

FACTORS RELATED TO FREQUENCY OF ENGAGING IN OUTSIDE ACTIVITIES AMONG ELDERLY PERSONS LIVING AN INDEPENDENT LIFE AT HOME

MIYUKI ISHIKAWA¹, KOJI TAMAKOSHI¹, HIROSHI YATSUYA¹, KAZUTAKA SUMA¹,
KEIKO WADA¹, REI OTSUKA¹, KUNIHIRO MATSUSHITA^{1,2}, HUIMING ZHANG¹,
CHIYOE MURATA³, TAKAAKI KONDO⁴ and HIDEAKI TOYOSHIMA¹

¹ Department of Public Health/Health Information Dynamics, Field of Social Life Science,
Nagoya University Graduate School of Medicine.

² Department of Cardiology, Nagoya University Graduate School of Medicine.

³ Department of Public Health, Hamamatsu University School of Medicine.

⁴ Department of Medical Technology, Nagoya University School of Health Science.

ABSTRACT

We examined by cross-sectional design the association between the frequency of outside activity and the demographic, health problem, lifestyle, psychosocial and environmental factors among 239 community-dwelling elderly Japanese people (105 men and 134 women) aged 65 years and older, who lived independently at home. The associations of the outside activities more than 6–7 days per week based on a categorical questionnaire choice with potential factors were expressed by odds ratio (OR) and 95% confidence interval (CI) calculated through logistic regression analysis by sex. The proportions of those engaging in outside activity more than 6–7 days per week were 38.1% and 21.6% among men and women, respectively. The associations of the factors belonging to various fields with the frequency of engaging in outside activities were clearly pronounced among men. Elderly men engaging in outside activities more often were scored less for depression and more socially active than men engaging in outside activities less often. Multiple regression analysis revealed meeting and talking often with friend (OR=4.18, 95% CI: 1.06–16.5), current alcohol consumption (3.01, 1.06–8.54), having any hobby (3.59, 0.94–13.7), and easy access to public transportation (3.43, 1.28–9.16) as significant or borderline significant factors related to engaging in outside activities more than 6–7 days per week. Women who were currently employed engaged in outside activities more frequently. The frequency of engaging in outside activities was associated with factors belonging to various fields among elderly people living independently, particularly among men, suggesting its usefulness as an indicator of comprehensive well-being.

Key Words: Community-dwelling elderly, Frequency of outside activities, Living an independent life, Cross-sectional study, Gender differences.

INTRODUCTION

Japan has been experiencing rapid demographic aging resulting in an alarming increase in frail elderly who need long-term care. The number of bedridden elderly is expected to reach

Address for correspondence: Hideaki Toyoshima

Department of Public Health/Health Information Dynamics, Field of Social Life Science, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

Phone: Japan 81-52 (744) 2128 Fax: Japan 81-52 (744) 2131

E-mail: toyosima@med.nagoya-u.ac.jp

1.7 million by the year 2010 and 2.3 million in the year 2025.¹⁾ Elderly people become bedridden for various reasons, and the two top causes are stroke and bone fracture. Recently, being homebound, a state in which an elderly is essentially confined to his or her home, is attracting attention since it is considered the risk or sign of physical and cognitive impairment related to being bedridden. Therefore, preventive efforts to reduce the number of bedridden should first target stroke and fracture prevention, but at the same time it would be important to identify factors within or surrounding elderly persons associated with being homebound. The homebound condition was evaluated using the frequency of going outdoors, and has been usually defined in many studies as leaving the house once or less than once a week, indicating a status of being almost totally confined to the house. Some previous studies including the subjects requiring any care or support have examined the characteristics of the homebound by comparing them with the non-homebound group and have shown that low functional and psychosocial status is associated with being homebound.²⁻¹⁵⁾

When the way of thinking is changed, what kinds of factors are related to high frequency of going out? To our knowledge, there are few reports on this issue. Physical and cognitive impairment must be associated with low frequency of going out. To exclude their effects, we chose to focus on the elderly who required no care and lived. Additionally, we paid attention to the factors related to going out for any purpose.

In this study, we investigated the relationship between a high frequency of their engaging in outside activities and demographic, health problem, lifestyle, psychosocial, and environmental factors among those living independently at home without any caregiver or support. Our findings lead us to propose possible measures by which these elderly persons maintain independent living, or avoid becoming progressively ill, frail, and disabled. They may also provide possible measures against being homebound and bedridden.

