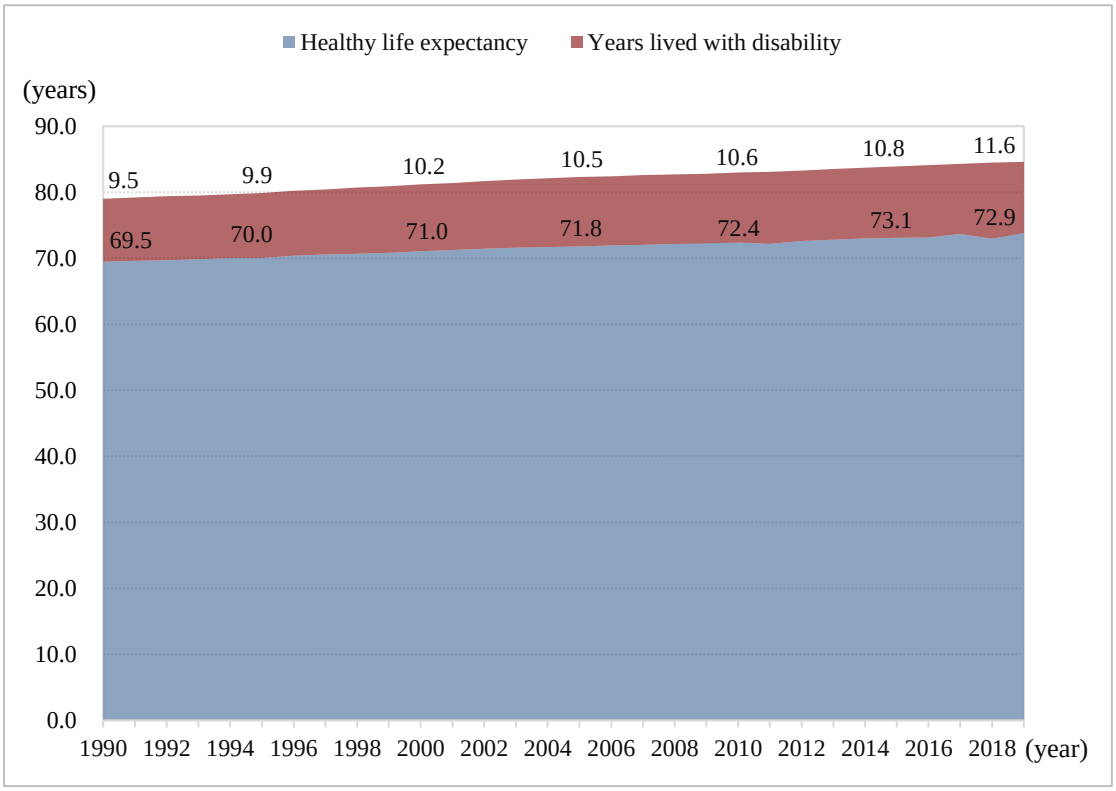

Figure 2 Healthy life expectancy and years lived with disability, Japan, 1990 to 2019

(Data source: Global Burden of Disease Study 2019 (GBD 2019) Results, Global Burden of Disease Collaborative Network.)

Lack of physical or social activities is a common risk factor for depressive symptoms

and functional disability among older adults (Zhang et al., 2021; Santini et al., 2015; Ginis et al., 2021; Tough et al., 2017). Nevertheless, as people age, various aspects of their lives change, for example, the quantity, quality and frequency of their social participation or physical exercise. A systematic review included thirty-one studies about trajectories of social activities in old age showed that three studies showed an increase of social engagement, especially at the beginning of old age (up to 75 years), twenty-one studies showed a reduction, and five studies showed a maintenance (Pinto and Neri, 2017). Another review paper about the trajectories of physical activities in older adults showed that seven out of eight studies identified a persistent physical activity, and those with a decreasing physical activity often fell to the level of the inactive (Lounassalo et al., 2019). The changes in behavioral activities among older adults was influenced by personal aspects (health, gender, income, education), environmental aspects (social support, physical barriers, and opportunities), and late-life events that characterize socially transient moments, such as, retirement and widowhood (Pinto and Neri, 2017). These influences may allow changes in behavioral activities to extend in a positive direction (increase or maintain in a higher level), or they may flourish in an adverse direction (decrease or maintain in a lower level). Given this, I hypothesis that positive change in behavioral activities can be an effective strategy to prevent the development or improve the prognosis of their disease and then prevent further morbidity and mortality.

This study includes three chapters. Chapter 1 will explore the association between changes in behavioral activities (social activities, exercise habits, and daily walking) and the incidence and persistence of depressive symptoms and then investigate if there is a difference in effect size among these three kinds of activities on depressive symptoms. Based on the results in Chapter 1, Chapter 2 will explore the association between changes in social activities and the incidence and persistence of depressive symptoms and then examine if the type and combination of social activities make a difference in depressive symptoms. Changes in behavioral activities are associated not only with the mental health of older adults but also with their functional health.

Additionally, depression is a significant risk factor for functional disability among older adults. Based on this, Chapter 3 will explore the association between changes in social activities and incident functional disability among depressed older adults and then examine if increasing or maintaining a higher level of social activities could prolong the disability-free survival time.

Chapter 1 Changes in behavioral activities and onset/persistence of depressive symptoms among age-specific older adults in the New Integrated Suburban Seniority Investigation Project

1-1. Introduction

Regular engagement in behavioral activities, such as contacting with friends or family members (Seung Hee and Kim, 2014), participating in leisure or religious activity (Choi et al., 2021; Hsu and Wright, 2014; Li et al., 2018; Isaac et al., 2009) and undertaking physical exercise (Zhang *et al.*, 2021) not only reduces the risk of onset of depressive disorders, but also improves symptoms in patients with a known diagnosis of depressive disorders (Hodgetts et al., 2017; Mau et al., 2020). However, the effects of behavioral activities on older adults with depressive symptoms may be dynamic, as the frequency of engagement in behavioral activities may change over time due to changes in physical function (e.g., disease) or social environment (e.g., retire, relocation or bereavement) (Yoshida et al., 2015). Although continued regular frequency of physical and social activities have been demonstrated negatively associated with the onset of depressive symptoms (Choi et al., 2015; Yoshida *et al.*, 2015). However, few studies have explored the association between changes in behavioral activities and the development of depressive symptoms.

Considering making treatment strategies of depressive symptoms in community-dwelling older adults, there is a need for inclusion of participants in depressive status at baseline, which gave the opportunity to study the development of depressive symptoms. Additionally, depressive status for community-dwelling older adults rarely focuses on a single risk factor, but a variety of risk factors with similar characteristics simultaneously (Fiske et al., 2009). Therefore, the combined effects of different kind of behavioral activities on depressive symptoms should be considered. A previous study has shown that more diverse participation in social activities further reduces the risk of depressive symptoms (Choi *et al.*, 2021). Another study about the combinatorial beneficial effects of social activity and physical activity in reducing

depressive symptoms showed that the effect is most pronounced in those who engage in at least two types of these activities (Roh et al., 2015). Few studies, however, have investigated the relationship between changes in combinations of behavioral activities in different frequency and transition of depressive symptoms over time.

In the present study, age-specific, older, Japanese community dwellers with and without depressive symptoms at baseline were included to examine the relationship between changes in behavioral activities and transition of depressive symptoms over a 6-year follow-up period. First, I hypothesized that older adults who engaged in behavioral activities at CRF, or IF would be less likely to have the onset or persistence of depressive symptoms. Second, I hypothesized that older adults who engaged in a wider variety of behavioral activities at CRF, or IF were less likely to experience new onset or worsening of depressive symptoms.

1-2. Methods

1-2.1 Study population

The study sample was obtained from the New Integrated Suburban Seniority Investigation (NISSIN) project, which is an ongoing, prospective cohort study that enrolled community-based, age-specific adults residing in Nisshin city.

The NISSIN project focused on people who would reach 65 years of age and aimed to investigate the predictors of mortality, morbidity, and other physical/mental outcomes among these age-specific younger elderly Japanese. The community-dwelling adults aged 64 years from Nisshin city were invited to participant a free comprehensive medical check-up and complete a self-administrated questionnaire in June every year from 1996 through 2005, and the responders were registered as the cohort participants. In total, 3,073 participants were included into this project. The comprehensive medical check-up included height and weight, systolic and diastolic,

clinical and laboratory test such as blood pressure, dipstick urinalyses, fecal occult blood etc. All clinical tests were performed at a single laboratory. The self-administrated questionnaire included items on demographical and lifestyle

characteristics, physical function, and quality of life.

Since 2002, another health check-ups and questionnaire surveys, similar to baseline, were conducted when participants reached 70 years. Participants who died or relocated out of the city were also followed according to the basic resident register of the city. In addition, from 2000 to now, this project is following-up the participants prospectively for the qualification as a Long-term Care Insurance recipient.

In the present study, of the total participant sample (n = 3,073), I excluded one participant whose competence of daily living questionnaire was invalid, 50 participants who had missing values on the GDS, and 19 participants who had missing data concerning behavioral activities. Therefore, 3,003 participants were eligible at baseline. 149 participants who relocated, 120 participants who died before the follow-up period were further excluded. Additionally, I excluded 1,010 participants who did not attend the check-ups at 70 years, 11 and 6 participants who had invalid or missing values on the GDS and behavioral activities, respectively. In total 1,707 participants (1,370 without depressive symptoms, 337 with depressive symptoms) were included in this study (**Figure 1-1**).

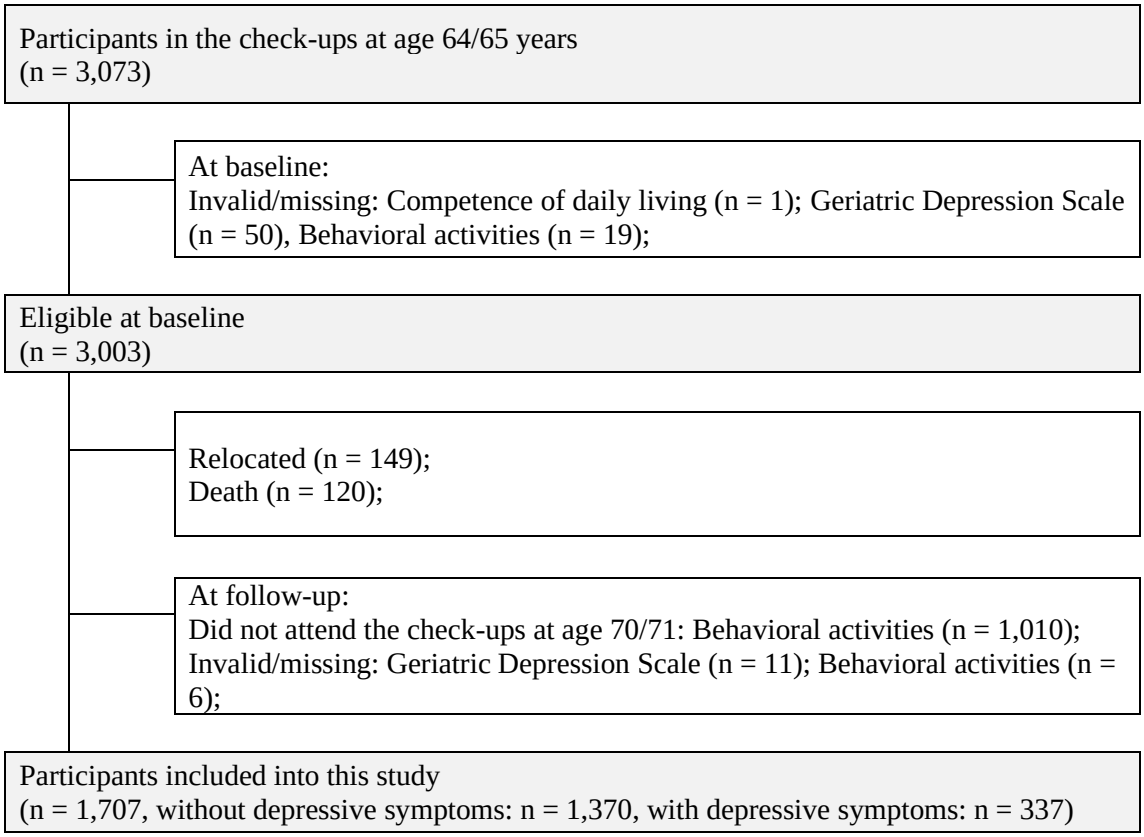

Figure 1-1 The flow chart of study subjects

1-2.2 Ethical issues

Informed consent was obtained from eligible respondents before the health check-up. For the questionnaire survey, oral consent was obtained using an opt-out approach until 2001, and written consent by an opt-in approach thereafter. The study protocol was approved by the Ethics Committee of Nagoya University Graduate School of Medicine, the National Center for Geriatrics and Gerontology of Japan, the Aichi Medical University School of Medicine, and Hokkaido University Graduate School of Medicine.

1-2.3 Assessment of depressive symptoms

Participants were screened for depressive symptoms at baseline and follow-up using

the Japanese version of the 15-item Geriatric Depression Scale (GDS), which has been validated in the Japanese population (Yatomi, 1994). The total score was calculated as the sum of scores for each of the 15 questions, ranging from 0 to 15. A higher score indicates a severity of depressive symptoms and a score ≥ 6 was considered to be having depressive symptoms (Schreiner et al., 2003).

1-2.4 Assessment of behavioral activities

Behavioral activities involved social activities, daily walking, and exercise habits, which were equally assessed at baseline and follow-up.

Social activities were measured based on 20 questions comprising three major categories: six questions were social-related activities, four questions were learning activities, and ten questions were personal activities (**Table 1-1**) (Hashimoto et al., 1997). For each question, scores of 3, 2, and 1 corresponding to "regularly doing," "occasionally doing," and "not doing" these activities, respectively. The total score of each participant was calculated as the sum of scores for the 20 questions, ranging from 20 to 60. I then categorized participants into quartile according to their total scores at baseline, and participants with scores that equal or lower than the median were assigned to the "low" group, the others were assigned to the "regular" group (Aoki et al., 1996). At follow-up, participants were similarly categorized using the same cut-off points.

Table 1-1 The Questionnaire of Social Activities

Categories		Regularly doing	Occasionally doing	Not doing
Social-related activities	1. Participation in activities for festivals, or some events in their cities/villages	3	2	1
	2. Participation in regional politics	3	2	1
	3. Membership in elderly activity groups	3	2	1
	4. Membership in hobbies groups	3	2	1
	5. Membership in volunteer groups	3	2	1
	6. Teaching one's skills	3	2	1
Learning activities	7. Schools for the elderly	3	2	1
	8. Study circles	3	2	1
	9. Listening to lectures	3	2	1
	10. Registering oneself at the civic center for the talented elderly	3	2	1
Personal activities	11. Contact with neighbors	3	2	1
	12. Shopping in their neighborhood	3	2	1
	13. Shopping in department stores	3	2	1
	14. Visiting friends and/or relatives living near their houses	3	2	1
	15. Visiting friends and/or relatives living far from their houses	3	2	1
	16. Traveling in Japan	3	2	1
	17. Traveling abroad	3	2	1
	18. Religious attendance	3	2	1
	19. Sports circles	3	2	1
	20. Recreation circles	3	2	1

Daily walking was assessed by asking participants “how many hours do you usually walk in a day, including the hours spent on housework or work?” Possible responses include “< 30 mins,” “30–60 mins,” “60–120 mins,” and “≥ 120 mins.” Previous intervention studies found a positive effect of daily walking time from 20 minutes to 60 minutes on depressive symptoms in adults (Mau *et al.*, 2020). A Japanese population-based study showed that a daily walking time of 75 min could mitigate the worsening of depressive symptoms in older adults aged 65 years and over (Tsuji et al., 2017). Thus, participants who responded as spending an hour or less on it were assigned to the “low” group, while the others were assigned to the “regular” group.

