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Does social participation increase the risk of influenza infection in older adults? : a cross-sectional study

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Title: **Does social participation increase the risk of influenza infection in older adults? : a cross-sectional study**

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ABSTRACT (276 words)

Objectives: Influenza infection can cause severe pneumonia, which is sometimes fatal, particularly in older adults. Social participation in the context of influenza infection is controversial because while social participation is beneficial in maintaining physical function and mental health, it also increases the risk of contact with infected people. The aim of this study is to examine the association between social participation and influenza infection in older adults.

Design: Cross-sectional study.

Setting: Japanese functionally independent adults aged 65 years or older.

Participants: 12,231 males and 14,091 females responded to the questions about influenza vaccination and influenza infection among the respondents of JAGES (Japan Gerontological Evaluation Study) 2013 survey from October through December 2013.

Outcome measures: We examined the association between social participation and influenza infection using data from the Japan Gerontological Evaluation Study (12,231 men and 14,091 women aged ≥65 years). The association between influenza infection and number of

groups in which respondents participated was investigated among elders aged ≥65 years stratified by vaccination status and sex.

Results: Unvaccinated female who participated in 2 or more social activities were 2.20 times (95% CI 1.47–3.29) as likely as those who reported no social participation to report an influenza infection. In contrast, vaccinated female who participated in 2 or more social groups had no additional risk of influenza infection as compared with female elders with no social participation. In male, participation in social activities was not significantly associated with an influenza infection regardless of vaccination status.

Conclusions: Social participation was associated with a higher risk of influenza infection among unvaccinated older female, which suggests a need for further efforts to promote influenza vaccination, particularly among socially active female elders.

ARTICLE SUMMARY

Strengths and limitations of this study

- The current study is the first to elucidate the association between social participation and influenza infection among elders even though social participation is highly recommended to older adults.
- Strength of the study lies the database from large scale social survey which we used has information of influenza infection, influenza vaccination, and social participation.
- The study is based on cross-sectional data, which does not allow determination of causal relationships between influenza infection and social participation.
- The current study has been done after stratifying by vaccination status because attitude to receiving influenza vaccination might be confounding with social behavior such as social participation.

Text:

INTRODUCTION

Influenza epidemics are estimated to result in 3 to 5 million cases of severe illness and about 250,000 to 500,000 deaths annually worldwide, [1] especially among older adults. [2-4] Older adults are vulnerable to influenza infection and development of secondary bacterial pneumonia due to complications of chronic conditions such as congestive heart failure and chronic obstructive pulmonary disease.[5] Influenza infection may also result in declines in major physical functions in frail elders. [6] Thus, influenza infection is one of the most important causes of death in an aging society.

Influenza infection is transmitted from person to person; thus, social contact might increase the risk of influenza infection.[7-10] However, social participation, which increases social contact, is beneficial for the physical and mental health of older adults.[11-13] To the best of our knowledge, no study has investigated the association between social participation and influenza infection among older adults.

Influenza vaccination must be considered in any study of the association between influenza infection and social participation among

older people aged ≥65 years. Influenza vaccination is recommended for older adults, to decrease the risk of preventable death, [1] even though the effectiveness of influenza vaccinations varies because the circulating type and subtype of the virus change every year, and because the influenza vaccine also must change to remain effective against the currently circulating strains. For elders in Japan, the vaccination fees are partly subsidized by the local government to increase vaccination coverage. Because social participation is positively associated with influenza vaccination, [14] the association between social participation and influenza infection might differ in relation to vaccination status. Also, contacting manner might be different in social participation between male and female. This study is the first to examine the association between social participation and influenza infection among elders stratified by influenza vaccination status and sex. In addition, we evaluated what type of social activity can affect more to influenza infection.

METHODS

Study population

This study used data from the Japan Gerontological Evaluation Study (JAGES) project, an ongoing prospective cohort study investigating social determinants of health among functionally independent adults aged 65 years or older. Several research studies have been done through this nationwide large scale project.[15 16] The cohort covers 30 municipalities in 13 prefectures in Japan. We used the 2013 wave of JAGES, in which questionnaires were mailed to a random sample of approximately 200,000 community-dwelling individuals aged 65 years and older from October through December 2013. Of those, 138,294 individuals responded to the survey (response rate, 70.8%). Aside from basic questions, there were five modules of the survey covering different topics. Module A covered nursing care, medical care, and life styles; module B assessed oral hygiene, optimism, and subjective health; module C covered social capital and history of abuse; module D evaluated subjective quality of life, sleep, and influenza infection; and module E assessed physical activity. We used module D, which includes questions about influenza vaccination and

influenza infection. Valid respondents to module D which comprised 12,231 males and 14,091 females were analyzed.

Influenza infection and vaccination

Influenza infection status was evaluated on the basis of participant response to a self-administered questionnaire. Respondents were asked, "Were you infected with influenza during the previous year? (yes, no)", to determine if they had been infected with influenza during the previous year. Vaccination status was also evaluated from the questionnaire. Respondents were asked, "Did you take influenza vaccination during the previous year? (yes, no)", to determine if they had been vaccinated during the previous year.

Social participation

Social participation was defined as the person's involvement in any social activities during the study period.[17] Respondents were asked how often they participated in volunteer groups, sport groups or clubs, leisure activity groups, senior citizen clubs, neighborhood associations, study or

cultural groups, nursing care prevention for health promotion groups, in teaching skills or passing on experiences to others, local events, protection for older people, assistance for older people, child-rearing support, local environment improvement activities, and other groups (frequency of participation: ≥4 times per week, 2-3 times per week, once a week, 1-3 times per month, several times per year, or never). We defined a participation frequency of at least 1-3 times per month as participation in a group, counted the number of groups in which the respondent participated, and categorized participation as 0, 1, or 2 or more groups.

Covariates

Physical health status, particularly the presence of respiratory disease, might be associated with social participation and influenza infection.[18 19] Self-rated health and respiratory disease as an underlying medical condition were assessed via questionnaire. Self-rated health was measured by the question, "What is your current health status? (excellent, good, fair, or poor)". We classified responses of excellent and good as "good" and responses of fair and poor as "not good". The presence of grandchildren

in the household, which might be associated with social participation and influenza infection, was ascertained via questionnaire. Socioeconomic status was considered as a possible confounder. Educational attainment was categorized as less than 6 years, 6-9 years, 10-12 years, more than 13 years, and other. Household income was equalized by the square root of the number of household members and classified as less than 1.99 million yen, 2-3.99 million yen, and more than 4 million yen. Age was categorized into 5 groups: 65-69 year-old, 70-74 year-old, 75-79 year-old, 80-84 year-old, and 85 year-old or older.

Analysis

Logistic regression analysis was used to examine the association between social participation and influenza infection, stratified by influenza vaccination status and sex. The interaction term between vaccination status and social participation was significantly associated with influenza infection. Also, the interaction term between sex and social participation was significantly associated with influenza infection. Possible confounding factors including age, self-rated health, underlying respiratory disease,

living with grandchildren, educational attainment and equivalent income were adjusted.

Additional analysis

To determine whether certain types of social activity were more likely to result in influenza infection, we set participation in each activity (volunteer groups, sport group or clubs, leisure activity groups, senior citizen clubs, neighborhood associations, study or cultural groups, nursing care prevention for health promotion, teaching skills or passing on experiences to others, local events, protection for older people, assistance for older people, child-rearing support, local environment improvement, and other group) as an explanatory variable, instead of participation in any social activity, which resulted in more than 15 models. The odds ratios (ORs) for influenza infection were calculated in relation to participation in each activity, stratified by vaccination status and by sex. All analyses were performed using STATA SE version 13 (StataCorp, College Station, TX, USA).

Ethical considerations

The questionnaire and an explanation of the study were sent to the participants by mail. The participants were informed that participation was voluntary and that returning the self-administered questionnaire would be interpreted as implying consent. Ethical approval for the study was obtained from the Ethics Committee at Nihon Fukushi University.

RESULTS

The characteristics of the study sample, stratified by vaccination status and by sex, are shown in Table 1. The vaccinated group was older than the unvaccinated group in male and female, respectively. Approximately one-third of vaccinated male (29.1%) and vaccinated (33.3%)/unvaccinated (28.4%) female participated in 2 or more groups, while less than one-fourth (22.6%) of unvaccinated male participated in 2 or more groups. A total of 355 cases (5.5%) and 372 cases (4.2%) of influenza infection were observed among vaccinated male and female, respectively, while 136 cases (2.4%) and 124 (2.3%) were observed in the unvaccinated male and female, respectively. The proportion of respondents with respiratory diseases was higher among vaccinated elders (7.6% in male and 5.0% in female) than among unvaccinated elders (4.0% in male and 3.4% in female). Vaccinated elders were more likely than unvaccinated elders to live with grandchildren (16.2% vs 11.2% in male and 21.1% vs 13.3% in female). The results of logistic analysis of influenza infection in respondents stratified by influenza vaccination status and by sex are shown in Table 2. Overall, unvaccinated female who participated in 2 or more

social activities were 2.20 times as likely as to develop influenza as unvaccinated females who did not participate in such activities (OR, 2.20; 95% confidence interval [CI], 1.47–3.29) after adjustment for age, self-rated health, presence of respiratory disease, living with grandchildren and socioeconomic status (educational attainment and equivalent income). However, among vaccinated females, social participation was not associated with influenza infection after adjustment (OR, 1.06; 95% CI, 0.83–1.36). In male, no significant association was found between social participation and influenza infection in both of the vaccinated and unvaccinated group. Participation in 1 group was not associated with influenza infection in either group. In male, presence of respiratory disease was significant factor to develop influenza infection in both of the vaccinated and unvaccinated group. Also in unvaccinated female, this was significantly associated with influenza infection. In female, poor self-rated health was significant factor in relation to influenza infection.