METHODS

Study population

We performed the study in N City, a rural community, in Gifu Prefecture, Japan. The population of this city was 54,934, and 22.1% were aged 65 years and older in 2002 (17.6% and 21.0% in 1995 and 2000, respectively). Total area was 275.98 km². The proportion of workers in primary industries (mainly agriculture), secondary industries (manufacturing industries), and tertiary industries were 4.7%, 43.4%, and 51.8%, respectively, in 2001.

To elucidate the factors related to the frequency with which elderly persons engage in outside activities, the local government office chose 10 persons per area at random among elderly persons aged 65 years and older who were recognized as not needing nursing care, that is, living independently by Long-term Care Screening Committee in 30 administrative areas in N city from June to August in 2000. Random sampling was performed according to the list of the persons whose application for nursing care was not approved by Long-Term Care Screening Committee. Although our study may have selection bias that present subjects were selected among the persons who applied for care at Long-Term Care Insurance Section, they are defined clearly as living independently. Finally, a total of 281 elderly persons participated in this study and answered the questionnaire through interview since 19 persons refused to participate. In November 2002, the frequency of outside activities and general condition were investigated again. At this time the questionnaire, more detailed than the first one, not only inquired about the frequency of engaging in outside activities, but also the demographics, health problems, depression, psychological and social factors, lifestyle, and their home environment; questions were also asked through interviews

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by a public health nurse. Of 281 elderly persons, 42 were excluded for the following reasons: death (n=12), receiving nursing care (n=10), hospitalization (n=2), mental disease (n=2), moving away from study area (n=5), refusing to participate in investigation (n=3), absence (n=1), and missing information (n=7). The remaining 239 elderly persons (105 men and 134 women; mean \pm standard deviation of age; men: 76.7 ± 6.5 , women: 76.9 ± 6.8) were included in the present analysis. All subjects were recognized as not needing nursing care (living independently) at the time of the interview. All subjects in the study gave their informed consent to the use of personal information for analysis. This study protocol was approved by the Ethics Committee of the Nagoya University Graduate School of Medicine, Nagoya, Japan.

Variables and instruments

Participants were asked, "How often do you usually go outside your home?" The answers to the question were categorized as 1) more than 6–7 times a week, 2) 4–5 times a week, 3) 2–3 times a week, 4) once a week, 5) 2–3 times a month, 6) once a month, and 7) less than once a month. In the questionnaire, shopping, hospital, bank, meeting place for hobby or amusement, friend's home, workplace, teahouse, a walking to neighborhood et al. were exemplified as places to go or reasons to engage in outside activities. Therefore, engaging in outside activities was defined as leaving one's home for any purpose.

Depression was assessed by the 30-item version of the Geriatric Depression Scale (GDS).^{16,17)} Scores of 0–9 are considered normal, 10–19 indicate mild depression and 20–30 indicate severe depression. Other psychological and social factors including social support were assessed by the following eight questions; 1) Perceived stress (Yes/No). 2) Meeting and talking as often as one would like with friend (Yes/No). 3) Having at least one person whose advice can really be trusted (Yes/No). 4) Participation in group activity (Yes/No). 5) Having any role in the group activity (Yes/No). 6) Having any role in the family (Yes/No). 7) Having something to live for (living a life worth living, living to some purpose) - "Ikigai" in Japanese (Yes/No).

The geographic environment around their homes was also assessed by the following three questions: 1) Access to nearby public transportation (Easy/Not easy). 2) Many hills around home (Yes/No). 3) Heavy traffic near house (Yes/No).

Our questionnaire also included several other items covering demographics such as: age, living alone (Yes/No), number of family members, education (<high school graduate/>=high school graduate), current employment (Yes/No); health problems: disease history such as stroke, heart attack/angina, hypertension, diabetes, lung disease, arthritis, and eye/ear disease, consciousness of physical pain (Yes/No); lifestyle: smoking status (Current/Former or Never), alcohol consumption (Current/Former or Never), having hobby (Yes/No).

Statistical methods

First, to elucidate the differences in study variables between men and women, we calculated proportions, means, and standard deviations by sex. Chi-square test or Student's t-test was performed to explore the potential association of gender with study variables. Further analyses were performed by gender since the frequency of engaging in outside activities differed significantly between men and women.

In the present study we aimed to elucidate the factors related to high frequency of outside activities. So we computed the odds ratios (ORs) and 95% confidence interval (CI) of engaging in outside activities more than 6–7 times per week (the highest category), which suggested outside activities were engaged in almost every day, for each study variable using logistic regression analysis with age as a covariate. Furthermore, multiple logistic regression analysis was performed to identify variables independently associated with engaging in outside activities.