Exercise habits were assessed by asking the participants “how many times did you engage in exercise during the previous week?”. Possible responses included “none,” “less than once a week,” and “more than once a week.” Most studies on exercise intervention for depression use the frequency equal to or higher than twice a week as the minimum requirements (Klil-Drori et al., 2020). Therefore, participants with responses of “none” or “< 2 times/week” were assigned to the “low” group, while the others were assigned to the “regular” group.

The combination of multiple behavioral activities was classified into four groups based on the frequency of each activity (**Table 1-2**). Group A included participants who had a low frequency of engagement in all three activities. Group B included participants who had a low frequency of engagement in two activities but a regular frequency of engagement in one activity. Group C included participants who had a low frequency of engagement in one activity but a regular frequency of engagement in two activities. Finally, Group D included participants who had a regular frequency of engagement in all three activities.

Table 1-2 Combination of multiple behavioral activities

Behavioral activities	Social activities	Daily walking	Exercise habits	Combination of multiple behavioral activities
Frequency groups	low	low	low	Group A
			regular	Group B
		regular	low	Group B
			regular	Group C
	Regular	low	low	Group B
			regular	Group C
		regular	low	Group C
			regular	Group D

1-2.5 Transition of depressive symptoms and changes in behavioral activities

Four transitions of depressive symptoms were examined over time: two are for participants who did not have depressive symptoms at baseline, namely "remaining not have depressive symptoms" and "onset of depressive symptoms"; and two are for participants who did have depressive symptoms at baseline, namely "improvement of depressive symptoms" and "persistence of depressive symptoms" (**Table 1-3**).

Table 1-3 Changes in depressive symptoms and behavioral activities

Items	Baseline	Follow-up	Changes in behavioral activities
Depressive symptoms	not have	not have	remaining not have
	not have	have	onset
	have	not have	improvement
	have	have	persistence
Frequency groups of behavioral activities	low	low	continued low frequency
	low	regular	increased frequency
	regular	low	decreased frequency
	regular	regular	continued regular frequency

Additionally, changes in behavioral activities at baseline and follow-up were classified into four categories: continued low frequency (CLF), continued regular frequency (CRF), Increased frequency (IF), and decreased frequency (DF). Changes

in combination of multiple behavioral activities included six categories (**Table 1-4**): remained in Group A, B, C, D, increased (increased the number of regular-frequency behavioral activities) and decreased (decreased the number of regular-frequency behavioral activities).

Table 1-4 Changes in combination of multiple behavioral activities

Baseline	Follow-up			
	Group A	Group B	Group C	Group D
Group A	remained in Group A	increased	increased	increased
Group B	decreased	remained in Group B	increased	increased
Group C	decreased	decreased	remained in Group C	increased
Group D	decreased	decreased	decreased	remained in Group D

1-2.6 Covariates

Data on covariates were collected from self-administered questionnaires and comprehensive health check-ups performed at baseline. Sociodemographic variables included sex, year of participation, marital status (i.e., married, other), educational background (i.e., junior high school or lower, high school, college or higher), residential status (i.e., living alone, other), and work status (i.e., working, others). Health-related variables included smoking (i.e., never, former, current), drinking (i.e., never, current), body mass index (BMI) (< 18.5; 18.5–25.0; > 25.0), history of chronic diseases, and competence of daily living. BMI was calculated as the weight in kilograms divided by the height in meters squared. Chronic disease included cancer, hypertension, diabetes, arthritis, and cardiovascular disease (CVD). Moreover, competence of daily living was evaluated using the Tokyo Metropolitan Institute of Gerontology Index of Competence questionnaire, which contains 13 close-ended questions and has been validated in the Japanese population (Koyano et al., 1991). The total score was calculated as the sum of scores for responses to each of the 13 questions, and a higher total score indicates a higher competence in daily living (Okabayashi et al., 2019).

1-2.7 Statistical analysis

Baseline demographic characteristics were compared among participants who showed changes in behavioral activities using a Chi-squared test or Fisher's exact test for categorical data and an analysis of variance (ANOVA) for continuous numerical data. A modified Poisson regression model for binary outcome data, with a log link function and robust error variance, was constructed to estimate the risk ratios (RRs) and 95% confidence intervals (95% CIs). These were used to determine the association between changes in single behavioral activities, changes in the multiple behavioral activities and transition of depressive symptoms, while adjusting for potential confounders. Statistical analyses were performed using the SAS statistical software package version 9.4 for Microsoft Windows (SAS Institute Inc., Cary, NC, USA). Statistical significance was set as $P < 0.05$.

1-3. Results

1-3.1 Baseline characteristics

Participants with a CRF or IF of behavioral activities were more likely to have higher educational background, higher competence of daily living, while they were less likely to be current smoker and have depressive symptoms. I also found that woman took higher proportion on CRF of social activities and daily walking, man took a higher proportion on CRF of exercise habits. In addition, for those who had a CRF or IF of daily walking or exercise habits, they were more likely to have a normal BMI, and be never drinker. About the work status, it seems that those who had a job were more likely to have an IF of social activities and exercise habits (**Table 1-5**).

Table 1-5 Baseline characteristics of participants

Baseline characteristics	Total	Changes in social activity				*P*	Changes in daily walking				*P*
		CLF	CRF	IF	DF		CLF	CRF	IF	DF	
Number of participants	1707	345	846	427	89		403	776	322	206	
Female	827 (48.5)	139 (40.3)	468 (55.3)	169 (39.6)	51 (57.3)	**<.0001**	129 (32.0)	467 (60.2)	134 (41.6)	97 (47.1)	**<.0001**
Participation year											
1996	125 (7.3)	32 (9.3)	56 (6.6)	32 (7.5)	5 (5.6)		39 (9.7)	47 (6.1)	23 (7.1)	16 (7.8)	
1997	146 (8.6)	35 (10.1)	60 (7.1)	48 (11.2)	3 (3.4)		41 (10.2)	60 (7.7)	25 (7.8)	20 (9.7)	
1998	151 (8.9)	27 (7.8)	77 (9.1)	36 (8.4)	11 (12.4)		31 (7.7)	72 (9.3)	30 (9.3)	18 (8.7)	
1999	178 (10.4)	37 (10.7)	85 (10.1)	42 (9.8)	14 (15.7)		37 (9.2)	85 (11.0)	39 (12.1)	17 (8.3)	
2000	157 (9.2)	28 (8.1)	79 (9.3)	40 (9.4)	10 (11.2)	0.365	42 (10.4)	71 (9.2)	32 (9.9)	12 (5.8)	0.058
2001	189 (11.1)	43 (12.5)	94 (11.1)	43 (10.1)	9 (10.1)		42 (10.4)	73 (9.4)	47 (14.6)	27 (13.1)	
2002	204 (12.0)	35 (10.1)	105 (12.4)	52 (12.2)	12 (13.5)		44 (10.9)	102 (13.1)	40 (12.4)	18 (8.7)	
2003	203 (11.9)	38 (11)	110 (13)	47 (11)	8 (9)		46 (11.4)	97 (12.5)	34 (10.6)	26 (12.6)	
2004	175 (10.3)	41 (11.9)	83 (9.8)	39 (9.1)	12 (13.5)		44 (10.9)	72 (9.3)	26 (8.1)	33 (16)	
2005	179 (10.5)	29 (8.4)	97 (11.5)	48 (11.2)	5 (5.6)		37 (9.2)	97 (12.5)	26 (8.1)	19 (9.2)	
BMI											
<18.5	70 (4.1)	19 (5.5)	32 (3.8)	15 (3.5)	4 (4.5)		14 (3.5)	39 (5.0)	8 (2.5)	9 (4.4)	
18.5-25.0	1259 (73.8)	250 (72.5)	636 (75.2)	313 (73.3)	60 (67.4)	0.522	281 (69.7)	581 (74.9)	252 (78.3)	145 (70.4)	**0.032**
>25.0	378 (22.1)	76 (22)	178 (21)	99 (23.2)	25 (28.1)		108 (26.8)	156 (20.1)	62 (19.3)	52 (25.2)	
Smoking											
never	937 (54.9)	152 (44.1)	527 (62.3)	207 (48.5)	51 (57.3)		170 (42.2)	496 (63.9)	165 (51.2)	106 (51.5)	
former	501 (29.4)	110 (31.9)	226 (26.7)	142 (33.3)	23 (25.8)	**<.0001**	151 (37.5)	183 (23.6)	108 (33.5)	59 (28.6)	**<.0001**
current	268 (15.7)	83 (24.1)	93 (11)	77 (18)	15 (16.9)		82 (20.4)	96 (12.4)	49 (15.2)	41 (19.9)	
missing	1 (0.1)	0 (0)	0 (0)	1 (0.2)	0 (0)		0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	
Drinking											
never	910 (53.3)	188 (54.5)	465 (55)	208 (48.7)	49 (55.1)	0.181	185 (45.9)	468 (60.3)	148 (46.0)	109 (52.9)	**<.0001**
current drinker	796 (46.6)	156 (45.2)	381 (45)	219 (51.3)	40 (44.9)		218 (54.1)	307 (39.6)	174 (54.0)	97 (47.1)	

missing	1 (0.1)	1 (0.3)	0 (0)	0 (0)	0 (0)		0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	
Marital status											
married	1540 (90.2)	305 (88.4)	769 (90.9)	385 (90.2)	81 (91)		372 (92.3)	690 (88.9)	295 (91.6)	183 (88.8)	
others	165 (9.7)	40 (11.6)	76 (9)	41 (9.6)	8 (9)	0.814	31 (7.7)	85 (11.0)	27 (8.4)	22 (10.7)	0.284
missing	2 (0.1)	0 (0)	1 (0.1)	1 (0.2)	0 (0)		0 (0.0)	1 (0.1)	0 (0.0)	1 (0.5)	
Education background											
junior high school or lower	479 (28.1)	130 (37.7)	190 (22.5)	127 (29.7)	32 (36)		81 (20.1)	248 (32.0)	78 (24.2)	72 (35.0)	
high school	778 (45.6)	136 (39.4)	409 (48.4)	194 (45.4)	39 (43.8)	**<.0001**	182 (45.2)	350 (45.1)	152 (47.2)	94 (45.6)	**<.0001**
college or higher	449 (26.3)	78 (22.6)	247 (29.2)	106 (24.8)	18 (20.2)		140 (34.7)	177 (22.8)	92 (28.6)	40 (19.4)	
missing	1 (0.1)	1 (0.3)	0 (0)	0 (0)	0 (0)		0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	
Residential status											
living alone	67 (3.9)	320 (92.8)	796 (94.1)	403 (94.4)	84 (94.4)		11 (2.7)	36 (4.6)	11 (3.4)	9 (4.4)	
others	1603 (93.9)	17 (4.9)	32 (3.8)	15 (3.5)	3 (3.4)	0.972	379 (94.0)	727 (93.7)	305 (94.7)	192 (93.2)	0.425
missing	37 (2.2)	8 (2.3)	18 (2.1)	9 (2.1)	2 (2.3)		13 (3.2)	13 (1.7)	6 (1.9)	5 (2.4)	
Work status											
working	704 (41.2)	186 (53.9)	517 (61.1)	228 (53.4)	57 (64)		176 (43.7)	298 (38.4)	129 (40.1)	101 (49.0)	
others	988 (57.9)	155 (44.9)	321 (37.9)	197 (46.1)	31 (34.8)	0.052	224 (55.6)	471 (60.7)	190 (59.0)	103 (50.0)	0.170
missing	15 (0.9)	4 (1.2)	8 (1)	2 (0.5)	1 (1.1)		3 (0.7)	7 (0.9)	3 (0.9)	2 (1.0)	
Cancer	62 (3.6)	15 (4.4)	37 (4.4)	8 (1.9)	2 (2.3)	0.107	17 (4.2)	28 (3.6)	10 (3.1)	7 (3.4)	0.877
Hypertension	388 (22.7)	83 (24.1)	177 (20.9)	103 (24.1)	25 (28.1)	0.278	99 (24.6)	170 (21.9)	73 (22.7)	46 (22.3)	0.779
Diabetes	125 (7.3)	83 (24.1)	177 (20.9)	103 (24.1)	25 (28.1)	0.432	33 (8.2)	50 (6.4)	21 (6.5)	21 (10.2)	0.247
Arthritis	86 (5.0)	21 (6.1)	39 (4.6)	22 (5.2)	4 (4.5)	0.757	15 (3.7)	41 (5.3)	14 (4.4)	16 (7.8)	0.166
CVD	267 (15.6)	57 (16.5)	137 (16.2)	61 (14.3)	12 (13.5)	0.727	86 (21.3)	93 (12.0)	46 (14.3)	42 (20.4)	**<.0001**
Depressive symptoms											
not have	1370 (80.3)	212 (61.5)	757 (89.5)	335 (78.5)	66 (74.2)	**<.0001**	314 (77.9)	638 (82.2)	254 (78.9)	164 (79.6)	0.294
have	337 (19.7)	133 (38.6)	89 (10.5)	92 (21.6)	23 (25.8)		89 (22.1)	138 (17.8)	68 (21.1)	42 (20.4)	
Competence of	12.18 ±	11.43 ±	12.56 ±	12.03 ±	12.13 ±	**<.0001**	12.02 ±	12.28 ±	12.21 ±	12.04 ±	**<.0001**

daily living	1.23	1.60	0.88	1.18	1.24	1.35	1.10	1.25	1.39

Difference among different changes in social activities tested by chi-square test and ANOVA test depending on the type of the variables. CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency, CVD: cardiovascular disease