Table 1. Characteristics of vaccinated and unvaccinated elders stratified by sex

		Male N=12,231					Female N=14,091				
		Vaccinated N=6,502		Unvaccinated N=5,729			Vaccinated N=8,801		Unvaccinated N=5,290		
Variables		N	%	N	%	P†	N	%	N	%	P†
Age, years old	65-69	1,438	(22.1%)	2,067	(36.1%)		1,916	(21.8%)	1,876	(35.5%)	
	70-74	1,845	(28.4%)	1,776	(31.0%)		2,663	(30.3%)	1,578	(29.8%)	
	75-79	1,658	(25.5%)	1,030	(18.0%)		2,163	(24.6%)	989	(18.7%)	
	80-84	1,067	(16.4%)	580	(10.1%)		1,376	(15.6%)	526	(9.9%)	
	85<	494	(7.6%)	276	(4.8%)	**<0.001**	683	(7.8%)	321	(6.1%)	**<0.001**
Participation to social activity	None	3,391	(52.2%)	3,408	(59.5%)		4,058	(46.1%)	2,813	(53.2%)	
	One	1,219	(18.7%)	1,026	(17.9%)		1,812	(20.6%)	974	(18.4%)	
	Two or more	1,892	(29.1%)	1,295	(22.6%)	**<0.001**	2,931	(33.3%)	1,503	(28.4%)	**<0.001**

Influenza infection within a year	Not infected	6,147	(94.5%)	5,593	(97.6%)		8,429	(95.2%)	5,166	(97.7%)	
	Infected	355	(5.5%)	136	(2.4%)	**<0.001**	372	(4.2%)	124	(2.3%)	**<0.001**
Self rated health	Unhealthy	4,972	(76.5%)	4,494	(78.4%)		6,911	(78.0%)	4,227	(79.9%)	
	Healthy	1,328	(20.4%)	1,036	(18.1%)		1,558	(17.6%)	824	(15.6%)	
	Missing	202	(3.1%)	199	(3.5%)	**0.003**	332	(3.8%)	239	(4.5%)	**0.001**
Any respiratory disease	No	6,009	(92.4%)	5,500	(96.0%)		8,357	(95.2%)	5,111	(96.6%)	
	Yes	493	(7.6%)	229	(4.0%)	**<0.001**	444	(5.1%)	179	(3.4%)	**<0.001**
Living with grandchild	No	5,447	(83.8%)	5,088	(88.8%)		6,948	(78.8%)	4,587	(86.7%)	
	Yes	1,055	(16.2%)	641	(11.2%)	**<0.001**	1,853	(21.1%)	703	(13.3%)	**<0.001**
Educational attainment, years	6>	89	(1.4%)	72	(1.3%)		195	(2.2%)	113	(2.1%)	
	6 - 9	2,431	(37.4%)	2,115	(36.9%)		3,847	(43.7%)	2,111	(39.9%)	
	10 - 12	2,271	(34.9%)	1,970	(34.4%)		3,308	(37.6%)	2,045	(38.7%)	
	13<	1,602	(24.6%)	1,446	(25.2%)		1,243	(14.1%)	834	(15.8%)	
	Others	40	(0.6%)	39	(0.7%)		51	(0.6%)	40	(0.8%)	
	Missing	69	(1.1%)	87	(1.5%)	0.296	157	(1.8%)	147	(2.8%)	**<0.001**
Equivalent income (million yen)	Low (-1.99)	2,875	(44.2%)	2,418	(42.2%)		3,595	(40.8%)	2,111	(39.9%)	
	Middle	2,222	(34.2%)	1,749	(30.5%)		2,421	(27.5%)	1,304	(24.7%)	

	(2-3.99)									
	High (4-)	654	(10.1%)	462	(8.1%)		692	(7.9%)	353	(6.7%)	
	Missing	751	(11.6%)	1,100	(19.2%)	**<0.001**	2,093	(23.8%)	1,522	(28.8%)	**<0.001**

† Chi-square test

Table 2. Risk of influenza infection in male and female stratified by influenza vaccination status

Variables		Male				Female			
		Unvaccinated		Vaccinated		Unvaccinated		Vaccinated	
		OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Participation in social activities (no. of groups)	None	Reference		Reference		Reference		Reference	
	One	0.94	(0.58-1.53)	1.02	(0.76-1.37)	0.95	(0.54-1.67)	1.14	(0.86-1.50)
	Two or more	1.27	(0.85-1.91)	1.08	(0.84-1.39)	**2.20**	**(1.47-3.29)**	1.06	(0.83-1.36)
Age, years	65-69	Reference		Reference		Reference		Reference	
	70-74	0.80	(0.53-1.22)	1.15	(0.85-1.56)	0.39	(0.24-0.63)	0.94	(0.71-1.25)
	75-79	0.98	(0.61-1.58)	0.94	(0.68-1.30)	0.54	(0.32-0.91)	0.84	(0.62-1.14)
	80-84	0.69	(0.35-1.35)	0.95	(0.66-1.36)	0.60	(0.31-1.17)	0.54	(0.37-0.80)
	85<	0.69	(0.27-1.76)	0.81	(0.50-1.31)	-		0.62	(0.38-1.00)
Self rated health	Good	Reference		Reference		Reference		Reference	
	Not good	0.80	(0.49-1.31)	0.98	(0.74-1.29)	**1.80**	**(1.12-2.87)**	**1.49**	**(1.15-1.92)**
	Missing	1.41	(0.60-3.29)	1.54	(0.92-2.59)	1.06	(0.38-2.93)	1.59	(0.98-2.59)
Respiratory disease	None	Reference		Reference		Reference		Reference	
	Any	**2.44**	**(1.28-4.68**	**1.94**	**(1.40-2.71**	1.14	(0.45-2.87)	**1.89**	**(1.31-2.73)**

		)		)			
Living with grandchildren	No	Reference		Reference		Reference	Reference
	Yes	1.56	(0.97-2.49)	1.21	(0.92-1.60)	0.91	(0.51-1.61)	0.98	(0.75-1.28)
Educational attainment, years	6>	Reference		Reference		Reference	Reference
	6 - 9	0.38	(0.11-1.29)	0.87	(0.37-2.04)	1.30	(0.17-9.76)	0.90	(0.43-1.89)
	10 - 12	0.58	(0.17-1.96)	0.73	(0.31-1.75)	1.20	(0.19-9.14)	0.77	(0.36-1.64)
	13<	0.39	(0.11-1.36)	0.80	(0.33-1.91)	1.03	(0.14-8.14)	0.74	(0.33-1.64)
	Others	1.07	(0.17-6.86)	1.20	(0.28-5.11)	1.86	(0.11-31.34)	0.75	(0.15-3.68)
	Missing	0.26	(0.03-2.57)	0.84	(0.23-3.14)	0.57	(0.03-9.36)	1.09	(0.39-3.01)
Equivalent income (million yen)	Low (-199)	Reference		Reference		Reference	Reference
	Middle (200-399)	0.87	(0.58-1.31)	0.87	(0.68-1.12)	1.09	(0.72-1.67)	1.09	(0.84-1.41)
	High (400-)	1.17	(0.65-2.11)	0.67	(0.43-1.03)	0.58	(0.25-1.39)	0.79	(0.50-1.25)
	Missing	0.66	(0.39-1.12)	1.17	(0.84-1.62)	0.62	(0.37-1.03)	0.94	(0.71-1.24)
Constant		0.06	(0.02-0.19)	0.07	(0.03-0.16)	0.02	(0-0.19)	0.05	(0.02-0.12)

In the analysis of the associations of participation in particular groups with influenza infection, social participation was not associated with influenza infection among vaccinated elders both in male and female except only participation in a "senior citizen club" or "neighborhood association" in males (OR, 1.56; 95% CI, 1.12–2.17; and OR, 1.54; 95% CI, 1.13–2.12; respectively; Fig. 1A). In contrast, among unvaccinated males, participation in 4 of 14 activities were significantly associated with influenza infection (namely, participation in a volunteer group, sports group or club, protection for older people, and assistance for older people). In unvaccinated female, 7 of 14 activities were significantly associated with influenza infection (namely, participation in a leisure activity group, senior citizen club, neighborhood association, nursing care prevention of health-building, protection for older people, assistance for older people, and other group).