Multiple logistic regression model included those independent variables found to be significant or borderline significant (p value <0.1) in the age-adjusted model.

All analyses were performed using the SPSS 11.0 statistical package. $P < 0.05$ was considered statistically significant.

RESULTS

Table 1 shows the characteristics of study subjects by gender. The means \pm standard deviations (SD) of age were 76.7 ± 6.5 and 76.9 ± 6.8 in men and women, respectively. The frequency of engaging in outside activities among men was significantly higher than among women ($p < 0.05$). As for psychological and social factors, there was no difference in GDS score (mildly and severely depressive: 43.4% and 3.8% in men, 44.8% and 5.2% in women, respectively) between men and women. The proportion of respondents having a friend whom he or she can meet and talk with as often as they liked was significantly higher among women than men. The proportion of having any role in group activity was higher among men, while more women had a role in family life.

Associations of variables with the frequency of engaging in outside activities are shown in Table 2. In demographic variables, only being employed was associated with high frequency of engaging in outside activities among women (OR=3.76, 95% CI: 1.32–10.7). With respect to health problems, all ORs of disease histories were below unity among men although they were not statistically significant. Consciousness of physical pain was inversely associated with a high frequency of engaging in outside activities (OR=0.36, 95% CI: 0.11–1.18). Women with eye or ear disease had a lower frequency (OR=0.23, 95% CI: 0.05–1.06), but women with hypertension engaged in outside activities more frequently than those without it (OR=2.95, 95% CI: 1.27–6.88). The associations of psychological and social factors with the frequency of engaging in outside activities were clearly pronounced among men. The number of depressive symptoms measured using GDS were significantly and inversely associated with high frequency of engaging in outside activities (trend $p=0.03$). The interpersonal support items (meeting and talking as often as one would like with a friend, OR=6.64, 95% CI: 2.02–21.9) and additional items (participation in group activity, OR=2.07, 95% CI: 0.90–4.77; having any role in the family, OR=2.72, 95% CI: 0.92–8.07) were significantly or borderline significantly related to a higher frequency of engaging in outside activities. Other ORs of social factors were above unity among men. Among women, the association of depression with the frequency of outside activities was similar to that among men, although not significant. The associations of lifestyle and environmental factors with the frequency of outside activities were also clear among men. As for lifestyle factors, alcohol consumption and having hobby were significantly associated with a high frequency of engaging in outside activities among men. Men with easy access to public transportation engaged in outside activities more frequently than those without it. Among women, no association of lifestyle and environmental factors was observed with the frequency of engaging in outside activities.

Table 3 shows the variables that were associated independently with the frequency of engaging in outside activities by sex, as determined by multiple logistic regression analyses. Variables included were those with significant or borderline significant relationships with a high frequency of engaging in outside activities in the age-adjusted model shown in Tables 2. Those found to be significantly or borderline significantly associated after adjusting for the effects of the other variables in the model included meeting and talking as often as they liked with a friend (OR=4.18, 95% CI: 1.06–16.5), current alcohol consumption (OR=3.01, 95% CI: 1.06–8.54), having any hobby (OR=3.59, 95% CI: 0.94–13.7), and easy access to public transportation

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Table 1 Characteristics of study population by gender.