Continued Table 1-5

Baseline characteristics	Total	Changes in exercise habits				*P*
		CLF	CRF	IF	DF	
Number of participants	1707	538	601	376	192	
Female	827 (48.5)	286 (53.2)	273 (45.4)	165 (43.9)	103 (53.7)	**0.007**
Participation year						
1996	125 (7.3)	42 (7.8)	38 (6.3)	25 (6.7)	20 (10.4)	
1997	146 (8.6)	59 (11)	34 (5.7)	34 (9.0)	19 (9.9)	
1998	151 (8.9)	42 (7.8)	60 (10.0)	40 (10.6)	9 (4.7)	
1999	178 (10.4)	51 (9.5)	59 (9.8)	38 (10.1)	30 (15.6)	
2000	157 (9.2)	61 (11.3)	48 (8.0)	25 (6.7)	23 (12.0)	**0.010**
2001	189 (11.1)	54 (10.0)	72 (12.0)	39 (10.4)	24 (12.5)	
2002	204 (12.0)	63 (11.7)	75 (12.5)	46 (12.2)	20 (10.4)	
2003	203 (11.9)	68 (12.6)	69 (11.5)	48 (12.8)	18 (9.4)	
2004	175 (10.3)	46 (8.6)	71 (11.8)	41 (10.9)	17 (8.9)	
2005	179 (10.5)	52 (9.7)	75 (12.5)	40 (10.6)	12 (6.3)	
BMI						
<18.5	70 (4.1)	29 (5.4)	17 (2.8)	17 (4.5)	7 (3.7)	
18.5-25.0	1259 (73.8)	387 (71.9)	466 (77.5)	276 (73.4)	130 (67.7)	**0.049**
>25.0	378 (22.1)	122 (22.7)	118 (19.6)	83 (22.1)	55 (28.7)	
Smoking						
never	937 (54.9)	319 (59.3)	316 (52.6)	193 (51.3)	109 (56.8)	**<.0001**
former	501 (29.4)	120 (22.3)	214 (35.6)	117 (31.1)	50 (26.0)	

current	268 (15.7)	99 (18.4)	70 (11.7)	66 (17.6)	33 (17.2)	
missing	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	
Drinking						
never	910 (53.3)	314 (58.4)	301 (50.1)	185 (49.2)	110 (57.3)	
current drinker	796 (46.6)	224 (41.6)	299 (49.8)	191 (50.8)	82 (42.7)	**0.036**
missing	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	
Marital status						
married	1540 (90.2)	481 (89.4)	546 (90.9)	341 (90.7)	172 (89.6)	
others	165 (9.7)	57 (10.6)	55 (9.2)	34 (9.0)	19 (9.9)	0.469
missing	2 (0.1)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.5)	
Education background						
junior high school or lower	479 (28.1)	179 (33.3)	125 (20.8)	109 (29)	66 (34.4)	
high school	778 (45.6)	233 (43.3)	297 (49.4)	168 (44.7)	80 (41.7)	**0.001**
college or higher	449 (26.3)	126 (23.4)	178 (29.6)	99 (26.3)	46 (24.0)	
missing	1 (0.1)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	
Residential status						
living alone	67 (3.9)	20 (3.7)	19 (3.2)	17 (4.5)	11 (5.7)	
others	1603 (93.9)	511 (95)	562 (93.5)	351 (93.4)	179 (93.2)	0.138
missing	37 (2.2)	7 (1.3)	20 (3.3)	8 (2.1)	2 (1.0)	
Work status						
working	704 (41.2)	247 (45.9)	183 (30.5)	200 (53.2)	74 (38.5)	
others	988 (57.9)	283 (52.6)	413 (68.7)	175 (46.5)	117 (60.9)	**<.0001**
missing	15 (0.9)	8 (1.5)	5 (0.8)	1 (0.3)	1 (0.5)	
Cancer	62 (3.6)	16 (3.0)	23 (3.8)	14 (3.7)	9 (4.7)	0.717
Hypertension	388 (22.7)	114 (21.2)	155 (25.8)	79 (21)	40 (20.8)	0.175
Diabetes	125 (7.3)	24 (4.5)	59 (9.8)	24 (6.4)	18 (9.4)	**0.003**
Arthritis	86 (5.0)	35 (6.5)	36 (6.0)	7 (1.9)	8 (4.2)	**0.008**
CVD	267 (15.6)	79 (14.7)	105 (17.5)	60 (16)	23 (12.0)	0.275

Depressive symptoms						
not have	1370 (80.3)	399 (74.2)	513 (85.4)	304 (80.9)	154 (80.2)	**<.0001**
have	337 (19.7)	139 (25.8)	88 (14.6)	72 (19.2)	38 (19.8)	
Competence of daily living	12.18 ± 1.23	12.01 ± 1.38	12.32 ± 1.11	12.11 ± 1.29	12.36 ± 0.96	**<.0001**

Difference among different changes in social activities tested by chi-square test and ANOVA test depending on the type of the variables. CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency, CVD: cardiovascular disease

1-3.2 Association between changes in behavioral activities and the onset of depressive symptoms

Table 1-6 shows the association between changes in behavioral activities and the onset of depressive symptoms among participants without depressive symptoms at baseline. There were 139 (10.1%) participants had the onset of depressive symptoms after 6 years follow-up period. For changes in social activities, participants with CRF (RR = 0.45, 95% CI = 0.29–0.69, P <0.01) and IF (RR = 0.41, 95% CI = 0.25–0.68, P <0.01) were less likely to have the onset of depressive symptoms than those with CLF. For changes in daily walking, compared with CLF, CRF (RR=0.55, 95% CI = 0.36–0.84, P <0.01) and IF (RR=0.48, 95% CI = 0.27–0.85, P <0.01) were significantly associated with the onset of depressive symptoms. Moreover, regarding the changes in exercise habits, a significant association was found between CRF (RR = 0.64, 95% CI = 0.42–0.99, P <0.01) and the onset of depressive symptoms.

For changes in combination of behavioral activities, compared with participants who remained in Group A from baseline to follow-up, those who remained in Groups D, as well as those who increased the number of behavioral activities at a regular frequency (e.g., moving from Group A at baseline to Group B at follow-up) experienced the protective effects of these activities on the onset of their depressive symptoms.

Table 1-6 Association between changes in behavioral activities and the onset of depressive symptoms among participants without depressive symptoms at baseline

Behavioral activities	Changes in behavioral activities	Total (n = 1370)	Onset (n = 139)	Model 1	Model 2	Model 3
				RRs (95% CI)	RRs (95% CI)	RRs (95% CI)
Social activity	CLF	212	44 (20.8)	1.00	1.00	1.00
	CRF	757	59 (7.8)	0.36 (0.24, 0.54) ***	0.37 (0.25, 0.56) ***	0.45 (0.29, 0.69) **
	IF	335	26 (7.8)	0.37 (0.23, 0.60) ***	0.38 (0.23, 0.62) **	0.41 (0.25, 0.68) **
	DF	66	10 (15.2)	0.72 (0.36, 1.43)	0.77 (0.38, 1.53)	0.84 (0.42, 1.71)
Daily walking	CLF	314	44 (14.0)	1.00	1.00	1.00
	CRF	638	51 (8.0)	0.54 (0.36, 0.82) **	0.53 (0.35, 0.80) **	0.55 (0.36, 0.84) **
	IF	254	17 (6.7)	0.47 (0.27, 0.83) **	0.47 (0.27, 0.83) **	0.48 (0.27, 0.85) *
	DF	164	27 (16.5)	1.15 (0.70, 1.86)	1.03 (0.63, 1.69)	1.07 (0.64, 1.78)
Exercise habit	CLF	399	52 (13.0)	1.00	1.00	1.00
	CRF	513	40 (7.8)	0.59 (0.39, 0.90) *	0.63 (0.41, 0.97) *	0.64 (0.42, 0.99) *
	IF	304	34 (11.2)	0.85 (0.55, 1.32)	0.90 (0.58, 1.39)	0.90 (0.58, 1.40)
	DF	154	13 (8.4)	0.67 (0.36, 1.23)	0.63 (0.34, 1.20)	0.68 (0.36, 1.29)
Combination of behavioral activities	remained in Group A	14	5 (35.7)	1.00	1.00	1.00
	remained in Group B	121	16 (13.2)	0.69 (0.30, 1.60)	0.71 (0.30, 1.66)	0.77 (0.32, 1.84)
	remained in Group C	269	28 (10.4)	0.47 (0.21, 1.07)	0.52 (0.23, 1.18)	0.60 (0.26, 1.39)
	remained in Group D	230	11 (4.8)	0.24 (0.09, 0.62) **	0.26 (0.10, 0.67) **	0.33 (0.12, 0.87) *
	increased	505	47 (9.3)	0.37 (0.17, 0.78) **	0.39 (0.18, 0.84) *	0.44 (0.20, 0.96) *
	decreased	231	32 (13.9)	0.55 (0.25, 1.22)	0.55 (0.25, 1.24)	0.65 (0.28, 1.49)

CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency; RRs = relative ratios, CI = confidence interval; Model 1 adjusted for gender and year of participation; Model 2 adjusted for sex, year of participation, smoking, drinking, marital status, education background residential status, and work status; Model 3 adjusted for sex, year of participation, smoking, drinking, marital status, education background, residential status, work status, BMI, cancer, hypertension, diabetes, arthritis, cardiovascular disease and competence of daily living; *P<0.05, **P<0.01, ***P<0.001

1-3.3 Association between changes in behavioral activities and the persistence of depressive symptoms

Table 1-7 shows the association between changes in behavioral activities and persistence of depressive symptoms among participants who had depressive symptoms at baseline. 163 (48.4%) older adults maintained the depressive status after 6 years follow-up period. Compared with behavioral activities at CLF, social activities, daily walking, and exercise habits at CRF, social activities and daily walking at IF were less likely to have the persistence of depressive symptoms, although there is no significant association after controlling all the confounders.

For changes in combination of behavioral activities, compared with participants who remained in Group A from baseline to follow-up, those who remained in the same group between baseline and follow-up or increased the number of behavioral activities at a regular frequency (e.g., moving from Group A at baseline to Group D at follow-up) may also protect them from the persistence of depressive symptoms.

Table 1-7 Association between changes in behavioral activities and the persistence of depressive symptoms among participants with depressive symptoms at baseline

Behavioral activities	Changes in behavioral activities	Total (n = 337)	Persistence (n = 163)	Model 1	Model 2	Model 3
				RRs (95% CI)	RRs (95% CI)	RRs (95% CI)
Social activity	CLF	133	77 (57.9)	1.00	1.00	1.00
	CRF	89	30 (33.7)	0.61 (0.40, 0.94) *	0.68 (0.43, 1.06)	0.75 (0.47, 1.20)
	IF	92	43 (46.7)	0.77 (0.53, 1.13)	0.81 (0.55, 1.20)	0.84 (0.57, 1.25)
	DF	23	13 (56.5)	0.94 (0.51, 1.74)	0.93 (0.50, 1.72)	0.99 (0.53, 1.85)
Daily walking	CLF	89	46 (51.7)	1.00	1.00	1.00
	CRF	138	62 (44.9)	0.90 (0.61, 1.35)	0.84 (0.56, 1.27)	0.87 (0.57, 1.34)
	IF	68	29 (42.6)	0.82 (0.52, 1.32)	0.84 (0.52, 1.36)	0.87 (0.53, 1.43)
	DF	42	26 (61.9)	1.22 (0.75, 1.98)	1.20 (0.72, 1.98)	1.18 (0.71, 1.98)
Exercise habit	CLF	139	75 (54.0)	1.00	1.00	1.00
	CRF	88	32 (36.4)	0.69 (0.45, 1.06)	0.65 (0.42, 1.02)	0.70 (0.44, 1.11)
	IF	72	39 (54.2)	1.01 (0.68, 1.50)	0.99 (0.66, 1.48)	1.07 (0.71, 1.63)
	DF	38	17 (44.7)	0.85 (0.50, 1.45)	0.85 (0.50, 1.47)	0.89 (0.51, 1.55)
Combination of behavioral activities	remained in Group A	19	12 (63.2)	1.00	1.00	1.00
	remained in Group B	34	22 (64.7)	0.93 (0.49, 1.77)	0.86 (0.44, 1.68)	0.93 (0.46, 1.88)
	remained in Group C	56	23 (41.1)	0.85 (0.40, 1.81)	0.77 (0.35, 1.68)	0.88 (0.39, 1.98)
	remained in Group D	23	7 (30.4)	0.38 (0.11, 1.34)	0.37 (0.10, 1.33)	0.46 (0.12, 1.70)
	increased	144	64 (44.4)	0.81 (0.45, 1.47)	0.79 (0.43, 1.47)	0.88 (0.46, 1.68)
	decreased	61	35 (57.4)	1.07 (0.55, 2.06)	1.03 (0.52, 2.04)	1.09 (0.53, 2.25)

CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency; RRs = relative ratios, CI = confidence interval; Model 1 adjusted for gender and year of participation; Model 2 adjusted for sex, year of participation, smoking, drinking, marital status, education background residential status, and work status; Model 3 adjusted for sex, year of participation, smoking, drinking, marital status, education background, residential status, work status, BMI, cancer, hypertension, diabetes, arthritis, cardiovascular disease and competence of daily living; *P<0.05, **P<0.01, ***P<0.001

1-4. Discussion

To my knowledge, this is the first comprehensive assessment of the effects of changes in behavioral activities on the transition of depressive symptoms among older community-dwelling adults with and without depressive symptoms, respectively. The findings indicated that participants without depressive symptoms at baseline engaged in social activities and daily walking at CRF and IF were less likely to have the onset of depressive symptoms over the 6-year follow-up period, compared with participants who engaged in activities at CLF. Additionally, participants with depressive symptoms who engaged in behavioral activities at CRF were less likely to have their symptoms exist. However, this effect was no longer significant once relevant confounders were adjusted. Further analysis of changes in combinations of behavioral activities in different frequencies and transition of depressive symptoms over the 6-year follow-up period showed that participants engaging in a greater variety of behavioral activities at regular frequency were less likely to experience new onset or persistence of depressive symptoms.

Considering the effects of changes in behavioral activities on the onset of depressive symptoms, a Korean study on participants aged ≥ 45 years showed that continued or new participation in social activities was negatively associated with the onset of depressive symptoms (Choi *et al.*, 2015). The results further in line with these results and demonstrate that social support or social respect received by older adults through participation in social activities can have a protective effect on the development of depressive symptoms. Another study that included participants aged ≥ 68 years found that walking for recreational purposes, rather than utilitarian purposes, was strongly associated with a reduction in the risk of developing depression (Julien et al., 2013). However, two studies among participants aged ≥ 60 years found that the maintenance, rather than increase or initiation, of exercise could protect older adults from depression (Yoshida *et al.*, 2015; Chang et al., 2017). The results are also in line with these findings. A review explained the reason of unprotected effect of increasing or

initiation of exercise on depressive symptoms that physical activity could optimize hippocampal neurogenesis, thereby exerting antidepressant effects (Zhang *et al.*, 2021). However, the natural course of depression disorders tended to worsen with increasing age (Schaakxs et al., 2018), and exercise-related improvements to the capacity for vascular hippocampal plasticity decreased with age (Maass et al., 2015). Therefore, as participants with depressive disorders age, exercise at IF may not be completely beneficial for the improvement of depressive symptoms.

Importantly, I found that social activities had the lowest risk ratio on the onset of depressive symptoms, followed by daily walking and exercise habits. The mechanism of social activities on the depressive symptom is that positive interpersonal interaction broadens older individuals' social lives, increases their confidence, self-efficacy, and self-esteem, and then brings protective factors against depression (Santini *et al.*, 2015; Lee et al., 2018). However, the higher frequency of interactions and intimacy obtained from physical activity, in addition to its anti-inflammatory effects, should not be underestimated in the mechanisms of depressive evidence in older adults (Zhang *et al.*, 2021; Yoshida *et al.*, 2015; Xiao et al., 2021; Chao, 2016). Hence, social interaction may have a stronger protective effect against the onset of depressive symptoms compared with other behavioral activities.