DISCUSSION

We found that social participation was positively associated with influenza infection among unvaccinated older females, but not among vaccinated elders and unvaccinated males, in Japan. Previous research on social participation showed wide-ranging health benefits for older adults. Older adults who participate in social activities have better self-rated health[11], have lower risks of disability, functional and mobility decline, depression and generalized anxiety disorders, cognitive decline, and dementia[20-25], and even longer life[12]. However, no study has investigated the risk of communicable diseases associated with social participation. In this study, we found that the risk of influenza infection was higher for unvaccinated elders, specifically in female, than for vaccinated elders, which indicates influenza vaccination might be effective to prevent influenza infection in active older adults, thus, suggests an urgent need for additional efforts to promote influenza vaccination among socially active elders especially in female.

In an analysis of real upper respiratory viruses, such as rhinovirus, in a quarantine setting, Cohen *et al.* found that individuals with diverse

social networks had greater resistance to upper respiratory illnesses due to unknown mechanism.[26] It is speculated that an immune status may operate as pathways, i.e. behavioral effects on the release of cytokines in the nasal passage. Similarly, building a social network through group activities might prevent virus infection. However, frequent contact with infected persons could result in infection even among people with robust social networks. In our study, we found that the OR for influenza infection was not higher among vaccinated elders when the chance of contact increases. For respiratory infectious agents other than influenza virus, vaccines, when available, might help prevent transmission, as is the case for the pneumococcal vaccine.[27] However, when no vaccine is available, other non-pharmaceutical interventions, such as respiratory hygiene and cough etiquette, [28 29] may be effective preventive measures. Further study of other infections is needed.

In this study, participation in social activities did not increase the risk of influenza infection among elders who took influenza vaccination, even after adjustment for confounding factors. In general, influenza vaccines provide protection against influenza infection.[30 31] Several other studies

reported that vaccination reduced hospitalizations and deaths in older adults.[32-34] Our results also support such vaccine effectiveness, but only in female. In Japan, influenza vaccination is recommended in elders aged 65 or older, [31 35] and the vaccination fees are partly subsidized by the local government. However, vaccine effectiveness varies by season, virus type, and recipient age.[36] Protection is sometimes greatly reduced or absent, especially in older adults. [37] This study is one of few evidences which showed positive effectiveness of influenza vaccination in older adults.

We stratified respondents by vaccination status because it may modify the association between social participation and influenza infection. Older people who participate in 2 or more groups are more likely to be vaccinated than are those who do not participate in such activities. It is believed that elders who participate in social activities have good access to health information, including how and where they can receive influenza vaccinations.[38-40] Gathering for any group activity means sharing information in participant interests, such as health information, even when the aim of the activity may not be directly related to such interests. In addition, socially active persons have better medical access, which includes

vaccinations and consultation with physicians.[38] This suggests that social persons who participate in groups are more likely than nonsocial persons to see a doctor when they develop a fever, especially in Japan, where medical resources are accessible to the entire population.

We also stratified respondents by sex. There are evidences that female typically develop higher antibody responses following vaccination than males.[41] Such differences are observed in response to various vaccines including influenza vaccine.[42 43] This might be one of the possible reasons for appearing different result by sex in this study. Behavioral difference between male and female might be also one of the reasons. Female tend to talk much when people gather than in male. Higher risk for influenza infection was shown only in female who participates two or more groups, but in unvaccinated ones, rather than in male.

The risk of influenza infection varied in relation to the type of social activity and by sex, but most activities significantly increased infection risk in the unvaccinated group. Participation in a volunteer group, sport group or club, protection for older people, or assistance for older people was associated with increased risk for infection among unvaccinated males.

Perhaps because these groups may have chance to contact closely and participants have much chance to be infected.[14] Differently in unvaccinated females, participation in a leisure activity group, senior citizen club, neighborhood association, nursing care prevention of health-building, protection for older people, assistance for older people, or other was associated with higher risk for influenza infection. These sex difference may be caused by behavioral characteristics in male or female. As we discussed above, female talks much more than male does when people gather, thus virus transmission can be easily occurred in female rather than in male. Transmission of the influenza virus between humans is mainly by respiratory droplets, although airborne transmission is also possible.[44 45] Thus, activities with fewer opportunities for conversation and direct contact have less infection risk. Similarly, the risk of transmission is higher for larger groups.[45 46] In contrast, the risk associated with group participation was low for vaccinated males, except for participation in a senior citizen group or neighborhood association. We speculate that speaking is the main activity in these groups and that these groups are large; thus, viral transmission is more likely to occur among the participants, however it is

unclear the reason why no significant increased risk of infection was shown in unvaccinated male who participate senior citizen club or neighborhood association. An effect of vaccination may be enhanced especially in a setting where close and frequent contacts occur as like in groups for sports, assistance for older people, or protection for older people. In such groups, discrepancy of odds ratio of influenza infection was clear between vaccinated and unvaccinated. In our study, group size and the number of people gathered were unknown. Further study is needed to determine why the risk of infection varied by group type and by sex.

Our study has several limitations. First, because this study is cross-sectional, causality cannot be inferred. A longitudinal study or randomized controlled trial is needed to prove a causal relationship between social participation and influenza infection. Second, diagnosis of influenza infection was based on self-reports rather than on the results of laboratory testing. However, in Japan commercial rapid diagnostic test kits are commonly used in clinical settings such as outpatient clinics. These kits have high sensitivity and specificity in the diagnosis of influenza infection.[47] [48] In addition, medical access is good because of the universal health

insurance system in Japan.[49] Older adults with an influenza-like illness in Japan are generally tested with rapid diagnostic tests with high sensitivity and high specificity.[47 50] Third, vaccination history was also self-reported. Fourth, previous influenza infection was not assessed.

In conclusion, social participation increased the risk of influenza infection among unvaccinated elders specifically in female, which suggests a need for greater efforts to encourage influenza vaccination among socially active elders.

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CONTRIBUTORSHIP STATEMENT

All authors meet the ICMJE criteria for authorship. YS and TK contributed to design this research. YS performed statistical analysis, and drafted the manuscript. TK advised on the analysis and interpretation. RS, KK, and TK

revised the manuscript. KK is the principal investigator of the JAGES project. AT helped to develop the idea of the study. All authors read and approved the final manuscript.

DECLARATION OF COMPETING INTERESTS

We have read and understood BMJ policy on declaration of interests and declare that we have no competing interests.

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No additional data available.

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Figure legends

Figure 1. Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among vaccinated male, unvaccinated male, vaccinated female and unvaccinated female.

The logistic regression adjusted for age, self-rated health, respiratory disease, living with grandchildren, and socioeconomic status. The odds ratios for influenza infection (95% confidence interval) are shown for vaccinated male (Figure 1A), unvaccinated male (Figure 1B), vaccinated

female (Figure 1C) and unvaccinated female (Figure 1D).

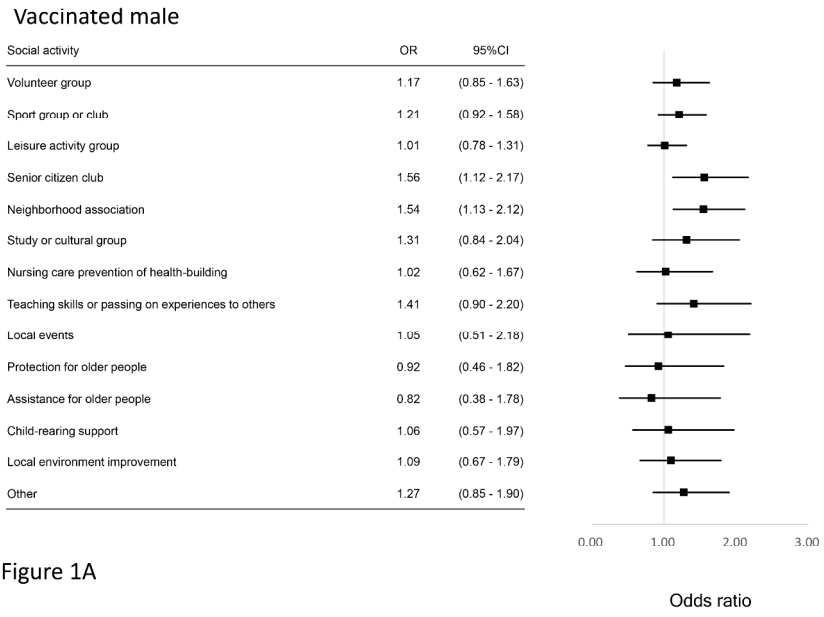

Figure 1A

Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among vaccinated male, unvaccinated male, vaccinated female and unvaccinated female. The logistic regression adjusted for age, self-rated health, respiratory disease, living with grandchildren, and socioeconomic status. The odds ratios for influenza infection (95% confidence interval) are shown for vaccinated male (Figure 1A), unvaccinated male (Figure 1B), vaccinated female (Figure 1C) and unvaccinated female (Figure 1D).