		Men	Women	p value ^{a)}
		n=105	n=134	
Demographics				
Age (year)				
65–74		45.7%	44.8%	ns
75–84		40.0%	43.3%	ns
85–		14.3%	11.9%	ns
	mean ± SD	76.7 ± 6.5	76.9 ± 6.8	ns
Living alone	Yes	36.2%	45.5%	ns
Number of family graduate	mean ± SD	1.78 ± 0.82	1.88 ± 1.18	ns
Education				
<High school graduate		76.0%	65.2%	0.07
≥High school graduate		24.0%	34.8%	
Current employment	Yes	32.7%	14.7%	<0.01
Health problems				
Disease history				
Stroke	Yes	10.5%	6.7%	ns
Heart attack/Angina	Yes	10.5%	7.5%	ns
Hypertension	Yes	21.9%	35.1%	ns
Diabetes	Yes	5.7%	11.2%	ns
Lung disease	Yes	11.4%	3.0%	<0.05
Arthritis	Yes	4.8%	4.5%	ns
Eye/Ear	Yes	15.2%	20.1%	ns
Consciousness of physical pain	Yes	18.1%	32.1%	<0.05
Psychological and social factors				
Depression				
–9		52.4%	50.0%	ns
10–19 (Mild depression)		43.4%	44.8%	
20+ (Severe depression)		3.8%	5.2%	
	mean ± SD	9.10 ± 5.25	10.2 ± 5.30	ns
Perceived stress	Yes	19.0%	20.5%	ns
Meeting and talking often with friend	Yes	70.5%	88.1%	<0.01
Having one person you can trust	Yes	91.4%	93.3%	ns
Participation in group activity	Yes	42.3%	44.0%	ns
Role in group activity	Yes	33.7%	14.9%	<0.01
Role in family life	Yes	76.9%	90.2%	<0.01
Something to live for (Ikigai)	Yes	64.4%	58.2%	ns
Lifestyle factors				
Smoking status	Current	32.0%	5.3%	<0.01
Alcohol consumption	Current	55.2%	16.4%	<0.01
Hobby	Yes	69.5%	73.7%	ns
Environmental factors				
Access to public transportation	Easy	42.6%	47.0%	ns
Hilly around your home	Yes	29.8%	42.4%	<0.05
Heavy traffic around your home	Yes	19.2%	27.8%	ns
Frequency of going outside activities				
More than 6–7 times/week		38.1%	21.6%	<0.05
4–5 times/week		18.1%	14.9%	
2–3 times/week		21.9%	36.6%	
Once per week		9.5%	14.9%	
2–3 times/month		9.5%	7.5%	
Once per month		2.9%	3.0%	
Less than once per month		0.0%	1.5%	

a) P values were calculated using chi-square test for categorical data and t-test for quantitative data.

Table 2 Age-adjusted odds ratios and 95% confidence intervals for engaging in outside activities more than 6–7 days per week by sex.

	Men		Women	
	OR	95% CI	OR	95% CI
Demographic factors				
Age (year)				
65–74	1.00	(reference)	1.00	(reference)
75–84	1.25	(0.25–6.30)	0.19	(0.03–1.23)
85–	1.86	(0.08–41.5)	0.23	(0.01–6.87)
	trend p=0.72		trend p=0.28	
Living alone (Yes/No)	0.86	(0.37–1.98)	1.38	(0.60–3.16)
Number of family members				
1	1.00	(reference)	1.00	(reference)
2	0.97	(0.41–2.27)	1.02	(0.41–2.50)
3+	1.37	(0.25–7.36)	0.37	(0.08–1.83)
	trend p=0.86		trend p=0.32	
Education (>=High school graduate/<High school graduate)	1.35	(0.53–3.41)	0.98	(0.41–2.37)
Current employment (Yes/No)	1.22	(0.52–2.84)	3.76	(1.32–10.7) ^{b)}
Health problems				
Disease history				
Stroke (Yes/No)	0.36	(0.07–1.80)	1.05	(0.20–5.46)
Heart attack or Angina (Yes/No)	0.30	(0.06–1.50)	0.38	(0.05–3.14)
Hypertension (Yes/No)	0.46	(0.16–1.30)	2.95	(1.27–6.88) ^{b)}
Diabetes (Yes/No)	0.63	(0.10–3.85)	0.52	(0.11–2.48)
Lung disease (Yes/No)	0.82	(0.22–2.95)	1.22	(0.12–12.3)
Arthritis (Yes/No)	0.91	(0.14–5.94)	1.88	(0.32–10.9)
Eye or Ear (Yes/No)	0.75	(0.24–2.39)	0.23	(0.05–1.06) ^{a)}
Consciousness of physical pain (Yes/No)	0.36	(0.11–1.18) ^{a)}	1.41	(0.59–3.37)
Psychological and social factors				
Depression (GDS score)				
–9	1.00	(reference)	1.00	(reference)
10–19	0.38	(0.16–0.89) ^{b)}	0.83	(0.34–1.86)
20+	0.36	(0.04–3.71)	0.53	(0.06–4.77)
	trend p=0.03		trend p=0.47	
Perceived stress (Yes/No)	1.52	(0.65–3.55)	1.65	(0.69–3.95)
Meeting and talking often with friend (Yes/No)	6.64	(2.02–21.9) ^{b)}	0.55	(0.17–1.77)
Having one person you can trust (Yes/No)	5.49	(0.66–45.7)	0.97	(0.19–4.93)
Participation in group activity (Yes/No)	2.07	(0.90–4.77) ^{a)}	0.71	(0.38–1.69)
Role in group activity (Yes/No)	1.60	(0.67–3.80)	0.88	(0.27–2.93)
Role in family life (Yes/No)	2.72	(0.92–8.07) ^{a)}	0.92	(0.23–3.62)
Something to live for (Ikigai) (Yes/No)	2.08	(0.86–5.04)	0.69	(0.29–1.63)
Lifestyle factors				
Smoking status (Current/Former or Never)	0.54	(0.22–1.30)	0.58	(0.07–5.02)
Alcohol consumption (Current/Former or Never)	2.66	(1.11–6.37) ^{b)}	0.32	(0.07–1.44)
Hobby (Yes/No)	2.84	(1.06–7.59) ^{b)}	0.72	(0.28–1.83)
Environmental factors				
Access to public transportation (Easy/Not easy)	3.24	(1.40–7.53) ^{b)}	1.29	(0.55–3.05)
Hilly around your home (Yes/No)	0.47	(0.18–1.21)	0.84	(0.36–1.98)
Heavy traffic around your home (Yes/No)	0.69	(0.24–2.02)	0.99	(0.39–2.48)