Longitudinal and interventional studies have shown that behavioral activities are negatively associated with the persistence of depressive symptoms (Isaac *et al.*, 2009; Zhang *et al.*, 2021; Robertson et al., 2012). In this study, the association between CRF of behavioral activities and the persistence in depressive symptoms was weakened once adjusted for BMI, competence of daily living, and history of chronic disease. It is plausible that physical disability or chronic disease could increase the risk of having depressive symptoms as these conditions restrict or reduce the participation in behavioral activities (Blazer, 2003). Moreover, participants were less likely to maintain the depressive status when they had IF of social activities and daily walking time, although this association was not significant. There may be several reasons for this. First, a type II error may have occurred due to the small sample number of

participants with depressive symptoms at baseline. Second, the effects of behavioral activities on the persistence of depressive symptoms may depend on the type, intensity, or duration of the activities (Li *et al.*, 2018; Isaac *et al.*, 2009; Mau *et al.*, 2020; Robertson *et al.*, 2012; Glass et al., 2006; Lucas et al., 2011; Tsuji *et al.*, 2017). Future longitudinal or interventional studies should focus on this aspect. The antidepressant effects of behavioral activities on the free of depressive symptoms may be more effective when combined with antidepressants medications or psychosocial interventions, which may also be confirmed by future studies.

In relation to changes in the cumulative of behavioral activities and transition of depressive symptoms, I found beneficial effects in increasing the variety of regular frequency activities or consistently maintaining a combination of activities in the same way. This finding points to the accumulation effect, whereby if older adults play multiple roles in a variety of activities, they will gain increased levels of self-esteem and social support (Choi *et al.*, 2021). This is also a hopeful finding in that older adults can select from a variety of activities to increase their adherence.

The age-specific participants in this study allow me effectively eliminated the age-derived biases. Moreover, most of Japanese employees retire about 65 years old, their lifestyles may be easily changed at this time. The real presence of these changes is therefore more significant to explore the association between changes in behavioral activities and transition of depressive symptoms.

Several limitations should be considered. First, depressive symptoms could also be a reason for reducing behavioral activities, but this study did not consider the inverse causation. The causality between transition of depressive symptoms and changes in behavioral activity remains unknown, and intervention studies are required to better understand the association. Second, coexisting cognitive impairment with depressive symptoms in older adults is common, and depressive symptoms may be both a risk factor and symptom of cognitive decline. Due to relatively few participants completing the assessment of cognitive function, it was not included as a covariate. I

attempted to perform the analysis in participants with valid cognitive function assessments. However, the results did not differ when cognitive functioning was included as a confounder. Third, the cohort only did two waves of investigation for six-year. We cannot assess changes in different waves during the six-year follow-up period. Future studies may consider it since the behavioral activities may fluctuate in a short period due to the physical or mental status. Additionally, there were some biases. The convenience sampling method may yield biased estimates of the target population because of the low generalizability. The lower response rate may cause a non-negligible selection bias. But the participants we included in this study were healthier than the non-participants. They were more likely to have a regular frequency of social activities, daily walking, and exercise habits, and they had a lower proportion of having depressive symptoms. The reality of the association between exposure and outcomes may be higher. The self-reported questionnaire might have led to recall biases because participants were asked to recall their behavioral activities during the past week. Hence, future studies could utilize public records of the use of facilities by participants, such as the church attendance records; or use wearable devices to record calories consumed or walking time. Finally, the assessment of social activities was done through questionnaires, and we divided participants into frequency groups based on the quartiles of the total scores of all participants' questionnaires, so we are unable to give participants specific recommendations on the frequency of social activity participation.

Chapter 2 Changes in social activities and onset/persistence of depressive symptoms among age-specific older adults in the New Integrated Suburban Seniority Investigation Project

2-1. Introduction

The results from chapter 1 showed that social interaction may had stronger effect size on depressive symptoms. Although previous studies have demonstrated that social participation, from which people could establish social networks and connections, increase their social interaction and get social support, has protective effects against depressive symptoms among older adults, the effect size is related to intensity and type of social participation (Shiba et al., 2021; Nakagomi et al., 2020; Watanabe et al., 2019). For example, informal social activities (date a friend, talking face-to-face with friends or children) have greater effects on reducing the risks of developing depressive symptoms compared with formal activities (religious or volunteer activities) (Steger and Kashdan, 2009; Seung Hee and Kim, 2014). Nevertheless, the same type of social activity may produce inconsistent results in terms of effects on depressive symptoms in different participants. An European study on adults aged 50 years and over found that participation in religious activities is associated with decreased depressive symptoms after four years, respectively (Croezen et al., 2015). An Asian study on adults aged 60 years and over reported the opposite results: attending religious activities is associated with increased depressive symptoms (Min et al., 2016). This suggested that the association between social activities and depressive symptoms may differ not only across different types of social activities, but also across different social cultures (Min *et al.*, 2016).

Thus, in examining the effects of social activities on depressive symptoms, although the specific types of social activities are easier to explore in terms of their effect on depressive symptoms, research on the comparison between different studies and the generalization across different races has been limited. Therefore, combing multiple social activities into a scale or measurement would be significant in exploring the

protection or intervention of depressive symptoms. First, participation in multiple social activities allows older adults to occupy various roles increasing their self-esteem and then benefit their mental health (Choi *et al.*, 2021). Moreover, different types of social activities may act differently on depressive symptoms, and there may be a cumulative or compensatory effect among multiple types of social activities. For example, engaging in more diverse activities with positive effects implies greater benefits on depressive symptoms; and increased participation in socializing with others may counteract the harmful effects of negative activities (Chao, 2016).

Although previous studies have explored the association between changes in social activity and depressive symptoms, (Choi *et al.*, 2015; Chao, 2016) these studies have only either the linear relation between changes in social activities without considering the onset or development in depressive symptoms, or only considered changes in single social activity, not the changes in the combination of different types of social activities.

The current study assessed social activities for community-dwelling older adults using a set of questions and divided them into three types based on the internal consistency of these activity types: social-related, learning, and personal activities. I explored the association between frequency changes in social activities and both the onset and persistence of depressive symptoms. I further explored the types and combinations of multiple types of social activities that have a greater influence on depressive symptoms.

2-2. Methods

2-2.1 Study design and participants

Please refer to the study design in Chapter one.

Of all the eligible participants (n = 3,073), I excluded 51 participants who had invalid response (n = 1) and missing values (n = 50) to the Geriatric Depression Scale (GDS) at baseline. I also excluded participants who relocated (n = 149) or died (n = 121) before follow-up. In addition, participants who did not attend the check-ups (n = 180),

who had missing values of GDS questionnaires (n = 26) and social activities (n = 86) at follow-up were also excluded. Thus, in this study, I included a total of 2,460 participants, of whom 1,938 had no depressive symptoms and 522 had depressive symptoms at baseline (**Figure 2-1**).

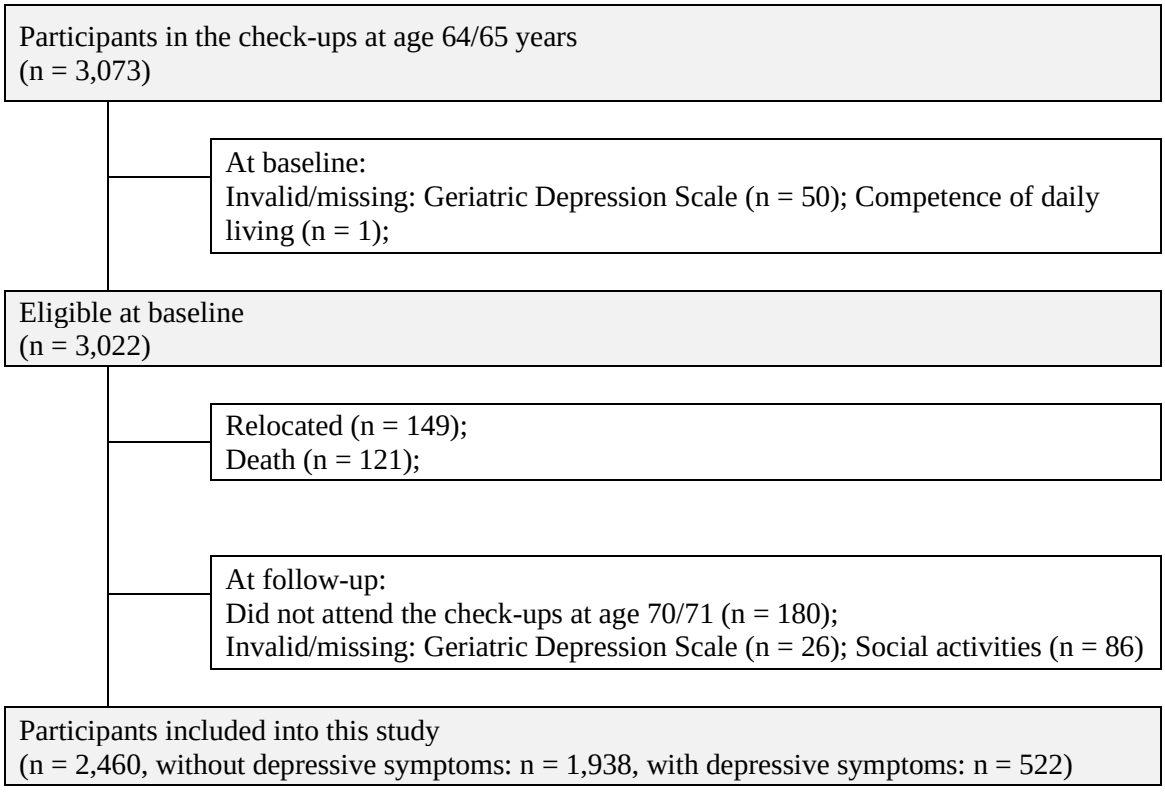

Figure 2-1 The flow chart of study subjects

2-2.2 Ethical issues

Please refer to Ethical issues in Chapter one.

2-2.3 Assessment of depressive symptoms

I used the same method to assess depressive symptoms as in Chapter one.

2-2.4 Assessment of social activities

The assessment of social activities is identical to that in Chapter one.

The combination of multiple social activities into four groups based on the frequency of each activity is similar to the group classification in Chapter one (Table 1-2).

2-2.5 Changes in depressive symptoms and changes in social activities

Change types of depressive symptoms are identical to that in Chapter one (**Table 1-3**). As with changes in behavioral activities in Chapter one, there are also four categories of changes in single social activities (CLF, CRF, IF, and DF) (**Table 1-3**) and six types of changes in multiple social activities (Group A, B, C, D, increased and decreased) (**Table 1-4**).

2-2.6 Covariates

The covariates that are controlled for in the models are the same as in Chapter one in addition to exercise habits (< 2/week, ≥ 2/week) and daily walking (< 60/day, ≥ 60/day).

2-2.7 Statistical analysis

I compared the baseline demographic characteristics among participants who showed changes in social activities using a Chi-squared test or Fisher's exact test for categorical data and an analysis of variance (ANOVA) for continuous numerical data. Due to the higher prevalence rate of our outcome (the onset (12.4%) and persistence (50.8%) of depressive symptoms), a modified Poisson regression model for binary outcome data, with a log link function and robust error variance, was constructed to estimate the risk ratios (RRs) and 95% confidence intervals (95% CIs). I used the RRs and CIs to determine the association between changes in social activities, changes in multiple social activities, and onset/persistence of depressive symptoms while adjusting for potential confounders. Statistical analyses were performed using SAS software package version 9.4 for Microsoft Windows (SAS Institute Inc., Cary, NC, USA). Statistical significance was set as $P < 0.05$.

2-3. Results

2-3.1 Baseline characteristics

Among participants who had changes in these three kinds of social activities, who with CRF in engagement were more likely to be woman, never smoker, never drinker,

have higher education backgrounds and competence of daily living, be free of depressive symptoms. Participants who had an IF of personal activities were more likely to be in a working state (**Table 2-1**).

Table 2-1 Baseline characteristics of participants

Baseline characteristics	Total	Changes in social-related activity				*P*	Changes in learning activity				*P*
		CLF	CRF	IF	DF		CLF	CRF	IF	DF	
Number of participants	2460	439	1300	557	164		892	828	504	236	
Female	1232(50.1)	201 (45.8)	678 (52.2)	268 (48.1)	85 (51.8)	0.088	395 (44.3)	486 (58.7)	221 (43.9)	130 (55.1)	**<.0001**
Participation year											
1996	193 (7.9)	37 (8.4)	94 (7.2)	51 (9.2)	11 (6.7)		72 (8.1)	57 (6.9)	50 (9.9)	14 (5.9)	
1997	200 (8.1)	41 (9.3)	99 (7.6)	49 (8.8)	11 (6.7)		65 (7.3)	69 (8.3)	53 (10.5)	13 (5.5)	
1998	214 (8.7)	26 (5.9)	115 (8.9)	58 (10.4)	15 (9.2)		67 (7.5)	80 (9.7)	44 (8.7)	23 (9.8)	
1999	260 (10.6)	50 (11.4)	135 (10.4)	49 (8.8)	26 (15.9)		92 (10.3)	89 (10.8)	52 (10.3)	27 (11.4)	
2000	250 (10.2)	59 (13.4)	119 (9.2)	55 (9.9)	17 (10.4)	0.088	96 (10.8)	75 (9.1)	52 (10.3)	27 (11.4)	0.189
2001	286 (11.6)	56 (12.8)	146 (11.2)	61 (11.0)	23 (14.0)		116 (13.0)	90 (10.9)	56 (11.1)	24 (10.2)	
2002	282 (11.5)	54 (12.3)	145 (11.2)	66 (11.9)	17 (10.4)		97 (10.9)	99 (12.0)	51 (10.1)	35 (14.8)	
2003	280 (11.4)	38 (8.7)	165 (12.7)	61 (11.0)	16 (9.8)		93 (10.4)	98 (11.8)	55 (10.9)	34 (14.4)	
2004	236 (9.6)	43 (9.8)	134 (10.3)	44 (7.9)	15 (9.2)		97 (10.9)	87 (10.5)	34 (6.8)	18 (7.6)	
2005	259 (10.5)	35 (8.0)	148 (11.4)	63 (11.3)	13 (7.9)		97 (10.9)	84 (10.1)	57 (11.3)	21 (8.9)	
BMI											
<18.5	113 (4.6)	30 (6.8)	50 (3.9)	25 (4.5)	8 (4.9)		45 (5.0)	40 (4.8)	18 (3.6)	10 (4.2)	
18.5-25.0	1791 (72.8)	318 (72.4)	953 (73.3)	399 (71.6)	121 (73.8)	0.251	639 (71.6)	620 (74.9)	365 (72.4)	167 (70.8)	0.456
>25.0	556 (22.6)	91 (20.7)	297 (22.9)	133 (23.9)	35 (21.3)		208 (23.3)	168 (20.3)	121 (24.0)	59 (25.0)	
Smoking											
never	1379 (56.1)	219 (49.9)	767 (59)	302 (54.2)	91 (55.5)		454 (50.9)	528 (63.8)	261 (51.8)	136 (57.6)	
former	669 (27.2)	131 (29.8)	336 (25.9)	162 (29.1)	40 (24.4)	**0.032**	237 (26.6)	219 (26.5)	151 (30.0)	62 (26.3)	**<.0001**
current	411 (16.7)	89 (20.3)	197 (15.2)	92 (16.5)	33 (20.1)		200 (22.4)	81 (9.8)	92 (18.3)	38 (16.1)	
missing	1 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)		1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	
Drinking											
never	1349 (54.8)	254 (57.9)	697 (53.6)	295 (53.0)	103 (62.8)	0.059	496 (55.6)	482 (58.2)	236 (46.8)	135 (57.2)	**<.0001**