355x266mm (300 x 300 DPI)

Unvaccinated male

Social activity	OR	95%CI
Volunteer group	1.88	(1.14 - 3.11)
Sport group or club	1.98	(1.31 – 3.00)
Leisure activity group	0.98	(0.64 - 1.50)
Senior citizen club	1.76	(0.95 - 3.28)
Neighborhood association	1.26	(0.72 - 2.19)
Study or cultural group	1.68	(0.83 - 3.40)
Nursing care prevention of health-building	1.94	(0.92 - 4.07)
Teaching skills or passing on experiences to others	1.87	(0.98 - 3.57)
Local events	2.24	(0.95 - 5.25)
Protection for older people	2.40	(1.03 - 5.63)
Assistance for older people	2.88	(1.22 - 6.77)
Child-rearing support	1.55	(0.61 - 3.91)
Local environment improvement	1.68	(0.86 - 3.26)
Other	1.37	(0.76 - 2.49)

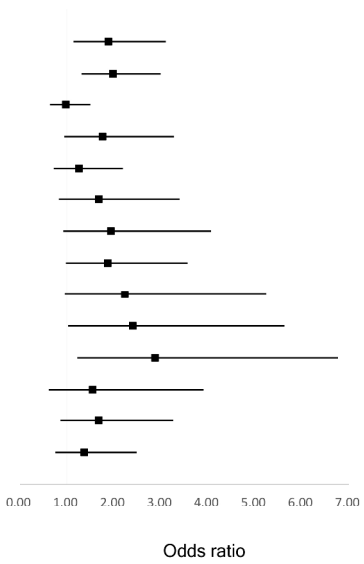

Figure 1B

355x266mm (300 x 300 DPI)

Vaccinated female

Social activity	OR	95%CI
Volunteer group	0.88	(0.61 - 1.28)
Sport group or club	1.07	(0.82 - 1.39)
Leisure activity group	1.05	(0.83 - 1.34)
Senior citizen club	1.05	(0.73 - 1.50)
Neighborhood association	1.18	(0.79 - 1.78)
Study or cultural group	0.93	(0.64 - 1.35)
Nursing care prevention of health-building	1.27	(0.91 - 1.78)
Teaching skills or passing on experiences to others	0.77	(0.44 - 1.37)
Local events	1.40	(0.64 - 3.05)
Protection for older people	0.61	(0.31 - 1.20)
Assistance for older people	1.04	(0.58 - 1.84)
Child-rearing support	1.13	(0.62 - 2.06)
Local environment improvement	1.24	(0.75 - 2.06)
Other	1.23	(0.80 - 1.91)

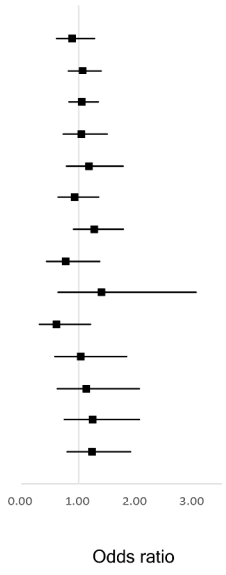

Figure 1C

355x266mm (300 x 300 DPI)

Unvaccinated female

Social activity	OR	95%CI
Volunteer group	1.52	(0.89 - 2.57)
Sport group or club	1.46	(0.95 - 2.26)
Leisure activity group	1.65	(1.12 - 2.45)
Senior citizen club	2.59	(1.46 - 4.58)
Neighborhood association	1.85	(1.01 - 3.37)
Study or cultural group	1.45	(0.82 - 2.57)
Nursing care prevention of health-building	2.05	(1.16 - 3.61)
Teaching skills or passing on experiences to others	1.04	(0.47 - 2.29)
Local events	1.62	(0.49 - 5.27)
Protection for older people	2.28	(1.15 - 4.48)
Assistance for older people	2.66	(1.34 - 5.28)
Child-rearing support	1.08	(0.43 - 2.73)
Local environment improvement	1.69	(0.77 - 3.73)
Other	2.07	(1.17 - 3.67)

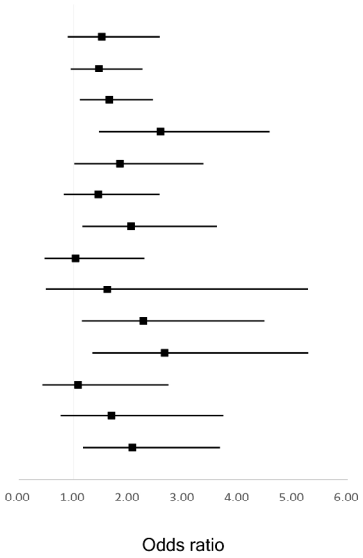

Figure 1D

355x266mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1✓	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
	P3-4	(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2✓ P6-7	Explain the scientific background and rationale for the investigation being reported
Objectives	3✓ P7-8	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4✓ P9	Present key elements of study design early in the paper
Setting	5✓ P8-9	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6✓ P9	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7✓ P9-11	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*✓ P9-11	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9✓ P10	Describe any efforts to address potential sources of bias
Study size	10✓ P9	Explain how the study size was arrived at
Quantitative variables	11✓ P9-11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12✓ P12-13i	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*✓ P14	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*✓ P14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*✓ P14	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16✓ P14-15	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17✓ P23	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18✓ P24	Summarise key results with reference to study objectives
Limitations	19✓ P28-29	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20✓ P24-27	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21✓ P25	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Social participation and risk of influenza infection in older adults: A cross-sectional study

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology, Infectious diseases, Respiratory medicine
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Title: **Social participation and risk of influenza infection in older adults: A cross-sectional study**

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ABSTRACT (296 words)

Objectives: Influenza infection can cause severe pneumonia, which is sometimes fatal, particularly in older adults. Influenza results in 3 to 5 million cases of severe illness and about 250,000 to 500,000 deaths annually worldwide. Social participation in the context of influenza infection is controversial because, although social participation is beneficial in maintaining physical function and mental health, it also increases the risk of contact with infected people. This study examined the association between social participation and influenza infection in Japanese adults aged 65 years or older.

Design: Cross-sectional study.

Setting: Japanese functionally independent adults aged 65 years or older.

Participants: Among the respondents to the Japan Gerontological Evaluation Study (JAGES) 2013 survey, which took place during the period from October through December 2013, 12,231 men and 14,091 women responded to questions on influenza vaccination and influenza infection.

Outcome measures: Using JAGES data for 12,231 men and 14,091 women aged ≥65 years, we examined the association between social

participation and influenza infection. The association between influenza infection and number of groups in which respondents participated was investigated among adults aged ≥65 years, stratified by vaccination status and sex.

Results: Unvaccinated women who participated in 2 or more social activities were 2.20 times (95% CI 1.47–3.29) as likely to report an influenza infection as those who reported no social participation. In contrast, vaccinated women who participated in 2 or more social groups had no additional risk of influenza infection as compared with female elders with no social participation. Among men, participation in social activities was not significantly associated with influenza infection, regardless of vaccination status.

Conclusions: Social participation was associated with a higher risk of influenza infection among unvaccinated older women, which suggests a need for further efforts to promote influenza vaccination, particularly among socially active elderly women.

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ARTICLE SUMMARY

Strengths and limitations of this study

- Although social participation is highly recommended for older adults, this study is the first to examine the association between social participation and influenza infection among this population.
- A strength of this study is that it used data from a large-scale social survey, which yielded information on influenza infection, influenza vaccination status, and social participation.
- The study is based on cross-sectional data, which does not allow determination of causal relationships between influenza infection and social participation.

INTRODUCTION

Influenza epidemics are estimated to result in 3 to 5 million cases of severe illness and about 250,000 to 500,000 deaths annually worldwide.[1] Older adults are disproportionally affected,[2-4] as they are vulnerable to influenza infection and development of secondary bacterial pneumonia due to complications of chronic conditions such as congestive heart failure and chronic obstructive pulmonary disease.[5] Influenza infection may also result in declines in critical physical functions in frail elders. [6] Influenza infection is thus one of the most important causes of death in an aging society.

Influenza infection is transmitted from person to person; therefore, social contact increases the risk of influenza infection.[7-10] However, social participation, which increases social contact, is beneficial for the physical and mental health of older adults.[11-13] Previous research on social participation showed wide-ranging health benefits for older adults. Older adults who participate in social activities have better self-rated health,[11] lower risks of disability, functional decline, mobility decline, depression, generalized anxiety disorders, cognitive decline, and dementia[14-19], and longer lifespans[12]. To our knowledge, no study has investigated the

association between social participation and influenza infection among older adults.