a) p <0.1.

b) p <0.05.

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Table 3 Multivariate odds ratios and 95% confidence intervals for engaging in outside activities more than 6–7 days per week by sex.

	OR	95% CI
Men		
Age (Years)	1.05	(0.97–1.15)
Consciousness of physical pain (Yes/No)	0.42	(0.09–2.04)
Depression (GDS score)		
–9	1.00	(reference)
10–19	0.55	(0.17–1.72)
20+	1.66	(0.09–29.3)
Meeting and talking often with friend (Yes/No)	4.18	(1.06–16.5) ^{b)}
Participation in group activity (Yes/No)	0.60	(0.19–1.86)
Role in family life (Yes/No)	1.55	(0.43–5.59)
Alcohol consumption (Current/Former or Never)	3.01	(1.06–8.54) ^{b)}
Hobby (Yes/No)	3.59	(0.94–13.7) ^{a)}
Access to public transportation (Easy/Not easy)	3.43	(1.28–9.16) ^{b)}
Women		
Age (Years)	1.00	(0.93–1.06)
Current employment (Yes/No)	3.25	(1.09–9.72) ^{b)}
History of hypertension (Yes/No)	2.64	(1.05–6.64) ^{b)}
History of eye or ear diseases (Yes/No)	0.25	(0.05–1.19) ^{a)}

a) $p < 0.1$.b) $p < 0.05$.

(OR=3.43, 95% CI: 1.28–9.16). Thus, many variables in different aspects were independently associated with a high frequency of engaging in outside activities among men. Among women, current employment (OR=3.25, 95%CI: 1.09–9.72), history of hypertension (OR=2.64, 95%CI: 1.05–6.64), and history of eye or ear diseases (OR=0.25, 95%CI: 0.05–1.19) were still significantly or borderline significantly associated with a high frequency of engaging in outside activities after multivariate-adjustment.

DISCUSSION

We elucidated some factors related to a high frequency of engaging in outside activities among elderly persons living independently. Additionally, we studied these issues from the viewpoint of gender differences since most of the previous studies on the frequency of outside activities and being homebound disregarded this issue.

We found some characteristics that were different between men and women. In the present study the frequency of engaging in outside activities was significantly higher among men than among women, although another study in Japan reported no such gender difference.¹³⁾ Our observations that men had more roles in group activity whereas women had more roles in familial life may explain the higher frequency of outside activities in men than in women. Additionally, in this area, there is the traditional thinking which does not encourage women's engaging in outside activities from ancient times. Compared with the frequency of outside activities in the previous study by Fujita et al.¹³⁾ (almost every day: 76.9% in men, 75.8% in women), that of our study subjects was low (38.1% in men, 21.6% in women). The lower proportions of being employed (current employment: 59.9% in men and 47.7% in women in the previous study¹³⁾ vs. 32.7% and 14.7%, respectively, in our study) may in part explain the lower frequency of

engaging in outside activities in our study. Our results should be interpreted in light of the above-mentioned situation.