current drinker	1110 (45.1)	184 (41.9)	603 (46.4)	262 (47.0)	61 (37.2)		396 (44.4)	346 (41.8)	268 (53.2)	100 (42.4)	
missing	1 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	
Marital status											
married	2206 (89.7)	381 (86.8)	1180 (90.8)	500 (89.8)	145 (88.4)		797 (89.4)	745 (90.0)	452 (89.7)	212 (89.8)	
others	250 (10.2)	57 (13.0)	118 (9.1)	56 (10.1)	19 (11.6)	0.392	94 (10.5)	83 (10.0)	50 (9.9)	23 (9.8)	0.622
missing	4 (0.2)	1 (0.2)	2 (0.2)	1 (0.2)	0 (0.0)		1 (0.1)	0 (0.0)	2 (0.4)	1 (0.4)	
Education background											
junior high school or lower	750 (30.5)	162 (36.9)	355 (27.3)	172 (30.9)	61 (37.2)		377 (42.3)	158 (19.1)	145 (28.8)	70 (29.7)	
high school	1099 (44.7)	181 (41.2)	587 (45.2)	255 (45.8)	76 (46.3)	**0.001**	359 (40.3)	407 (49.2)	230 (45.6)	103 (43.6)	**<.0001**
college or higher	610 (24.8)	95 (21.6)	358 (27.5)	130 (23.3)	27 (16.5)		155 (17.4)	263 (31.8)	129 (25.6)	63 (26.7)	
missing	1 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)		1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	
Residential status											
living alone	91 (3.7)	21 (4.8)	41 (3.2)	22 (4.0)	7 (4.3)		31 (3.5)	38 (4.6)	15 (3.0)	7 (3.0)	
others	2314 (94.1)	406 (92.5)	1234 (94.9)	519 (93.2)	155 (94.5)	0.449	842 (94.4)	772 (93.2)	475 (94.3)	225 (95.3)	0.664
missing	55 (2.2)	12 (2.7)	25 (1.9)	16 (2.9)	2 (1.2)		19 (2.1)	18 (2.2)	14 (2.8)	4 (1.7)	
Work status											
working	1027 (41.8)	173 (39.4)	544 (41.9)	243 (43.6)	67 (40.9)		390 (43.7)	314 (37.9)	232 (46.0)	91 (38.6)	
others	1411 (57.4)	260 (59.2)	748 (57.5)	309 (55.5)	94 (57.3)	0.478	493 (55.3)	507 (61.2)	268 (53.2)	143 (60.6)	0.073
missing	22 (0.9)	6 (1.4)	8 (0.6)	5 (0.9)	3 (1.8)		9 (1.0)	7 (0.9)	4 (0.8)	2 (0.9)	
Cancer	90 (3.7)	16 (3.6)	47 (3.6)	18 (3.2)	9 (5.5)	0.604	32 (3.6)	33 (4.0)	15 (3.0)	10 (4.2)	0.764
Hypertension	595 (24.2)	113 (25.7)	304 (23.4)	143 (25.7)	35 (21.3)	0.488	230 (25.8)	188 (22.7)	125 (24.8)	52 (22.0)	0.402
Diabetes	179 (7.3)	35 (8.0)	87 (6.7)	44 (7.9)	13 (7.9)	0.706	67 (7.5)	56 (6.8)	42 (8.3)	14 (5.9)	0.601
Arthritis	117 (4.8)	21 (4.8)	61 (4.7)	28 (5.0)	7 (4.3)	0.979	35 (3.9)	48 (5.8)	24 (4.8)	10 (4.2)	0.323
CVD	174 (7.1)	27 (6.2)	88 (6.8)	44 (7.9)	15 (9.2)	0.493	70 (7.9)	63 (7.6)	31 (6.2)	10 (4.2)	0.194

Depressive symptoms											
not have	1938 (78.8)	280 (63.8)	1106 (85.1)	424 (76.1)	128 (78.1)	**<.0001**	635 (71.2)	722 (87.2)	397 (78.8)	184 (78.0)	**<.0001**
have	522 (21.2)	159 (36.2)	194 (14.9)	133 (23.9)	36 (22.0)		257 (28.8)	106 (12.8)	107 (21.2)	52 (22.0)	
Exercise habit											
<2/week	1338 (54.4)	289 (65.8)	315 (56.6)	98 (59.8)	636 (48.9)		549 (61.6)	297 (58.9)	127 (53.8)	365 (44.1)	
≥2/week	1119 (45.5)	149 (33.9)	241 (43.3)	65 (39.6)	664 (51.1)	**<.0001**	341 (38.2)	206 (40.9)	109 (46.2)	463 (55.9)	**<.0001**
missing	3 (0.1)	1 (0.2)	1 (0.2)	1 (0.6)	0 (0.0)		2 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	
Daily walking											
<60/day	1050 (42.7)	193 (44)	237 (42.6)	79 (48.2)	541 (41.6)		376 (42.2)	216 (42.9)	91 (38.6)	367 (44.3)	
≥60/day	1396 (56.8)	243 (55.4)	317 (56.9)	85 (51.8)	751 (57.8)	0.696	511 (57.3)	285 (56.6)	145 (61.4)	455 (55)	0.588
missing	14 (0.6)	3 (0.7)	3 (0.5)	0 (0.0)	8 (0.6)		5 (0.6)	3 (0.6)	0 (0.0)	6 (0.7)	
Competence of daily living	12.16 ± 1.28	11.52 ± 1.67	12.42 ± 1.04	12.02 ± 1.31	12.24 ± 1.03	**<.0001**	11.83 ± 1.49	12.49 ± 0.99	12.15 ± 1.20	12.25 ± 1.19	**<.0001**

Difference among different changes in social activities tested by chi-square test and ANOVA test depending on the type of the variables. CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency, CVD: cardiovascular disease

Continued Table 2-1

Baseline characteristics	Total	Changes in personal activity				*P*
		CLF	CRF	IF	DF	
Number of participants	2460	512	1210	515	223	
Female	1232 (50.1)	205 (40.0)	684 (56.5)	207 (40.2)	136 (61.0)	**<.0001**
Participation year						
1996	193 (7.9)	50 (9.8)	84 (6.9)	35 (6.8)	24 (10.8)	
1997	200 (8.1)	42 (8.2)	98 (8.1)	46 (8.9)	14 (6.3)	0.102
1998	214 (8.7)	49 (9.6)	100 (8.3)	45 (8.7)	20 (9.0)	

1999	260 (10.6)	54 (10.6)	128 (10.6)	44 (8.5)	34 (15.3)	
2000	250 (10.2)	62 (12.1)	122 (10.1)	41 (8.0)	25 (11.2)	
2001	286 (11.6)	59 (11.5)	133 (11.0)	69 (13.4)	25 (11.2)	
2002	282 (11.5)	48 (9.4)	144 (11.9)	66 (12.8)	24 (10.8)	
2003	280 (11.4)	59 (11.5)	143 (11.8)	61 (11.8)	17 (7.6)	
2004	236 (9.6)	46 (9.0)	119 (9.8)	46 (8.9)	25 (11.2)	
2005	259 (10.5)	43 (8.4)	139 (11.5)	62 (12.0)	15 (6.7)	
BMI						
<18.5	113 (4.6)	29 (5.7)	51 (4.2)	25 (4.9)	8 (3.6)	
18.5-25.0	1791 (72.8)	374 (73.1)	894 (73.9)	361 (70.1)	162 (72.7)	0.532
>25.0	556 (22.6)	109 (21.3)	265 (21.9)	129 (25.1)	53 (23.8)	
Smoking						
never	1379 (56.1)	236 (46.1)	759 (62.7)	250 (48.5)	134 (60.1)	
former	669 (27.2)	146 (28.5)	300 (24.8)	172 (33.4)	51 (22.9)	**<.0001**
current	411 (16.7)	130 (25.4)	150 (12.4)	93 (18.1)	38 (17.0)	
missing	1 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	
Drinking						
never	1349 (54.8)	268 (52.3)	681 (56.3)	261 (50.7)	139 (62.3)	
current drinker	1110 (45.1)	243 (47.5)	529 (43.7)	254 (49.3)	84 (37.7)	**0.023**
missing	1 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	
Marital status						
married	2206 (89.7)	450 (87.9)	1096 (90.6)	460 (89.3)	200 (89.7)	
others	250 (10.2)	62 (12.1)	114 (9.4)	52 (10.1)	22 (9.9)	0.054
missing	4 (0.2)	0 (0.0)	0 (0.0)	3 (0.6)	1 (0.5)	
Education background						
junior high school or lower	750 (30.5)	203 (39.7)	303 (25)	159 (30.9)	85 (38.1)	
high school	1099 (44.7)	194 (37.9)	596 (49.3)	221 (42.9)	88 (39.5)	**<.0001**
college or higher	610 (24.8)	115 (22.5)	311 (25.7)	134 (26.0)	50 (22.4)	
missing	1 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	

Residential status						
living alone	91 (3.7)	21 (4.1)	45 (3.7)	14 (2.7)	11 (4.9)	
others	2314 (94.1)	480 (93.8)	1134 (93.7)	491 (95.3)	209 (93.7)	0.653
missing	55 (2.2)	11 (2.2)	31 (2.6)	10 (1.9)	3 (1.4)	
Work status						
working	1027 (41.8)	221 (43.2)	464 (38.4)	250 (48.5)	92 (41.3)	
others	1411 (57.4)	286 (55.9)	735 (60.7)	261 (50.7)	129 (57.9)	**0.013**
missing	22 (0.9)	5 (1.0)	11 (0.9)	4 (0.8)	2 (0.9)	
Cancer	90 (3.7)	19 (3.7)	49 (4.1)	15 (2.9)	7 (3.1)	0.679
Hypertension	595 (24.2)	126 (24.6)	277 (22.9)	132 (25.6)	60 (26.9)	0.451
Diabetes	179 (7.3)	40 (7.8)	84 (6.9)	36 (7.0)	19 (8.5)	0.803
Arthritis	117 (4.8)	27 (5.3)	61 (5.0)	19 (3.7)	10 (4.5)	0.604
CVD	174 (7.1)	36 (7.0)	81 (6.7)	40 (7.8)	17 (7.6)	0.862
Depressive symptoms						
not have	1938 (78.8)	322 (62.9)	1052 (86.9)	395 (76.7)	169 (75.8)	**<.0001**
have	522 (21.2)	190 (37.1)	158 (13.1)	120 (23.3)	54 (24.2)	
Exercise habit						
<2/week	1338 (54.4)	351 (68.6)	326 (63.3)	127 (57)	534 (44.1)	
≥2/week	1119 (45.5)	160 (31.3)	188 (36.5)	96 (43.1)	675 (55.8)	**<.0001**
missing	3 (0.1)	1 (0.2)	1 (0.2)	0 (0.0)	1 (0.1)	
Daily walking						
<60/day	1050 (42.7)	240 (46.9)	234 (45.4)	99 (44.4)	477 (39.4)	
≥60/day	1396 (56.8)	271 (52.9)	277 (53.8)	123 (55.2)	725 (59.9)	0.053
missing	14 (0.6)	1 (0.2)	4 (0.8)	1 (0.5)	8 (0.7)	
Competence of daily living	12.16 ± 1.28	11.23 ± 1.71	12.6 ± 0.76	11.96 ± 1.31	12.33 ± 1.10	**<.0001**

Difference among different changes in social activities tested by chi-square test and ANOVA test depending on the type of the variables. CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency, CVD: cardiovascular disease

2-3.2 Association between changes in social activities and the onset of depressive symptoms among participants without depressive symptoms at baseline

A total of 241 (12.4%) developed depressive symptoms after six-year follow-up period. Compared with participants who partook in activities at CLF, those who participated in social-related (RR_{CRF}=0.61, 95% CI= 0.43–0.87; RR_{IF} = 0.58, 95% CI = 0.39–0.88), learning activities (RR_{CRF}=0.63, 95% CI= 0.45–0.88; RR_{IF} = 0.60, 95% CI = 0.41–0.88), and personal activities (RR_{CRF}=0.40, 95% CI= 0.28–0.57; RR_{IF} = 0.49, 95% CI = 0.33–0.72) at CRF or IF were less likely to develop depressive symptoms. Those who had DF of social-related activities (RR = 1.62, 95% CI = 1.05–2.49) also showed significant association with the onset of depressive symptoms (**Table 2-2**).

On the association between changes in combination of multiple social activities and the onset of depressive symptoms, compared with participants who remained in Group A, those who remained in the same group or increase the number of regular activities were less likely to develop depressive symptoms (**Table 2-2**).

Table 2-2 Association between changes in social activities and the onset of depressive symptoms among participants without depressive symptoms at baseline

Behavioral activities	Changes in social activities	Total (n = 1938)	Onset (n = 241)	Model 1	Model 2	Model 3
				RRs (95% CI)	RRs (95% CI)	RRs (95% CI)
Social-related activities	CLF	280	53 (18.9)	1.00	1.00	1.00
	CRF	424	43 (10.1)	0.51 (0.36, 0.71) ***	0.53 (0.38, 0.74) **	0.61 (0.43, 0.87) **
	IF	128	37 (28.9)	0.53 (0.35, 0.79) **	0.56 (0.37, 0.84) **	0.58 (0.39, 0.88) *
	DF	1106	108 (9.8)	1.51 (0.99, 2.30)	1.48 (0.97, 2.26)	1.62 (1.05, 2.49) *
Learning activities	CLF	635	105 (16.5)	1.00	1.00	1.00
	CRF	397	37 (9.3)	0.51 (0.37, 0.70) ***	0.55 (0.40, 0.77) **	0.63 (0.45, 0.88) **
	IF	184	36 (19.6)	0.57 (0.39, 0.82) **	0.59 (0.41, 0.87) **	0.60 (0.41, 0.88) **
	DF	722	63 (8.7)	1.16 (0.79, 1.71)	1.20 (0.82, 1.77)	1.31 (0.89, 1.94)
Personal activities	CLF	322	77 (23.9)	1.00	1.00	1.00
	CRF	395	41 (10.4)	0.31 (0.23, 0.43) ***	0.34 (0.24, 0.46) ***	0.40 (0.28, 0.57) ***
	IF	169	41 (24.3)	0.43 (0.30, 0.63) ***	0.46 (0.31, 0.67) ***	0.49 (0.33, 0.72) **
	DF	1052	82 (7.8)	0.98 (0.67, 1.44)	1.02 (0.69, 1.51)	1.15 (0.76, 1.72)
Combination of social activities	remained in Group A	86	29 (33.7)	1.00	1.00	1.00
	remained in Group B	117	13 (11.1)	0.33 (0.17, 0.63) **	0.33 (0.17, 0.65) **	0.38 (0.19, 0.74) **
	remained in Group C	204	19 (9.3)	0.27 (0.15, 0.49) ***	0.29 (0.16, 0.52) ***	0.35 (0.19, 0.64) **
	remained in Group D	438	27 (6.2)	0.17 (0.10, 0.30) ***	0.19 (0.11, 0.33) ***	0.25 (0.14, 0.45) ***
	increased	789	84 (10.6)	0.31 (0.20, 0.48) ***	0.34 (0.22, 0.52) ***	0.39 (0.24, 0.61) ***
	decreased	304	69 (22.7)	0.66 (0.42, 1.02) *	0.69 (0.44, 1.07)	0.82 (0.51, 1.32)

CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency; RRs = relative ratios, CI = confidence interval; Model 1 adjusted for gender and year of participation; Model 2 adjusted for sex, year of participation, smoking, drinking, marital status, education background residential status, and work status; Model 3 adjusted for sex, year of participation, smoking, drinking, marital status, education background, residential status, work status, BMI, cancer, hypertension, diabetes, arthritis, cardiovascular disease, competence of daily living, exercise habits and daily walking time; *P<0.05, **P<0.01, ***P<0.001

2-3.3 Association between changes in social activities and the persistence of depressive symptoms among those with depressive symptoms at baseline

A total 265 (50.8%) participants reported persistent depressive symptoms after the six-year follow-up period. Compared with participants who engaged in activities at CLF, those who reported CRF and IF for personal activities were less likely to have persistent depressive symptoms in the model1 (**Table 2-3**).