Influenza vaccination status must be considered in any study of the association between influenza infection and social participation among adults aged ≥65 years. Influenza vaccination is recommended for older adults,[20 21] as it decreases the risk of preventable death.[1] For elders in Japan, vaccination fees are partly subsidized by the local government, to increase vaccination coverage.[14 15] The influenza vaccine must be altered to remain effective against currently circulating strains. The effectiveness of influenza vaccinations varies because the circulating type and subtype of the virus change every year. Thus, protection is sometimes greatly reduced or absent, especially in older adults.[22] This study is one of the few to show the effectiveness of influenza vaccination in older adults. Because social participation is positively associated with influenza vaccination,[23] the association between social participation and influenza infection might vary in relation to vaccination status. In addition, modes of contact during social participation might differ between men and women.

The Japan Gerontological Evaluation Study (JAGES) project is one of

the largest cohort studies of social determinants of health among Japanese adults aged ≥65 years. This study used part of the 2013 wave data from the 138,294 respondents to the survey (response rate, 70.8%). This study is the first to examine the association between social participation and influenza infection among elders stratified by influenza vaccination status and sex. In addition, we attempted to identify social activities that were associated with influenza infection.

METHODS

Study population

This study used data from the JAGES project, an ongoing prospective cohort study of the social determinants of health among functionally independent adults aged ≥65 years. Several studies have utilized data from this large-scale nationwide project.[24 25] The cohort covers 30 municipalities in 13 prefectures in Japan. We used the 2013 wave of JAGES, in which questionnaires were mailed to a random sample of approximately 200,000 community-dwelling individuals aged 65 years and older from October through December 2013. In addition to the basic items, 5 survey modules covered a variety of other topics. Module A covered nursing care, medical care, and lifestyle; module B assessed oral hygiene, optimism, and subjective health; module C covered social capital and history of abuse; module D evaluated subjective quality of life, sleep, and influenza infection; and module E assessed physical activity. We used module D, which included questions on influenza vaccination and influenza infection. All valid responses (from 12,231 men and 14,091 women) to module D were analyzed.

Influenza infection and vaccination

Influenza infection status was determined by participant response to a self-administered questionnaire. To determine influenza infection status, respondents were asked, "Were you infected with influenza during the previous year? (yes, no)". Vaccination status was evaluated by asking respondents, "Did you receive an influenza vaccination during the previous year? (yes, no)".

Social participation

Social participation was defined as involvement in any social activity during the study period.[26] Respondents were asked how often they took part in volunteer groups, sport groups or clubs, leisure activity groups, senior citizen clubs, neighborhood associations, study or cultural groups, nursing care prevention for health promotion groups, in teaching skills or passing on experiences to others, local events, protection for older people, assistance for older people, child-rearing support, local environment improvement activities, and other groups (frequency of participation: ≥4

times per week, 2-3 times per week, once a week, 1-3 times per month, several times per year, or never). We defined a participation frequency of at least 1-3 times per month as participation in a group, counted the number of groups in which the respondent participated, and categorized participation as 0, 1, or ≥2 groups.

Covariates

Physical health status, particularly presence of respiratory disease, might be associated with social participation and influenza infection.[27 28] Self-rated health and respiratory disease as an underlying medical condition were assessed via questionnaire. Self-rated health was assessed by the question, "What is your current health status? (excellent, good, fair, or poor)". Responses of excellent and good were classified as "good" and responses of fair and poor as "not good". Presence of grandchildren in the household, which might be associated with social participation and influenza infection, was ascertained via questionnaire. Socioeconomic status was analyzed as a possible confounder. Educational attainment was categorized as <6 years, 6-9 years, 10-12 years, ≥13 years, and other.

Household income was equalized by the square root of the number of household members and classified as <1.99 million yen, 2-3.99 million yen, and >4 million yen. Age was categorized into 5 groups: 65-69, 70-74, 75-79, 80-84, and ≥85 years.

Analysis

Logistic regression analysis was used to examine the association between social participation and influenza infection. When an interaction term between a factor and social participation was significantly associated with influenza infection, analyses were done after stratifying respondents by that factor. We adjusted for the possible confounding factors age, self-rated health, underlying respiratory disease, living with grandchildren, educational attainment, and equivalent income.

Additional analysis

To determine whether certain types of social activity were more likely to result in influenza infection, we set participation in each activity as an explanatory variable, instead of participation in any social activity, and

this yielded more than 15 models. Data from respondents who participated in 1 or more group activities were analyzed. Number of participating activities was included as a covariate, to measure the effect of participating in each activity. Odds ratios (ORs) for influenza infection were calculated in relation to participation in each activity, stratified by vaccination status and sex. All analyses were performed with STATA SE version 13 (StataCorp, College Station, TX, USA).

Ethical considerations

The questionnaire and an explanation of the study were sent to participants by mail. The recipients were informed that participation was voluntary and that returning the self-administered questionnaire would be interpreted as consent to participate. Ethical approval for the study was obtained from the Ethics Committee at Nihon Fukushi University.

RESULTS

The interaction term between vaccination status and social participation was significantly associated with influenza infection, as was the interaction term between sex and social participation. Thus, all analyses of the groups were stratified by vaccination status and sex. The characteristics of the study sample, stratified by vaccination status and by sex, are shown in Table 1. The vaccinated group was older than the unvaccinated group, and this was true for men and women. In particular, 49.5% of vaccinated men and 32.9% of unvaccinated men were 75 years or older; the respective values were 48.0% and 34.7% for women. Approximately one-third of vaccinated men (29.1%) and vaccinated (33.3%) women participated in 2 or more groups, while less than one-fourth (22.6%) of unvaccinated men participated in 2 or more groups.

A total of 355 cases (5.5%) and 372 cases (4.2%) of influenza infection were observed among vaccinated men and women, respectively, and 136 cases (2.4%) and 124 cases (2.3%) of influenza infection were observed in unvaccinated men and women, respectively. The proportion of respondents with respiratory diseases was higher among vaccinated elders

(7.6% in men and 5.0% in women, P<0.001) than among unvaccinated elders (4.0% in men and 3.4% in women, P<0.001). Vaccinated elders were more likely than unvaccinated elders to live with grandchildren (men: 16.2% vs 11.2%, P<0.001; women: 21.1% vs 13.3%, P<0.001).

Table 2 shows the results of logistic analysis of influenza infection in respondents stratified by influenza vaccination status and sex. Overall, unvaccinated women who participated in 2 or more social activities were more likely to develop influenza than were unvaccinated women who did not participate in such activities (OR, 2.20; 95% confidence interval [CI], 1.47–3.29), after adjustment for age, self-rated health, presence of respiratory disease, living with grandchildren, and socioeconomic status (educational attainment and equivalent income). However, among vaccinated women, social participation in 2 or more activities was not associated with influenza infection after adjustment (OR, 1.06; 95% CI, 0.83-1.36). Social participation was not associated with influenza infection among vaccinated or unvaccinated men. Participation in 1 group was not associated with influenza infection in either group. Presence of respiratory disease was significantly associated with influenza infection among

vaccinated men (OR, 1.94; 95% CI, 1.40–2.71), unvaccinated men (OR, 2.44; 95% CI, 1.28–4.68), and vaccinated women (OR, 1.89; 95% CI, 1.31–2.73). Poor self-rated health was significantly associated with influenza infection in vaccinated (OR, 1.49; 95% CI, 1.15–1.92) and unvaccinated women (OR, 1.80; 95% CI, 1.12–2.87).

Table 1. Characteristics of vaccinated and unvaccinated elders stratified by sex

		Men N=12,231					Women N=14,091				
		Vaccinated N=6,502		Unvaccinated N=5,729			Vaccinated N=8,801		Unvaccinated N=5,290		
Variables		N	%	N	%	P†	N	%	N	%	P†
Age, years	65-69	1,438	(22.1%)	2,067	(36.1%)		1,916	(21.8%)	1,876	(35.5%)	
	70-74	1,845	(28.4%)	1,776	(31.0%)		2,663	(30.3%)	1,578	(29.8%)	
	75-79	1,658	(25.5%)	1,030	(18.0%)		2,163	(24.6%)	989	(18.7%)	
	80-84	1,067	(16.4%)	580	(10.1%)		1,376	(15.6%)	526	(9.9%)	
	85<	494	(7.6%)	276	(4.8%)	**<0.001**	683	(7.8%)	321	(6.1%)	**<0.001**
Participation in social activity, no.	0	3,391	(52.2%)	3,408	(59.5%)		4,058	(46.1%)	2,813	(53.2%)	
	1	1,219	(18.7%)	1,026	(17.9%)		1,812	(20.6%)	974	(18.4%)	
	≥2	1,892	(29.1%)	1,295	(22.6%)	**<0.001**	2,931	(33.3%)	1,503	(28.4%)	**<0.001**
Influenza infection in past year	Not infected	6,147	(94.5%)	5,593	(97.6%)		8,429	(95.8%)	5,166	(97.7%)	
	Infected	355	(5.5%)	136	(2.4%)	**<0.001**	372	(4.2%)	124	(2.3%)	**<0.001**