The associations of study variables with the frequency of outside activities differed by gender. They were clear among men, and the related factors belonged to various fields. By age-adjusted model, health problem (consciousness of physical pain) or psychological factors (higher GDS) were likely to discourage the elderly from engaging in outside activities, while social factors (meeting and talking often with friends, participation in group activity, role in family life), lifestyle factor (current alcohol consumption, having hobby), and environmental factors (easy access to public transportation) were likely to promote it. After mutually adjusting for these variables, social factors (meeting and talking as often as one liked with a friend), lifestyle factors (current alcohol consumption, having hobby), and environmental factors (easy access to public transportation) were still significantly or borderline significantly associated with the high frequency of engaging in outside activities. Particularly, these three factors except for alcohol consumption should be recalled when considering administrative measures. Creating more opportunities for meeting and talking with friends and having hobby and providing easier access to public transportation may enable the elderly to leave home more often. The positive association of alcohol consumption with a high frequency of engaging in outside activities has been reported in the previous study¹³⁾ but it is difficult to consider it a causal relationship. Elderly men with a habit of alcohol consumption may go out in order to drink or those who frequently go out may consequently have more opportunities for drinking.

On the other hand, only three factors were associated with the high frequency of engaging in outside activities among women by age-adjusted model. Their associations were also observed after multivariate-adjustment. It would be only natural that being employed promoted and eye or ear disease interfered with outside activities, consistent with previous results.¹³⁾ However, the association of hypertension with increased frequency of outside activities was unexpected. Going to the hospital or walking for treatment may be one of a few reasons for women in this study area to go outside given their very low employment rate.

As for psychological status among our subjects, the fact that the proportions of mildly and severely depressive men were 43.4% and 3.8%, and 44.8% and 5.2% in women, respectively, is a grave situation. A high GDS score indicative of being more depressed was significantly and inversely associated with the frequency of engaging in outside activities in the age-adjusted model and was consistent with previous reports on the association of depression with being homebound.^{3,6,7,18,19)} Kono *et al.*¹²⁾ examined 112 Japanese frail elderly persons and reported that elderly people frequently engaging in outside activities often scored as less depressed than those going outdoors less often. We verified the association of depression with less engagement in outside activities even among elders living an independent life, although the association was diminished after multi-adjustment. The causal relationship between depression, outside activities and other factors is complex, and the pursuit of the causes of depression is beyond the scope of this study.

A large number of screening questionnaires are available to screen the elderly with functional decline and less psychosocial activity.²⁰⁻²⁴⁾ However, it is difficult to screen all elderly people in an administrative district since many of the questionnaires are lengthy and time consuming. When 7 categories of the frequency of engaging in outside activities were combined into 3 categories (more than 6–7 times a week, 2–5 times a week, once or less than once a week), the factors which were significantly associated with a high frequency of engaging in outside activities showed stepwise trends with the new categories in this order [the proportion of ‘Yes’; (Men; Meeting and talking often with friend: 90.0%, 61.9%, and 52.2%; Current alcohol consumption: 70.0%, 50.0%, and 39.1%; Easy access to public transportation: 60.5%, 32.5%, and 30.4%), (Women;

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Current employment: 30.8%, 10.3%, and 11.4%; History of hypertension: 55.2%, 31.9%, and 25.0%]. These results indicated the possibility that the frequency of engaging in outside activities may well serve as a simple, useful and comprehensive indicator even among the elderly living independently, particularly men. Kono et al.¹²⁾ suggested that the decreased frequency of engaging in outdoors may predict functional and psychological impairment among Japanese ambulatory but frail elderly. Thus, further study must be done on the association of the frequency of outside activities with the factors variously related to general condition of the elderly among different populations and in different areas by cross-sectional or longitudinal studies.

This study has several limitations. First, our data are cross-sectional and therefore can not prove a causal relationship between the frequency of engaging in outside activities and its related factors such as depression. Only easy access to public transportation may cause older people to leave home more frequently. Second, the subjects in this study comprised elderly persons living independently at home. Therefore, our results may not apply to those who have disabilities or require any care. Previous studies^{9,10)} on the subject including elderly people requiring care have reported an association of being homebound with functional and psychosocial factors but did not show gender differences. The gender differences observed in the present study may be specific to subjects living independently or our study area. Third, our study subjects were from a single cultural and geographic context, that is, residents of a rural Japanese community. Further studies should take the geographic characteristics into consideration.

Finally, in addition to the above-mentioned issues, we propose some problems with respect to the actual conditions among the elderly living an independent life. The proportion of homebound defined as leaving home once or less a week was 24.7% of the elderly living independently. Moreover, half of the subjects were depressed. Our study suggested that the frequency of engaging in outside activities among the elderly living independently is a useful and simple indicator for screening persons with psychosocial problems. Moreover, encouraging them to go out more often may improve their general health. However, these conclusions should be verified in a longitudinal study and tested by interventional trials with due consideration of gender and geographic differences.

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