On the association between changes in combination of multiple social activities and the persistence of depressive symptoms, compared with participants who remained in Group A, those who remained in Group D showed significant association with the persistence of depressive symptoms in model1 (**Table 2-3**).

Table 2-3 Association between changes in social activities and the persistence of depressive symptoms among participants with depressive symptoms at baseline

Behavioral activities	Changes in social activities	Total (n = 522)	Persistence (n = 265)	Model 1	Model 2	Model 3
				RRs (95% CI)	RRs (95% CI)	RRs (95% CI)
Social-related activities	CLF	159	90 (56.6)	1.00	1.00	1.00
	CRF	133	74 (55.6)	0.75 (0.56, 1.02)	0.77 (0.57, 1.06)	0.86 (0.62, 1.19)
	IF	36	19 (52.8)	0.99 (0.72, 1.35)	1.00 (0.73, 1.37)	1.05 (0.75, 1.45)
	DF	194	82 (42.3)	0.93 (0.56, 1.53)	0.97 (0.58, 1.61)	1.05 (0.62, 1.76)
Learning activities	CLF	257	139 (54.1)	1.00	1.00	1.00
	CRF	107	47 (43.9)	0.83 (0.59, 1.16)	0.92 (0.65, 1.30)	0.96 (0.68, 1.37)
	IF	52	32 (61.5)	0.82 (0.59, 1.15)	0.86 (0.62, 1.21)	0.89 (0.63, 1.25)
	DF	106	47 (44.3)	1.17 (0.79, 1.72)	1.25 (0.84, 1.87)	1.33 (0.88, 2.00)
Personal activities	CLF	190	114 (60.0)	1.00	1.00	1.00
	CRF	120	49 (40.8)	0.74 (0.55, 1.00) *	0.76 (0.56, 1.03)	0.89 (0.63, 1.26)
	IF	54	33 (61.1)	0.68 (0.49, 0.96) *	0.69 (0.49, 0.98) *	0.74 (0.52, 1.06)
	DF	158	69 (43.7)	1.00 (0.67, 1.49)	1.00 (0.67, 1.50)	1.13 (0.74, 1.72)
Combination of social activities	remained in Group A	73	46 (63.0)	1.00	1.00	1.00
	remained in Group B	57	32 (56.1)	0.91 (0.58, 1.44)	0.91 (0.57, 1.45)	0.99 (0.61, 1.59)
	remained in Group C	35	19 (54.3)	0.91 (0.53, 1.55)	0.88 (0.51, 1.53)	1.10 (0.61, 1.98)
	remained in Group D	43	13 (30.2)	0.50 (0.27, 0.93) *	0.54 (0.29, 1.02)	0.66 (0.34, 1.29)
	increased	227	107 (47.1)	0.78 (0.55, 1.10)	0.78 (0.55, 1.12)	0.86 (0.59, 1.26)
	decreased	87	48 (55.2)	0.90 (0.60, 1.36)	0.90 (0.59, 1.37)	1.02 (0.65, 1.60)

CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency; RRs = relative ratios, CI = confidence interval; Model 1 adjusted for gender and year of participation; Model 2 adjusted for sex, year of participation, smoking, drinking, marital status, education background residential status, and work status; Model 3 adjusted for sex, year of participation, smoking, drinking, marital status, education background, residential status, work status, BMI, cancer, hypertension, diabetes, arthritis, cardiovascular disease, competence of daily living, exercise habits and daily walking time; *P<0.05, **P<0.01, ***P<0.001

2-4. Discussion

This study explored the association between changes in social activities and the onset and persistence of depressive symptoms. Regarding the changes in each social activity, I found that older adults without depressive symptoms, who participated in social-related, learning, and personal activities at CRF or IF had a significant association with the onset of depressive symptoms. However, for older adults with depressive symptoms at baseline, only the IF of personal activities showed an association with the persistence of depressive symptoms, but this association was not significant when included all the covariates into the model. Regarding the changes in the combination of multiple social activities, I found that participants were less likely to develop depressive symptoms if they maintained the same level of participation or increased the number of regular frequency social activities to two or three. However, for those who had depressive symptoms, maintaining all three kinds of activities at a regular frequency may have an association with the persistence of depressive symptoms.

A prospective study on Koreans aged 45 years or older found that continued or new participation in social activities is negatively associated with the onset of depressive symptoms (Choi *et al.*, 2015). They also found that the strength of the negative association varies across types of social activities, with stronger negative effects of leisure, culture or sports club, and family or school reunion activities compared with volunteer or political activities (Choi *et al.*, 2015). The present results also confirmed that the effect size of the negative relation between CRF or IF of social activities and depressive symptoms varied across different types of social activities. Personal activities had the strongest effect, followed by socially relevant activities and then learning activities. Cross-sectional and prospective studies have demonstrated that a higher level of perceived emotional support could protect people from depressive symptoms, whereas a lower level is associated with the presence or development of depressive symptoms (Santini *et al.*, 2015). Another longitudinal study on adults aged 60 years and over also found that decreased participation in social activities is

associated with higher score on the Center for Epidemiological Studies-Depression scale (higher scores indicate severe depressive symptoms) (Chao, 2016). The present results similarly demonstrated that decreased social-related activities was associated with the onset of depressive symptoms. This longitudinal study also found the cumulative and compensatory effects of different types of leisure activities on depressive symptoms, which means a gain in certain activities may compensate for losses in other activities (Chao, 2016). The results on changes in the accumulation of social activities and the onset of depressive symptoms also suggested that even with a low frequency of one or two activities, maintaining the same combination status during follow-up showed significant association with the development depressive symptoms, which may suggest a compensatory effect among different frequency groups of social activities.

Early research has revealed that the strength and direction of the association of social activities with persistent depressive symptoms are also related to the type of activity (Ryu et al., 2021; Croezen *et al.*, 2015; Min *et al.*, 2016). Increased participation in sports, social clubs, and other club activities is associated with a contemporary decline in depressive symptoms but does not predict changes in depressive symptoms after multi-year follow-up period. A possible explanation is that the short-term benefits of social engagement on depressive symptoms diminish over time; another is that depressive symptoms affect engagement in social activities (Croezen *et al.*, 2015). In my study, I found an association of CRF or IF of personal activities with the persistence of depressive symptoms. The measurement of changes in social activities and persistence of depressive symptoms in my study were at the same wave; the association also seemed contemporaneous. More longitudinal studies are needed to explain the association between changes in social activities and the improvement of depressive symptoms.

The age-specific participants allowed me to eliminate the confounding factor of age. In addition, I used a set of questions rather than a single question to assess social activities from multiple perspectives, which makes the results more generalizable.

Several limitations also should be considered. First, the self-reported questions on social activity assessment may lead to recalled biases. Second, social activities and depressive symptoms may interact with each other over time, the exposure and outcome in my study were measured at the same time; as much, I could not consider causality. Future studies should carefully consider the statistical methods or use prospective or intervention studies to explore this interaction between social activity and depressive symptoms over time, especially for participants with depressive symptoms at baseline. Third, cognitive function was not included as a confounding factor because relatively few participants completed the assessments.

Chapter 3 An increased frequency of social activities prolong disability-free survival among age-specific older adults with depressive symptoms in the New Integrated Suburban Seniority Investigation Project

3-1. Introduction

Depressed older adults with executive dysfunction, higher level of inflammation, and poor adherence to a healthy lifestyle had an increased risk for functional disability compared to non-depressed older adults (Rogers et al., 2004; Johnson et al., 2007; Schmidt et al., 2014; Sander et al., 2018; Chen et al., 2020). However, randomized clinical trials have been demonstrated that effective treatment of depressive disorders can improve functional outcomes (Ormel et al., 1994). For example, participating in social activities where older adults receive social support has been demonstrated to be a more effective buffer against functional decline among older adults with clinical depressive symptoms than among asymptomatic older adults (Hays et al., 1997; Travis et al., 2004; Hays et al., 2001).

Nevertheless, social participation is an important modifiable health determinant, changes in physical behaviors among older adults may avoid, retard, or reverse the outcome of incident disability (Levasseur et al., 2010; Okabayashi *et al.*, 2019). Previous studies have shown that participating in social activities increasingly or continuously had a lower risk of functional disability (Agahi et al., 2013; Chen et al., 2016). Based on the results in previous two chapters, maintenance or increase of social activity participation may help depressed older adults relieve their symptoms. Therefore, a beneficial effect of an IF or CRF of social activities on incident functional disability among depressed older adults could be expected. In addition, the positive health effects of social activities on functional disability also depending on the type, frequency, and diversity of social activities (Ide et al., 2020; Kanamori et al., 2014; van Hees et al., 2020; Ukawa et al., 2020; Gao et al., 2018). But the uncertainty remains regarding the effect of changes in single and combination of social activities on incident functional disability among depressed older adults.

Therefore, this study aimed to examine the association between changes in single and multiple social activities between 65 to 70 years and incident functional disability between 70 to 80 years among depressed older adults, and to explore which type of social activities have a larger effect size on incident functional disability. I further estimated the association between changes in single and multiple social activities and disability-free survival time, to explore whether increased or continued regular frequency of social activities can prolong their disability-free survival time.

3-2. Methods

3-2.1 Study design and participants

The study design is shown in Chapter one.

Figure 3-1 showed the flow chart for this study population. Of 3,073 participants, I excluded those with missing or invalid values of GDS questionnaire (n = 50) and competence of daily living (n = 1). The participants who did not have depressive symptoms at baseline (n = 2,349) were also excluded. Then 673 participants were eligible at baseline, 43 relocated and 36 died were excluded before follow-up. In addition, 47 participants who did not attend the second check-ups, six who had missing values of the GDS scale, 16 who were certified needing LTCI before 70 years old were also excluded. In total, 525 depressed older adults were included into this study.

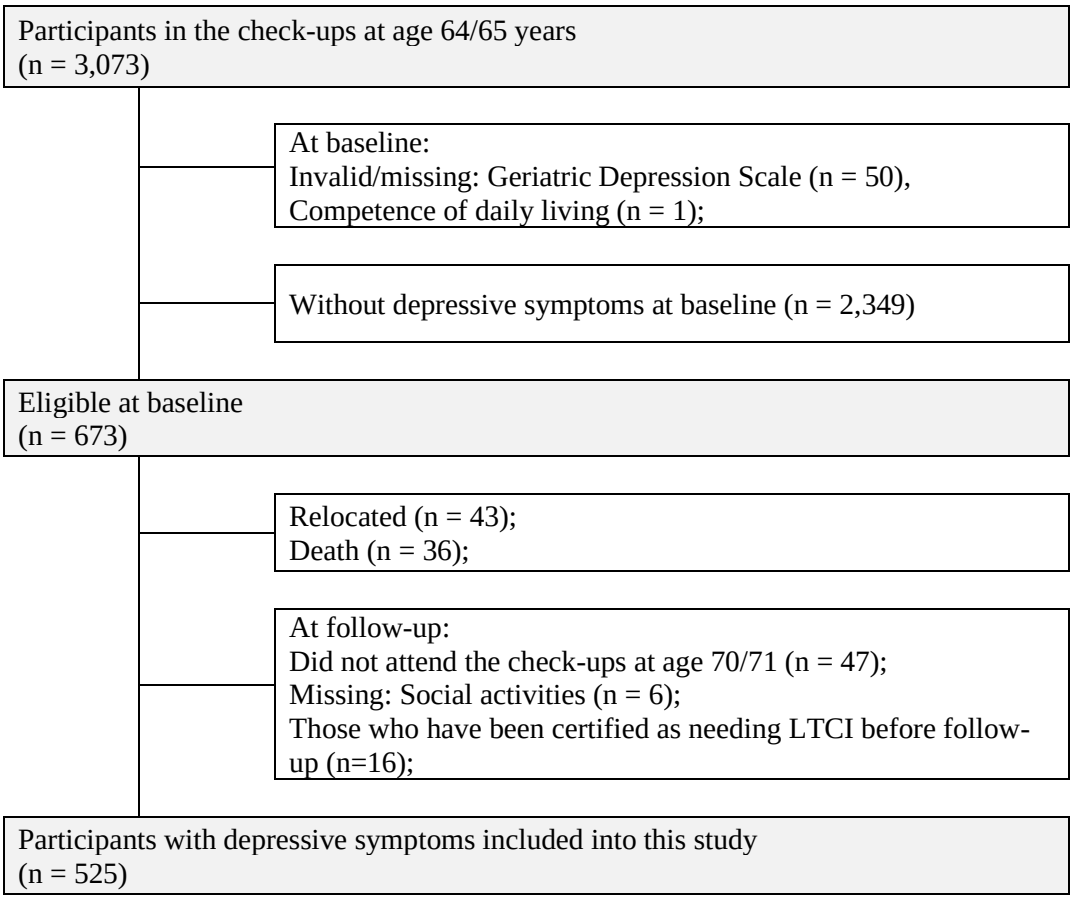

Fig. 3-1 The flow chart of study subjects

3-2.2 Ethical issues

Please refer to Ethical issues in Chapter one.

3-2.3 Exposure assessments

Depressed participants were assessed by the same method as in Chapter one. The measurement of social activities and changes in single/multiple social activities are the same as in Chapter one.

3-2.4 Follow up and outcomes

Functional disability was defined according to the Japan's Long-term Care Insurance System (LTCI) (Matsunaga et al., 2017). The certification of LTCI benefit is evaluated according to a nationally standardized process that includes a physician's examination

and an assessment of physical and cognitive functioning (Tsutsui and Muramatsu, 2007). There are seven levels of the LTCI certification: support levels 1-2 and care levels 1-5. The higher the level, the severity the disability (Matsunaga *et al.*, 2017). In my study, I separated all the seven levels into two outcomes: one is mild disability that includes the newly certified participants who developed as need support levels 1-2 and care level 1, another one is severe disability that includes the newly certified participants who developed as need care levels 2-5.

Disability-free survival was defined as survival without disability during the follow-up period. Therefore, the outcome was the first onset of mild or severe disability.

3-2.5 Covariates

Data on covariates were collected the same as in Chapter two.

3-2.6 Statistical analysis

Baseline characteristics were compared among participants with changes in social activities using the Chi-squared test or Fisher's exact test for categorical variables and the analysis of variance (ANOVA) for continuous variables.

I counted person-years of follow-up for each participant from the second day of the second survey (70/71 years) until the date of LTCI certification, death, or relocation from Nisshin city, or the end of the study period (December 31st, 2020, 80/81 years), whichever occurred first.