Self-rated health	Good	4,972	(76.5%)	4,494	(78.4%)		6,911	(78.5%)	4,227	(79.9%)	
	Not good	1,328	(20.4%)	1,036	(18.1%)		1,558	(17.7%)	824	(15.6%)	
	Missing	202	(3.1%)	199	(3.5%)	**0.003**	332	(3.8%)	239	(4.5%)	**0.001**
Any respiratory disease	No	6,009	(92.4%)	5,500	(96.0%)		8,357	(95.0%)	5,111	(96.6%)	
	Yes	493	(7.6%)	229	(4.0%)	**<0.001**	444	(5.0%)	179	(3.4%)	**<0.001**
Living with grandchild	No	5,447	(83.8%)	5,088	(88.8%)		6,948	(78.9%)	4,587	(86.7%)	
	Yes	1,055	(16.2%)	641	(11.2%)	**<0.001**	1,853	(21.1%)	703	(13.3%)	**<0.001**
Educational attainment, years	6>	89	(1.4%)	72	(1.3%)		195	(2.2%)	113	(2.1%)	
	6 - 9	2,431	(37.4%)	2,115	(36.9%)		3,847	(43.7%)	2,111	(39.9%)	
	10 - 12	2,271	(34.9%)	1,970	(34.4%)		3,308	(37.6%)	2,045	(38.7%)	
	13<	1,602	(24.6%)	1,446	(25.2%)		1,243	(14.1%)	834	(15.8%)	
	Others	40	(0.6%)	39	(0.7%)		51	(0.6%)	40	(0.8%)	
	Missing	69	(1.1%)	87	(1.5%)	0.296	157	(1.8%)	147	(2.8%)	**<0.001**
Equivalent income (million yen)	Low (-1.99)	2,875	(44.2%)	2,418	(42.2%)		3,595	(40.8%)	2,111	(39.9%)	
	Middle (2-3.99)	2,222	(34.2%)	1,749	(30.5%)		2,421	(27.5%)	1,304	(24.7%)	
	High (4-)	654	(10.1%)	462	(8.1%)		692	(7.9%)	353	(6.7%)	
	Missing	751	(11.6%)	1,100	(19.2%)	**<0.001**	2,093	(23.8%)	1,522	(28.8%)	**<0.001**

† Chi-square test

Table 2. Risk of influenza infection in men and women stratified by influenza vaccination status

Variables		Men				Women			
		Vaccinated		Unvaccinated		Vaccinated		Unvaccinated	
		OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Participation in social activities (no. of groups)	0	Reference		Reference		Reference		Reference	
	1	1.02	(0.76-1.37)	0.94	(0.58-1.53)	1.14	(0.86-1.50)	0.95	(0.54-1.67)
	≥2	1.08	(0.84-1.39)	1.27	(0.85-1.91)	1.06	(0.85-1.36)	**2.20**	**(1.47-3.29)**
Age, years	65-69	Reference		Reference		Reference		Reference	
	70-74	1.15	(0.85-1.56)	0.80	(0.53-1.22)	0.94	(0.74-1.25)	0.39	(0.24-0.63)
	75-79	0.94	(0.68-1.30)	0.98	(0.61-1.58)	0.84	(0.63-1.14)	0.54	(0.32-0.91)
	80-84	0.95	(0.66-1.36)	0.69	(0.35-1.35)	0.54	(0.37-0.80)	0.60	(0.31-1.17)
	85<	0.81	(0.50-1.31)	0.69	(0.27-1.76)	0.62	(0.36-1.06)	-	
Self-rated health	Good	Reference		Reference		Reference		Reference	
	Not good	0.98	(0.74-1.29)	0.80	(0.49-1.31)	**1.49**	**(1.15-1.92)**	**1.80**	**(1.12-2.87)**
	Missing	1.54	(0.92-2.59)	1.41	(0.60-3.29)	1.59	(0.98-2.59)	1.06	(0.38-2.93)
Any	No	Reference		Reference		Reference		Reference	

respiratory disease	Yes	**1.94**	**(1.40-2.71)**	**2.44**	**(1.28-4.68)**	**1.89**	**(1.31-2.73)**	1.14	(0.45-2.87)
Living with grandchild	No	Reference		Reference		Reference		Reference	
	Yes	1.21	(0.92-1.60)	1.56	(0.97-2.49)	0.98	(0.71-1.28)	0.91	(0.51-1.61)
Educational attainment, years	6>	Reference		Reference		Reference		Reference	
	6 - 9	0.87	(0.37-2.04)	0.38	(0.11-1.29)	0.90	(0.44-1.89)	1.30	(0.17-9.76)
	10 - 12	0.73	(0.31-1.75)	0.58	(0.17-1.96)	0.77	(0.38-1.64)	1.20	(0.16-9.14)
	13<	0.80	(0.33-1.91)	0.39	(0.11-1.36)	0.74	(0.37-1.64)	1.03	(0.13-8.14)
	Others	1.20	(0.28-5.11)	1.07	(0.17-6.86)	0.75	(0.19-3.68)	1.86	(0.11-31.34)
	Missing	0.84	(0.23-3.14)	0.26	(0.03-2.57)	1.09	(0.39-3.01)	0.57	(0.03-9.36)
Equivalent income (million yen)	Low (-199)	Reference		Reference		Reference		Reference	
	Middle (200-399)	0.87	(0.68-1.12)	0.87	(0.58-1.31)	1.09	(0.84-1.41)	1.09	(0.72-1.67)
	High (400-)	0.67	(0.43-1.03)	1.17	(0.65-2.11)	0.79	(0.53-1.25)	0.58	(0.25-1.39)
	Missing	0.66	(0.84-1.62)	0.66	(0.39-1.12)	0.94	(0.71-1.24)	0.62	(0.37-1.03)
Constant		0.07	(0.03-0.16)	0.06	(0.02-0.19)	0.05	(0.02-0.12)	0.02	(0-0.19)

Each social participation was not associated with influenza infection among vaccinated elderly men or women (Fig. 1A and 1B). Among unvaccinated elders (Fig. 1C and 1D), only men who participated in a sports group or club had a significantly increased risk of influenza infection (OR, 2.10; 95% CI, 1.17–3.78; Fig. 1C).

DISCUSSION

In this study, risk of influenza infection was higher for unvaccinated elders, particularly women, than for vaccinated Japanese elders. This suggests that influenza vaccination is effective in preventing influenza infection among active older adults and highlights the urgent need for additional efforts to promote influenza vaccination among socially active elders, especially women.

In an analysis of upper respiratory tract viruses, such as rhinovirus, in a quarantine setting, Cohen *et al.* found that for unknown reasons individuals with diverse social networks had greater resistance to upper respiratory illnesses.[29] It is hypothesized that certain immune mechanism operates as pathways and that behavior affects release of cytokines in nasal passages. Similarly, establishing a social network through group activities might prevent viral infection. However, frequent contact with infected persons could result in infection even among people with robust social networks. In our study, the risk of influenza infection was not higher among vaccinated elders when the likelihood of contact increased. When available, vaccines might help prevent transmission of infectious

respiratory agents other than influenza virus, as is the case for the pneumococcal vaccine.[30] However, when no vaccine is available, non-pharmaceutical interventions such as respiratory hygiene and cough etiquette[31 32] may be effective preventive measures. Future studies should investigate infections other than influenza.

In this study, participation in social activities did not increase the risk of influenza infection among vaccinated elders, even after adjustment for confounding factors. In general, influenza vaccines provide protection against influenza infection.[21 33] Several previous studies reported that vaccination reduced hospitalizations and deaths in older adults.[34-36] Our results confirm the effectiveness of influenza vaccines, but only in women. Protection is sometimes greatly reduced or absent, especially in older adults.[22] This study is one of the few that have confirmed the effectiveness of influenza vaccination in older adults.

Respondents were stratified by vaccination status because it may modify the association between social participation and influenza infection. Older people who participate in 2 or more groups are more likely to be vaccinated than are those who do not participate in such activities. It is

believed that elders who participate in social activities have good access to health information, including how and where they can receive influenza vaccinations.[20 37 38] Gathering for any group activity means sharing information in participant interests, such as health information, even when the aim of the activity may not be directly related to such interests. In addition, socially active persons have better medical access, which includes vaccinations and consultation with physicians.[20] This suggests that social persons who participate in groups are more likely than nonsocial persons to see a doctor when they develop a fever, especially in Japan, where medical resources are accessible to the entire population.

We also stratified respondents by sex. Evidence indicates that antibody responses after vaccination are stronger for women than for men.[39] Such differences in response were observed for various vaccines, including influenza vaccine.[40 41] This could explain the sex differences observed in this study. Behavioral differences between men and women may also have a role. Women tend to talk more than men during social activities. The risk of influenza infection was higher in unvaccinated women who participated in 2 or more groups.

The risk of influenza infection varied in relation to the type of social activity and by sex, but most activities did not significantly increase infection risk in vaccinated or unvaccinated elders. Only participation in a sports group was associated with increased risk for infection, among unvaccinated men, perhaps because such groups have more opportunities for close contact.[23] One reason for the lack of a significant association with most activities was reduced statistical power due to the focus on elders who participated in 1 or more activities. A larger-scale study is needed in order to evaluate the effects of participation in particular activities on influenza infection among participants stratified by sex and vaccination status. Transmission of the influenza virus between humans is mainly by respiratory droplets, although airborne transmission is possible.[42 43] Thus, activities with fewer opportunities for conversation and direct contact have less infection risk. Similarly, the risk of transmission is higher for larger groups.[43 44] In our study, group size and number of people gathered were unknown. Future studies should investigate why infection risk varies by group type and sex.

Our study has several limitations. First, because it is cross-sectional,

causality cannot be inferred. A longitudinal study or randomized controlled trial is needed in order to prove a causal relationship between social participation and influenza infection. Second, diagnosis of influenza infection was based on self-reports rather than on the results of laboratory testing. However, in Japan, commercial rapid diagnostic test kits are commonly used in clinical settings such as outpatient clinics. These kits have high sensitivity and specificity in the diagnosis of influenza infection.[45 46] In addition, medical access is good because of the universal health insurance system in Japan.[47] Older adults with an influenza-like illness in Japan are generally tested with rapid diagnostic tests.[45 48] Third, vaccination history was self-reported. Fourth, previous influenza infection was not assessed.

In conclusion, social participation increased the risk of influenza infection among unvaccinated elders, particularly women, which suggests that additional efforts are needed in order to encourage influenza vaccination among socially active elders.

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CONTRIBUTORSHIP STATEMENT

All authors meet ICMJE criteria for authorship. YS and TK contributed to the study design. YS performed statistical analysis and drafted the manuscript. TK advised on data analysis and interpretation. RS, KK, and TK revised the manuscript. KK is the principal investigator of the JAGES project. AT helped to develop the idea of the study. All authors read and approved the final manuscript.

DECLARATION OF COMPETING INTERESTS

We have read and understand BMJ policy on declaration of interests and declare that we have no competing interests.

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DATA SHARING STATEMENT

No additional data available.

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Figure legends

Figure 1. Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among vaccinated men, unvaccinated men, vaccinated women, and unvaccinated women who participated in 1 or more activities.

Logistic regression was adjusted for age, number of participating groups, self-rated health, respiratory disease, living with grandchildren, and socioeconomic status. The ORs for influenza infection (95% confidence interval) are shown for vaccinated men (Figure 1A), vaccinated women (Figure 1B), unvaccinated men (Figure 1C), and unvaccinated women (Figure 1D).

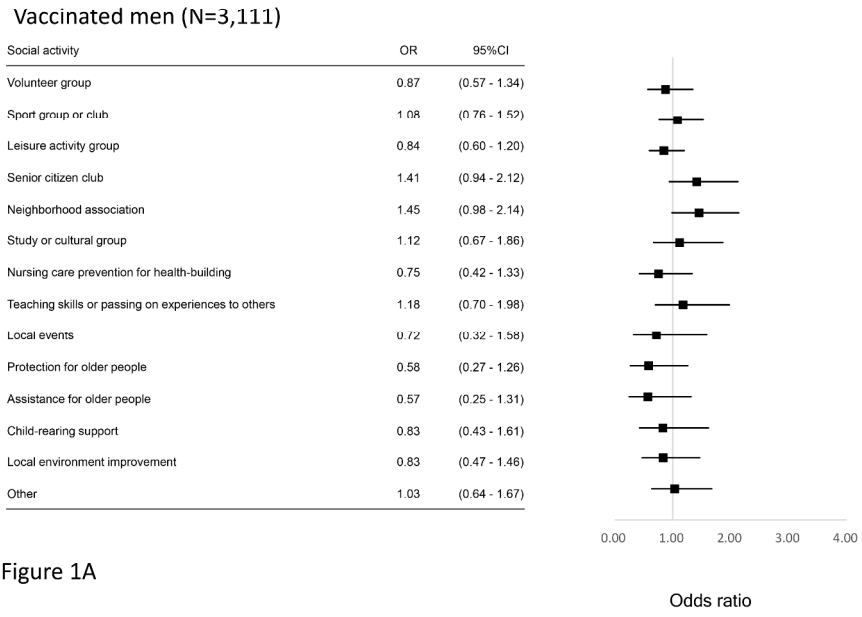

Figure 1A

Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among vaccinated men, unvaccinated men, vaccinated women, and unvaccinated women who participated in 1 or more activities.
Logistic regression was adjusted for age, number of participating groups, self-rated health, respiratory disease, living with grandchildren, and socioeconomic status. The ORs for influenza infection (95% confidence interval) are shown for vaccinated men (Figure 1A), vaccinated women (Figure 1B), unvaccinated men (Figure 1C), and unvaccinated women (Figure 1D).

355x266mm (300 x 300 DPI)

Vaccinated women (N=4,743)

Social activity	OR	95%CI
Volunteer group	0.82	(0.52 - 1.28)
Sport group or club	1.02	(0.74 - 1.42)
Leisure activity group	0.97	(0.69 - 1.35)
Senior citizen club	0.96	(0.64 - 1.45)
Neighborhood association	1.16	(0.73 - 1.82)
Study or cultural group	0.84	(0.54 - 1.30)
Nursing care prevention for health-building	1.30	(0.86 - 1.95)
Teaching skills or passing on experiences to others	0.70	(0.37 - 1.31)
Local events	1.47	(0.63 - 3.43)
Protection for older people	0.53	(0.25 - 1.12)
Assistance for older people	1.00	(0.53 - 1.87)
Child-rearing support	1.15	(0.62 - 2.13)
Local environment improvement	1.28	(0.74 - 2.23)
Other	1.37	(0.83 - 2.27)

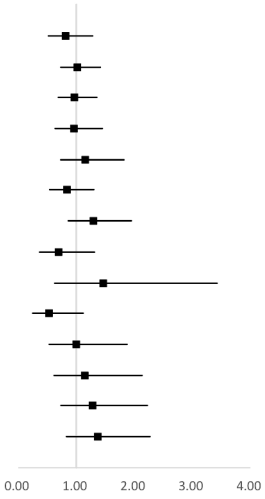

Figure 1B

355x266mm (300 x 300 DPI)

Unvaccinated men (N=2,321)

Social activity	OR	95%CI
Volunteer group	1.14	(0.57 - 2.29)
Sport group or club	2.10	(1.17 - 3.78)
Leisure activity group	0.59	(0.34 - 1.02)
Senior citizen club	1.14	(0.54 - 2.39)
Neighborhood association	0.69	(0.34 - 1.40)
Study or cultural group	0.96	(0.42 - 2.17)
Nursing care prevention for health-building	0.89	(0.35 - 2.25)
Teaching skills or passing on experiences to others	1.16	(0.53 - 2.54)
Local events	0.97	(0.34 - 2.78)
Protection for older people	0.99	(0.34 - 2.92)
Assistance for older people	1.31	(0.45 - 3.78)
Child-rearing support	0.72	(0.24 - 2.12)
Local environment improvement	0.85	(0.37 - 1.96)
Other	0.83	(0.39 - 1.74)

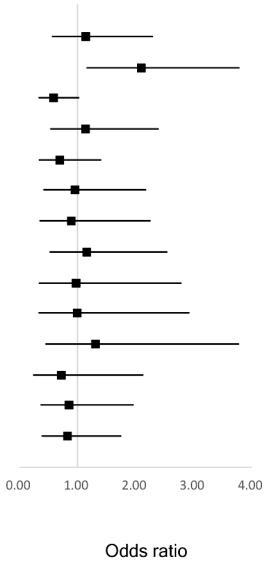

Figure 1C

355x266mm (300 x 300 DPI)

Unvaccinated women (N=2,477)

Social activity	OR	95%CI
Volunteer group	0.66	(0.32 - 1.39)
Sport group or club	0.90	(0.53 - 1.53)
Leisure activity group	0.98	(0.57 - 1.67)
Senior citizen club	1.61	(0.83 - 3.14)
Neighborhood association	1.07	(0.54 - 2.12)
Study or cultural group	0.79	(0.40 - 1.56)
Nursing care prevention for health-building	1.19	(0.60 - 2.35)
Teaching skills or passing on experiences to others	0.44	(0.18 - 1.11)
Local events	0.76	(0.21 - 2.78)
Protection for older people	1.24	(0.53 - 2.93)
Assistance for older people	1.64	(0.74 - 3.64)
Child-rearing support	0.66	(0.25 - 1.75)
Local environment improvement	0.90	(0.37 - 2.20)
Other	1.23	(0.62 - 2.44)