A competing risk model was used to estimate the hazard ratios (HRs) and 95% confidence intervals (95% CIs). I treated death as competing events, that is, those who was not certified as needing LTCI benefits before the mortality event, because mortality and functional disability may share a common risk factor of the decreased or continued low frequency of social activity participation (Ukawa *et al.*, 2020). HRs adjusted sex and year of participation in model1; in model 2, HRs adjusted covariates in model 1 plus BMI, smoking, drinking, educational background, marital status, residential status, work status, competence of daily living, history of chronic disease, exercise habits and daily walking.

A Laplace regression model was used to quantify year differences in disability-free survival time based on the category of different change types of social activities, using the period until the outcome occurred as the time scale. Percentile of survival range between 1% to 99%, but the choice of percentile determined by the number of events (Orsini et al., 2012). During the study period, 20% of participants developed mild disability, and 10% of participants developed severe disability. Therefore, I estimated differences in the first 25% of the population developed the incident mild or severe disability adjusted for the same items as those in the Cox model.

3-3. Results

3-3.1 Baseline characteristics

Table 3-1 showed that participants with CRF of all these three social activities were more likely to had higher level of exercise habits and competence of daily living. In CRF of learning and personal activities, they were more likely to have higher education background. In addition, most of participants at CRF of personal activities were woman, and they were more likely to be never smoker.

Table 3-1 Baseline characteristics of participants with depressive symptoms

Baseline characteristics	Total	Changes in social-related activity				*P*	Changes in learning activity				*P*
		CLF	CRF	IF	DF		CLF	CRF	IF	DF	
Number of participants	525	165	189	139	32		263	105	110	47	
Female	290 (55.2)	85 (51.5)	108 (57.1)	75 (54.0)	22 (68.8)	0.301	134 (51.0)	64 (61.0)	65 (59.1)	27 (57.5)	0.251
Participation year											
1996	52 (9.9)	18 (10.9)	20 (10.6)	13 (9.4)	1 (3.1)		28 (10.7)	9 (8.6)	13 (11.8)	2 (4.3)	
1997	43 (8.2)	15 (9.1)	12 (6.4)	13 (9.4)	3 (9.4)		23 (8.8)	7 (6.7)	11 (10.0)	2 (4.3)	
1998	42 (8.0)	8 (4.9)	12 (6.4)	18 (13.0)	4 (12.5)		20 (7.6)	8 (7.6)	9 (8.2)	5 (10.6)	
1999	56 (10.7)	24 (14.6)	16 (8.5)	10 (7.2)	6 (18.8)		26 (9.9)	14 (13.3)	12 (10.9)	4 (8.5)	
2000	72 (13.7)	31 (18.8)	20 (10.6)	17 (12.2)	4 (12.5)	0.061	40 (15.2)	11 (10.5)	15 (13.6)	6 (12.8)	0.867
2001	67 (12.8)	20 (12.1)	19 (10.1)	22 (15.8)	6 (18.8)		35 (13.3)	13 (12.4)	14 (12.7)	5 (10.6)	
2002	40 (7.6)	10 (6.1)	16 (8.5)	11 (7.9)	3 (9.4)		17 (6.5)	8 (7.6)	8 (7.3)	7 (14.9)	
2003	46 (8.8)	9 (5.5)	25 (13.2)	11 (7.9)	1 (3.1)		21 (8.0)	14 (13.3)	8 (7.3)	3 (6.4)	
2004	56 (10.7)	16 (9.7)	27 (14.3)	11 (7.9)	2 (6.3)		30 (11.4)	13 (12.4)	7 (6.4)	6 (12.8)	
2005	51 (9.7)	14 (8.5)	22 (11.6)	13 (9.4)	2 (6.3)		23 (8.8)	8 (7.6)	13 (11.8)	7 (14.9)	
BMI											
<18.5	24 (4.6)	10 (6.1)	6 (3.2)	6 (4.3)	2 (6.3)		14 (5.3)	3 (2.9)	4 (3.6)	3 (6.4)	
18.5-25.0	383 (73.0)	125 (75.8)	138 (73.0)	98 (70.5)	22 (68.8)	0.644	196 (74.5)	82 (78.1)	77 (70.0)	28 (59.6)	0.237
>25.0	118 (22.5)	30 (18.2)	45 (23.8)	35 (25.2)	8 (25.0)		53 (20.2)	20 (19.1)	29 (26.4)	16 (34.0)	
Smoking											
Never	310 (59.1)	86 (52.1)	120 (63.5)	81 (58.3)	23 (71.9)		146 (55.5)	68 (64.8)	69 (62.7)	27 (57.5)	
Former	121 (23.1)	40 (24.2)	42 (22.2)	35 (25.2)	4 (12.5)	0.147	57 (21.7)	27 (25.7)	23 (20.9)	14 (29.8)	0.072
Current	94 (17.9)	39 (23.6)	27 (14.3)	23 (16.6)	5 (15.6)		60 (22.8)	10 (9.5)	18 (16.4)	6 (12.8)	
Drinking											
never	320 (61.0)	101 (61.2)	110 (58.2)	84 (60.4)	25 (78.1)	0.339	160 (60.8)	65 (61.9)	66 (60.0)	29 (61.7)	0.111
current drinker	204 (38.9)	63 (38.2)	79 (41.8)	55 (39.6)	7 (21.9)		103 (39.2)	40 (38.1)	44 (40.0)	17 (36.2)	

missing	1 (0.2)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	
Marital status											
marries	452 (86.1)	141 (85.5)	166 (87.8)	119 (85.6)	26 (81.3)		227 (86.3)	94 (89.5)	93 (84.6)	38 (80.9)	
others	71 (13.5)	23 (13.9)	23 (12.2)	19 (13.7)	6 (18.8)	0.861	35 (13.3)	11 (10.5)	16 (14.6)	9 (19.2)	0.727
missing	2 (0.4)	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)		1 (0.4)	0 (0.0)	1 (0.9)	0 (0.0)	
Education background											
Junior high school or lower	222 (42.3)	75 (45.5)	78 (41.3)	57 (41.0)	12 (37.5)		133 (50.6)	31 (29.5)	45 (40.9)	13 (27.7)	
High school	206 (39.2)	57 (34.6)	75 (39.7)	59 (42.5)	15 (46.9)	0.796	93 (35.4)	48 (45.7)	43 (39.1)	22 (46.8)	**0.003**
College or higher	97 (18.5)	33 (20.0)	36 (19.1)	23 (16.6)	5 (15.6)		37 (14.1)	26 (24.8)	22 (20.0)	12 (25.5)	
Residential status											
living alone	26 (5.0)	8 (4.9)	6 (3.2)	9 (6.5)	3 (9.4)		11 (4.2)	5 (4.8)	6 (5.5)	4 (8.5)	
others	486 (92.6)	153 (92.7)	178 (94.2)	127 (91.4)	28 (87.5)	0.754	245 (93.2)	97 (92.4)	103 (93.6)	41 (87.2)	0.739
missing	13 (2.5)	4 (2.4)	5 (2.7)	3 (2.2)	1 (3.1)		7 (2.7)	3 (2.9)	1 (0.9)	2 (4.3)	
Work status											
working	193 (36.8)	56 (33.9)	76 (40.2)	48 (34.5)	13 (40.6)		90 (34.2)	40 (38.1)	45 (40.9)	18 (38.3)	
others	331 (63.1)	109 (66.1)	112 (59.3)	91 (65.5)	19 (59.4)	0.619	172 (65.4)	65 (61.9)	65 (59.1)	29 (61.7)	0.826
missing	1 (0.2)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	
Cancer	21 (4.0)	8 (4.9)	7 (3.7)	6 (4.3)	0 (0.0)	0.632	13 (4.9)	6 (5.7)	1 (0.9)	1 (2.1)	0.205
Hypertension	142 (27.1)	55 (33.3)	47 (24.9)	33 (23.7)	7 (21.9)	0.175	75 (28.5)	25 (23.8)	30 (27.3)	12 (25.5)	0.825
Diabetes	32 (6.1)	10 (6.1)	10 (5.3)	9 (6.5)	3 (9.4)	0.837	19 (7.2)	3 (2.9)	4 (3.6)	6 (12.8)	0.062
Arthritis	30 (5.7)	13 (7.9)	6 (3.2)	10 (7.2)	1 (3.1)	0.198	15 (5.7)	5 (4.8)	9 (8.2)	1 (2.1)	0.468
CVD	79 (15.1)	25 (15.2)	27 (14.3)	21 (15.1)	6 (18.8)	0.934	35 (13.3)	18 (17.1)	17 (15.5)	9 (19.2)	0.656
Exercise habit											
<2/week	336 (64.0)	111 (67.3)	105 (55.6)	98 (70.5)	22 (68.8)	**0.028**	183 (69.6)	53 (50.5)	71 (64.6)	29 (61.7)	**0.013**

≥2/week	188 (35.8)	53 (32.1)	84 (44.4)	41 (29.5)	10 (31.3)		79 (30)	52 (49.5)	39 (35.5)	18 (38.3)	
missing	1 (0.2)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	
Daily walking											
<60/day	240 (45.7)	75 (45.5)	90 (47.6)	60 (43.2)	15 (46.9)		115 (43.7)	54 (51.4)	48 (43.6)	23 (48.9)	
≥60/day	281 (53.5)	87 (52.7)	98 (51.9)	79 (56.8)	17 (53.1)	0.730	146 (55.5)	49 (46.7)	62 (56.4)	24 (51.1)	0.514
missing	4 (0.8)	3 (1.8)	1 (0.5)	0 (0.0)	0 (0.0)		2 (0.8)	2 (1.9)	0 (0.0)	0 (0.0)	
Competence of daily living	11.61 ± 1.61	11.04 ± 1.82	12.01 ± 1.33	11.66 ± 1.59	12.03 ± 1.20	**<.0001**	11.36 ± 1.78	11.86 ± 1.42	11.83 ± 1.31	11.98 ± 1.39	**0.004**

Difference among different changes in social activities tested by chi-square test and ANOVA test depending on the type of the variables. CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency, CVD: cardiovascular disease

Continue 3-1

Baseline characteristics	Total	Changes in personal activity				*P*
		CLF	CRF	IF	DF	
Number of participants	525	192	156	125	52	
Female	290 (55.2)	84 (43.8)	100 (64.1)	68 (54.4)	38 (73.1)	**<.0001**
Participation year						
1996	52 (9.9)	19 (9.9)	13 (8.3)	13 (10.4)	7 (13.5)	
1997	43 (8.2)	19 (9.9)	12 (7.7)	9 (7.2)	3 (5.8)	
1998	42 (8)	14 (7.3)	9 (5.8)	12 (9.6)	7 (13.5)	
1999	56 (10.7)	24 (12.5)	19 (12.2)	7 (5.6)	6 (11.5)	
2000	72 (13.7)	29 (15.1)	23 (14.7)	15 (12.0)	5 (9.6)	0.639
2001	67 (12.8)	28 (14.6)	17 (10.9)	16 (12.8)	6 (11.5)	
2002	40 (7.6)	9 (4.7)	10 (6.4)	14 (11.2)	7 (13.5)	
2003	46 (8.8)	13 (6.8)	18 (11.5)	13 (10.4)	2 (3.9)	
2004	56 (10.7)	19 (9.9)	19 (12.2)	13 (10.4)	5 (9.6)	

2005	51 (9.7)	18 (9.4)	16 (10.3)	13 (10.4)	4 (7.7)	
BMI						
<18.5	24 (4.6)	10 (5.2)	5 (3.2)	4 (3.2)	5 (9.6)	
18.5-25.0	383 (73.0)	148 (77.1)	114 (73.1)	87 (69.6)	34 (65.4)	0.191
>25.0	118 (22.5)	34 (17.7)	37 (23.7)	34 (27.2)	13 (25.0)	
Smoking						
Never	310 (59.1)	94 (49.0)	109 (69.9)	72 (57.6)	35 (67.3)	
Former	121 (23.1)	52 (27.1)	27 (17.3)	35 (28.0)	7 (13.5)	**0.002**
Current	94 (17.9)	46 (24)	20 (12.8)	18 (14.4)	10 (19.2)	
Drinking						
never	320 (61)	107 (55.7)	107 (68.6)	75 (60)	31 (59.6)	
current drinker	204 (38.9)	84 (43.8)	49 (31.4)	50 (40)	21 (40.4)	0.269
missing	1 (0.2)	1 (0.5)	0 (0)	0 (0)	0 (0)	
Marital status						
marries	452 (86.1)	169 (88)	136 (87.2)	106 (84.8)	41 (78.9)	
others	71 (13.5)	23 (12)	20 (12.8)	17 (13.6)	11 (21.2)	0.148
missing	2 (0.4)	0 (0.0)	0 (0.0)	2 (1.6)	0 (0.0)	
Education background						
Junior high school or lower	222 (42.3)	85 (44.3)	51 (32.7)	56 (44.8)	30 (57.7)	**0.011**
High school	206 (39.2)	66 (34.4)	70 (44.9)	53 (42.4)	17 (32.7)	
College or higher	97 (18.5)	41 (21.4)	35 (22.4)	16 (12.8)	5 (9.6)	
Residential status						
living alone	26 (5.0)	6 (3.1)	10 (6.4)	5 (4.0)	5 (9.6)	
others	486 (92.6)	182 (94.8)	142 (91)	116 (92.8)	46 (88.5)	0.523
missing	13 (2.5)	4 (2.1)	4 (2.6)	4 (3.2)	1 (1.9)	
Work status						
working	193 (36.8)	74 (38.5)	49 (31.4)	51 (40.8)	19 (36.5)	
others	331 (63.1)	117 (60.9)	107 (68.6)	74 (59.2)	33 (63.5)	0.477
missing	1 (0.2)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	

Cancer	21 (4.0)	8 (4.2)	7 (4.5)	4 (3.2)	2 (3.9)	0.956
Hypertension	142 (27.1)	57 (29.7)	34 (21.8)	35 (28.0)	16 (30.8)	0.350
Diabetes	32 (6.1)	11 (5.7)	9 (5.8)	8 (6.4)	4 (7.7)	0.955
Arthritis	30 (5.7)	13 (6.8)	8 (5.1)	8 (6.4)	1 (1.9)	0.574
CVD	79 (15.1)	31 (16.2)	17 (10.9)	19 (15.2)	12 (23.1)	0.179
Exercise habit						
<2/week	336 (64)	138 (71.9)	74 (47.4)	87 (69.6)	37 (71.2)	
≥2/week	188 (35.8)	53 (27.6)	82 (52.6)	38 (30.4)	15 (28.9)	**<.0001**
missing	1 (0.2)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	
Daily walking						
<60/day	240 (45.7)	95 (49.5)	63 (40.4)	54 (43.2)	28 (53.9)	
≥60/day	281 (53.5)	96 (50.0)	92 (59.0)	70 (56.0)	23 (44.2)	0.292
missing	4 (0.8)	1 (0.5)	1 (0.6)	1 (0.8)	1 (1.9)	
Competence of daily living	11.61 ± 1.61	10.81 ± 1.77	12.43 ± 0.85	11.68 ± 1.61	11.96 ± 1.30	**<.0001**

Difference among different changes in social activities tested by chi-square test and ANOVA test depending on the type of the variables. CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency, CVD: cardiovascular disease

3-3.2 Changes in social activities and mild disability

From the resulting 4,342 person-years for mild disability, the number of people who developed as it was 108 (20.6%) (**Table 3-2**).

In comparison with participants who had CLF of changes in social activities, the HRs (95% CI) for mild disability were 0.44 (0.24, 0.82) at IF of learning activities in the fully adjusted model 2. The inverse association were also showed for IF of social-related and personal activities, CRF of social-related, learning, and personal activities, but the associations were not statistically significant. In the Laplace regression model, compared with CLF of changes in social activities, IF and CRF of learning and personal activities were associated with longer disability-free survival time. But after controlling all the covariates, only IF of learning activities (25% PD=3.11, 95% CI (1.41, 4.82)) showed significant association.

Regarding the changes in combination of social activities, when compared with participants who remained in Group A, participants who remained in Group C, D and increased the number of regular frequency social activities had a lower risk of mild disability. But the Laplace regression results showed only when participants increased the number of regular activities were more likely to increase the disability-free survival time. However, these associations were not statistically significant.

Table 3-2 Association of changes in social activities on incident mild disability and disability free survival time among participants with depressive symptoms at baseline

Social activities	Changes in social activities	Person-years (n = 4342)	Number of events (n = 108)	Cox regression model		Laplace regression model	
				model1	model2	model1	model2
				HRs (95%CI)	HRs (95%CI)	25th PDs (years) (95%CI)	25th PDs (years) (95%CI)
Social-related activities	CLF	1355	39/165	1.00	1.00	0.00	0.00
	CRF	1128	28/139	0.66 (0.41, 1.06)	0.76 (0.44, 1.34)	0.44 (-1.77, 2.65)	0.09 (-3.53, 3.71)
	IF	245	10/32	0.86 (0.53, 1.39)	0.93 (0.54, 1.60)	0.06 (-2.77, 2.90)	-0.04 (-3.97, 3.89)
	DF	1614	31/189	1.39 (0.67, 2.88)	1.55 (0.72, 3.36)	-1.51 (-4.01, 0.99)	-1.36 (-5.21, 2.48)
Learning activities	CLF	2119	63/263	1.00	1.00	0.00	0.00
	CRF	977	13/110	0.74 (0.45, 1.23)	0.77 (0.44, 1.35)	1.41 (-0.47, 3.28)	0.94 (-1.89, 3.78)
	IF	365	12/47	0.44 (0.24, 0.80) **	0.44 (0.24, 0.82) **	3.26 (1.26, 5.26) **	3.11 (1.41, 4.82) ***
	DF	881	20/105	1.21 (0.65, 2.24)	1.22 (0.62, 2.40)	-0.7 (-36.49, 35.08)	-0.21 (-2.78, 2.36)
Personal activities	CLF	1546	46/192	1.00	1.00	0.00	0.00
	CRF	1062	22/125	0.60 (0.37, 0.97) *	0.78 (0.45, 1.35)	0.80 (-1.08, 2.67)	0.43 (-2.41, 3.27)
	IF	412	15/52	0.70 (0.42, 1.16)	0.77 (0.45, 1.33)	1.55 (-0.98, 4.07)	1.76 (-0.73, 4.25)
	DF	1323	25/156	1.15 (0.63, 2.09)	1.23 (0.66, 2.28)	-2.02 (-3.77, -0.27) *	-1.14 (-4.00, 1.72)
Combination of social activities	remained in Group A	620	18/77	1.00	1.00	0.00	0.00
	remained in Group B	478	16/58	1.23 (0.61, 2.47)	1.58 (0.74, 3.37)	-0.14 (-4.77, 4.50)	-0.67 (-4.91, 3.57)
	remained in Group C	294	2/35	0.23 (0.05, 0.96) *	0.36 (0.08, 1.61)	1.58 (-2.51, 5.68)	-0.65 (-6.47, 5.17)
	remained in Group D	347	6/41	0.57 (0.23, 1.44)	0.81 (0.28, 2.31)	0.38 (-4.07, 4.82)	-0.46 (-7.35, 6.42)
	increased	1986	40/234	0.70 (0.40, 1.23)	0.84 (0.45, 1.57)	1.18 (-3.30, 5.66)	0.95 (-3.17, 5.06)
	decreased	617	26/80	1.45 (0.78, 2.67)	1.82 (0.91, 3.66)	-1.83 (-6.39, 2.73)	-1.61 (-6.67, 3.46)

CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency; HRs: hazard ratios, CI: confidence interval; 25th PDs: the 25th percentile differences; Model 1 adjusted for sex and year of participation; Model 2 Model 3 adjusted for sex, year of participation, smoking, drinking, marital status, education background, residential status, and work status, BMI, cancer, hypertension, diabetes, arthritis, cardiovascular disease and competence of daily living, exercise habits, and daily walking; *P<0.05, **P<0.01, ***P<0.001

3-3.3 Changes in social activities and severe disability

From the resulting 4,465 person-years for severe disability, the number of people who developed it was 54 (10.3%) (**Table 3-3**).

Compared with participants with CLF of social activities, those who had CRF of learning and personal activities showed a reduced risk of severe disability in model1. Although the IF of learning activities was also more likely to decrease the risk of severe disability, there is no significant difference. The Laplace regression results showed that the CRF of learning activities was significantly associated with a longer disability-free survival time in model1.

Although there is no significant difference, compared with participants who remained in Group A, the other three groups that people who remained in the same group were more likely to have the lower risk of severe disability. But the Laplace regression, with different results with the Cox models, showed a longer disability-free survival time among participants who remained in Group B, and who increased their number of regular frequency activities.

Table 3-3 Association of changes in social activities on severe disability and disability free survival time among participants with depressive symptoms at baseline

Social activities	Changes in social activities	Person-years (n = 4465)	Number of events (n = 54)	Cox regression model		Laplace regression model	
				model1	model2	model1	model2
				HRs (95%CI)	HRs (95%CI)	25th PDs (years) (95%CI)	25th PDs (years) (95%CI)
Social-related activities	CLF	1406	17/165	1.00	1.00	0.00	0.00
	CRF	1159	17/139	0.90 (0.45, 1.77)	1.29 (0.56, 2.98)	0.48 (-2.88, 3.85)	-1.37 (-4.91, 2.16)
	IF	261	3/32	1.23 (0.63, 2.41)	1.58 (0.77, 3.25)	-0.96 (-4.23, 2.31)	-0.97 (-3.83, 1.90)
	DF	1640	17/189	1.03 (0.29, 3.70)	1.44 (0.37, 5.67)	0.18 (-5.86, 6.23)	-1.01 (-7.49, 5.47)
Learning activities	CLF	2175	35/263	1.00	1.00	0.00	0.00
	CRF	974	8/110	0.35 (0.14, 0.88) *	0.42 (0.15, 1.18)	5.11 (0.4, 9.83) *	1.93 (-0.86, 4.73)
	IF	389	6/47	0.54 (0.25, 1.17)	0.66 (0.29, 1.54)	3.22 (-0.60, 7.05)	3.46 (-0.08, 7.00)
	DF	928	5/105	1.00 (0.43, 2.33)	1.21 (0.47, 3.09)	-0.22 (-4.42, 3.98)	1.73 (-3.72, 7.19)
Personal activities	CLF	1593	23/192	1.00	1.00	0.00	0.00
	CRF	1064	17/125	0.43 (0.19, 0.97) *	0.65 (0.25, 1.68)	4.03 (-0.07, 8.14)	0.67 (-2.94, 4.28)
	IF	443	6/52	1.18 (0.63, 2.19)	1.38 (0.71, 2.67)	-0.61 (-3.62, 2.41)	0.01 (-2.51, 2.52)
	DF	1365	8/156	1.00 (0.40, 2.53)	1.15 (0.45, 2.98)	-0.21 (-4.85, 4.44)	-1.03 (-5.25, 3.2)
Combination of social activities	remained in Group A	629	11/77	1.00	1.00	0.00	0.00
	remained in Group B	510	5/58	0.63 (0.21, 1.94)	0.92 (0.24, 3.55)	2.32 (-3.22, 7.86)	2.59 (-2.56, 7.74)
	remained in Group C	293	2/35	0.41 (0.09, 1.80)	0.68 (0.13, 3.50)	4.22 (-3.33, 11.77)	-2.02 (-6.51, 2.46)
	remained in Group D	362	2/41	0.34 (0.08, 1.51)	0.75 (0.12, 4.71)	4.94 (-2.69, 12.58)	-2.34 (-9.5, 4.81)
	increased	2011	24/234	0.75 (0.36, 1.56)	1.08 (0.46, 2.54)	1.54 (-2.01, 5.08)	0.25 (-3.2, 3.70)
	decreased	661	10/80	0.96 (0.39, 2.35)	1.51 (0.49, 4.64)	0.11 (-4.36, 4.57)	-1.41 (-6.65, 3.83)

CLF: continued low frequency, IF: increased frequency, DF: decreased frequency, CRF: continued regular frequency; HRs: hazard ratios, CI: confidence interval; 25th PDs: the 25th percentile differences; Model 1 adjusted for sex and year of participation; Model 2 Model 3 adjusted for sex, year of participation, smoking, drinking, marital status, education background, residential status, and work status, BMI, cancer, hypertension, diabetes, arthritis, cardiovascular disease and competence of daily living, exercise habits, and daily walking; *P<0.05, **P<0.01, ***P<0.001

3-4. Discussion

To the best of my knowledge, this is the first study exploring the relationship between changes in single, multiple social activities and incident functional disability and disability-free survival time among age-specific depressed older adults in Japan. This study revealed evidence that compared to participants with CLF of learning activities, those who with IF of learning activities had a reduced risk of developing mild disability, and IF of learning activities also significantly prolong their mild disability-free survival. Those who with CRF of learning activities had a reduced risk of developing severe disability, but this association was not significant after controlling all the confounding factors. Similarly, the association between CRF of learning activities and severe disability-free survival time also did not show a significance in the multivariable models.

Regarding the changes in different type of social activities and incident functional disability among depressed older adults, the results showed that IF of learning activities not only had a lower hazard ratio of the incidence of mild disability, but also prolonged the disability-free survival time. This is in line with the previous studies that intellectual activities (play cards/mahjong/chess, reading books) could protect against functional decline among common older adults (Gao *et al.*, 2018; Fujiwara et al., 2009). Although the subjects in the current study are different from that in previous studies, there is a common mechanism that a higher level of participation in intellectual activities had more significant benefits for cognitive function among older adults, because these activities may help them exercise their reflexes and memory, thereby delaying function deterioration (Glei et al., 2005; Gao *et al.*, 2018). Furthermore, the higher levels and increased level of learning activities have positive effects on depressed older adults (Isaac *et al.*, 2009; Shan et al., 2022). The improvement in depressive symptoms was associated with improved functional disability (Nyunt et al., 2012).

Additionally, CRF of personal activities showed a significant association with mild

and severe disability in model 1. The results in Chapter two also demonstrated that personal activities had a stronger effect on depressive symptom, the reason may be a higher level of perceived emotional support that people could get from personal activities than the other two kind of activities, since perceived social support not only buffers the neuroendocrine effects of depression but also encourages depressed patients to remain physically active, decreasing the potential severity of their impairment (Hays *et al.*, 2001). However, in the present study, the association was not significant after all the covariates controlled. This may be due to the lower incidence rate or the comorbid disease that weakened the relationship. Additionally, about the combination of social activities, the results between Cox and Laplace regression were not consistent, this also may because the lower sample size. Still need more studies to explore this association.

Regarding the severity degree of disability, although the results showed associations between changes in learning activities and incident disability among depressed older adults, there are differences among different change types of social activities on incident mild or severe disability. Among participants who developed mild disability, IF of learning activities showed a significant association. However, among participants who developed severe disability, CRF of learning activities demonstrated a significant association in model1. This may suggest that the risk of mild disability can be reduced by increasing the frequency of learning activities even if the frequency of learning activities in earlier life is low. However, for depressed participants with severe disability, maintaining higher frequency of learning activity may reduce the risk of disability. It may because a low frequency of social engagement at baseline could persist or exacerbate depressive symptoms. Thus, even increasing the frequency of social activities does not help to protect against the following disability. Future studies still need to demonstrate this association, because the lower prevalence of disability that who developed severe disability may cause underestimation of the association between changes in social activities and disability in this study.

A set of social activities makes me detect the effect of the different type and

combination of social activities on incident functional disability, which also making the results more easily to generalize in different race. Social participation among community-dwelling older adults differed by their age and gender (Saito et al., 2015; Finkel et al., 2018; Tomioka et al., 2022). The participants in the present study were older adults of a specific age, which allowed us to eliminate age bias. However, due to the low prevalence of disability, there were missing values when assessing gender differences, so I did not explore gender differences in the relationship between changes in social activity and the incident disability. In addition, social activities and depressive symptoms were assessed by the self-reported questionnaire, which may lead to recalled biases. Furthermore, the effect of changes in social activities on depressive symptoms is a dynamic process, continued regular or increased social activities may improve the depressive status. However, this cohort only did two waves of investigation for six-years. Therefore, I did not consider the trajectories of social activities and depressive status on incident disability. Finally, as I discussed intellectual activities could improve the cognitive function then decrease the risk of disability, cognitive function should be treated as a confounding factor. However, due to relatively few participants completed the assessment of cognitive function, it was not included as a covariate.

Conclusions

Findings

- Chapter one found that Japanese community-dwelling older adults who engaged in one or more behavioral activities with continued regular frequency were negatively associated with the onset of depressive symptoms. Similarly, depressed participants may also benefit from the continued regular frequency of one or multiple behavioral activities.
- Chapter two demonstrated that Japanese community-dwelling older adults with a continued regular or an increased frequency of single and multiple social activities associated with the onset of depressive symptoms. And participating in personal activities had a greater impact on depressive symptoms than social-related and learning activities, whether they had depressive symptoms or not at baseline.
- Chapter three further revealed that depressed community-dwelling older adults who had increased frequency of learning activities were more likely to reduce the risk of incident mild disability and prolong their disability-free survival time.

Significance

This study not only elucidated the relationship between changes in behavioral activities and depressive symptoms among community-dwelling older adults but also identified the association between changes in social activities and functional disability among depressed community-dwelling older adults. For Japanese community-dwelling older adults, these findings encourage them to make positive behavioral and lifestyle changes to protect them from future disease onset or improve the prognosis of disease. For policy makers, these findings provide them some recommendations of guidelines on behavioral activities to promote older people's health. In addition, for clinicians, they can purposefully target this emerging evidence to clinical adjuvant therapy, which enable to relieve and treat the depressive symptoms or functional disability in older adults.

Future study

Although the association between changes in behavioral activities and depressive symptom, disability have been demonstrated in this study, to better put these findings into practice, my future studies will further explore the dose effect between them. First, as I discussed in chapter two, it was difficult to compare studies due to the utilization of single social activity that are distinct and not necessarily comparable even the same kind of activity but different question. Thus, the best comparisons were derived studies that utilize a comprehensive questionnaire that covering a variety of social activities, rather than one or two single variables. However, the questionnaire I used did not validated in the other nations. Therefore, I plan to improve the current questionnaire and validate it in more countries or ethnic groups as soon as possible. This would pave the way for a more robust research base for social activities and ultimately strengthen the comparability across studies that included different race of people. Second, about the physical activities, it is better to use the wearable devices to measure the calories consume or exercise time etc., which not only reduce the biases but also enhance executability. Although there are multiple of studies have provided guidance on physical activity in older adults, these findings remain controversial, especially in older adults with depression or disability. Therefore, future studies on promoting healthy aging through physical activities should focus more on older adults with chronic diseases.

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Disclosure of conflict of interest

The author declares no conflicts of interest.

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