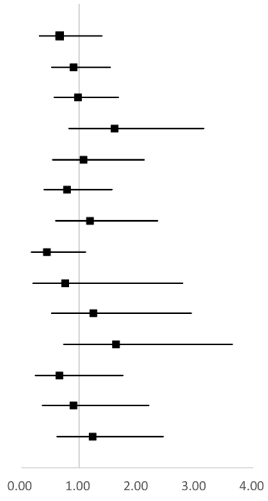

Figure 1D

355x266mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1✓	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
	P3-4	(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2✓ P6-7	Explain the scientific background and rationale for the investigation being reported
Objectives	3✓ P7-8	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4✓ P9	Present key elements of study design early in the paper
Setting	5✓ P8-9	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6✓ P9	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7✓ P9-11	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*✓ P9-11	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9✓ P10	Describe any efforts to address potential sources of bias
Study size	10✓ P9	Explain how the study size was arrived at
Quantitative variables	11✓ P9-11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12✓ P12-13i	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*✓ P14	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*✓ P14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*✓ P14	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16✓ P14-15	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17✓ P23	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18✓ P24	Summarise key results with reference to study objectives
Limitations	19✓ P28-29	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20✓ P24-27	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21✓ P25	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Social participation and risk of influenza infection in older adults: A cross-sectional study

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology, Infectious diseases, Respiratory medicine
Keywords:	influenza, social participation, vaccination, older people, social capital

Title: **Social participation and risk of influenza infection in older adults: A cross-sectional study**

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Keywords: influenza; social participation; vaccination; older people; social capital

Word count: 2462

ABSTRACT (296 words)

Objectives: Influenza infection can cause severe pneumonia, which is sometimes fatal, particularly in older adults. Influenza results in 3 to 5 million cases of severe illness and about 250,000 to 500,000 deaths annually worldwide. Social participation in the context of influenza infection is controversial because, although social participation is beneficial in maintaining physical function and mental health, it also increases the risk of contact with infected people. This study examined the association between social participation and influenza infection in Japanese adults aged 65 years or older.

Design: Cross-sectional study.

Setting: Japanese functionally independent adults aged 65 years or older.

Participants: Among the respondents to the Japan Gerontological Evaluation Study (JAGES) 2013 survey, which took place during the period from October through December 2013, 12,231 men and 14,091 women responded to questions on influenza vaccination and influenza infection.

Outcome measures: Using JAGES data for 12,231 men and 14,091 women aged ≥65 years, we examined the association between social

participation and influenza infection. The association between influenza infection and number of groups in which respondents participated was investigated among adults aged ≥65 years, stratified by vaccination status and sex.

Results: Unvaccinated women who participated in 2 or more social activities were 2.20 times (95% CI 1.47–3.29) as likely to report an influenza infection as those who reported no social participation. In contrast, vaccinated women who participated in 2 or more social groups had no additional risk of influenza infection as compared with female elders with no social participation. Among men, participation in social activities was not significantly associated with influenza infection, regardless of vaccination status.

Conclusions: Social participation was associated with a higher risk of influenza infection among unvaccinated older women, which suggests a need for further efforts to promote influenza vaccination, particularly among socially active elderly women.

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ARTICLE SUMMARY

Strengths and limitations of this study

- Although social participation is highly recommended for older adults, this study is the first to examine the association between social participation and influenza infection among this population.
- A strength of this study is that it used data from a large-scale social survey, which yielded information on influenza infection, influenza vaccination status, and social participation.
- The study is based on cross-sectional data, which does not allow determination of causal relationships between influenza infection and social participation.

INTRODUCTION

Influenza epidemics are estimated to result in 3 to 5 million cases of severe illness and about 250,000 to 500,000 deaths annually worldwide.[1] Older adults are disproportionally affected,[2-4] as they are vulnerable to influenza infection and development of secondary bacterial pneumonia due to complications of chronic conditions such as congestive heart failure and chronic obstructive pulmonary disease.[5] Influenza infection may also result in declines in critical physical functions in frail elders. [6] Influenza infection is thus one of the most important causes of death in an aging society.

Influenza infection is transmitted from person to person; therefore, social contact increases the risk of influenza infection.[7-10] However, social participation, which increases social contact, is beneficial for the physical and mental health of older adults.[11-13] Previous research on social participation showed wide-ranging health benefits for older adults. Older adults who participate in social activities have better self-rated health,[11] lower risks of disability, functional decline, mobility decline, depression, generalized anxiety disorders, cognitive decline, and dementia[14-19], and longer lifespans[12]. To our knowledge, no study has investigated the

association between social participation and influenza infection among older adults.

Influenza vaccination status must be considered in any study of the association between influenza infection and social participation among adults aged ≥65 years. Influenza vaccination is recommended for older adults,[20 21] as it decreases the risk of preventable death.[1] For elders in Japan, vaccination fees are partly subsidized by the local government, to increase vaccination coverage.[14 15] The influenza vaccine must be altered to remain effective against currently circulating strains. The effectiveness of influenza vaccinations varies because the circulating type and subtype of the virus change every year. Thus, protection is sometimes greatly reduced or absent, especially in older adults.[22] This study is one of the few to show the effectiveness of influenza vaccination in older adults. Because social participation is positively associated with influenza vaccination,[23] the association between social participation and influenza infection might vary in relation to vaccination status. In addition, modes of contact during social participation might differ between men and women.

The Japan Gerontological Evaluation Study (JAGES) project is one of

the largest cohort studies of social determinants of health among Japanese adults aged ≥65 years. This study used part of the 2013 wave data from the 138,294 respondents to the survey (response rate, 70.8%). This study is the first to examine the association between social participation and influenza infection among elders stratified by influenza vaccination status and sex. In addition, we attempted to identify social activities that were associated with influenza infection.

METHODS

Study population

This study used data from the JAGES project, an ongoing prospective cohort study of the social determinants of health among functionally independent adults aged ≥65 years. Several studies have utilized data from this large-scale nationwide project.[24 25] The cohort covers 30 municipalities in 13 prefectures in Japan. We used the 2013 wave of JAGES, in which questionnaires were mailed to a random sample of approximately 200,000 community-dwelling individuals aged 65 years and older from October through December 2013. In addition to the basic items, 5 survey modules covered a variety of other topics. Module A covered nursing care, medical care, and lifestyle; module B assessed oral hygiene, optimism, and subjective health; module C covered social capital and history of abuse; module D evaluated subjective quality of life, sleep, and influenza infection; and module E assessed physical activity. We used module D, which included questions on influenza vaccination and influenza infection. All valid responses (from 12,231 men and 14,091 women) to module D were analyzed.

Influenza infection and vaccination

Influenza infection status was determined by participant response to a self-administered questionnaire. To determine influenza infection status, respondents were asked, "Were you infected with influenza during the previous year? (yes, no)". Vaccination status was evaluated by asking respondents, "Did you receive an influenza vaccination during the previous year? (yes, no)".

Social participation

Social participation was defined as involvement in any social activity during the study period.[26] Respondents were asked how often they took part in volunteer groups, sport groups or clubs, leisure activity groups, senior citizen clubs, neighborhood associations, study or cultural groups, nursing care prevention for health promotion groups, in teaching skills or passing on experiences to others, local events, protection for older people, assistance for older people, child-rearing support, local environment improvement activities, and other groups (frequency of participation: ≥4

times per week, 2-3 times per week, once a week, 1-3 times per month, several times per year, or never). We defined a participation frequency of at least 1-3 times per month as participation in a group, counted the number of groups in which the respondent participated, and categorized participation as 0, 1, or ≥2 groups.

Covariates

Physical health status, particularly presence of respiratory disease, might be associated with social participation and influenza infection.[27 28] Self-rated health and respiratory disease as an underlying medical condition were assessed via questionnaire. Self-rated health was assessed by the question, "What is your current health status? (excellent, good, fair, or poor)". Responses of excellent and good were classified as "good" and responses of fair and poor as "not good". Presence of grandchildren in the household, which might be associated with social participation and influenza infection, was ascertained via questionnaire. Socioeconomic status was analyzed as a possible confounder. Educational attainment was categorized as <6 years, 6-9 years, 10-12 years, ≥13 years, and other.

Household income was equalized by the square root of the number of household members and classified as <1.99 million yen, 2-3.99 million yen, and >4 million yen. Age was categorized into 5 groups: 65-69, 70-74, 75-79, 80-84, and ≥85 years.

Analysis

Logistic regression analysis was used to examine the association between social participation and influenza infection. When an interaction term between a factor and social participation was significantly associated with influenza infection, analyses were done after stratifying respondents by that factor. We adjusted for the possible confounding factors age, self-rated health, underlying respiratory disease, living with grandchildren, educational attainment, and equivalent income.

Additional analysis

To determine whether certain types of social activity were more likely to result in influenza infection, we set participation in each activity as an explanatory variable, instead of participation in any social activity, and

this yielded 14 models. Data from all the respondents were analyzed. Number of participating activities was included as a covariate, to measure the effect of participating in each activity. Odds ratios (ORs) for influenza infection were calculated in relation to participation in each activity, stratified by vaccination status and sex. All analyses were performed with STATA SE version 13 (StataCorp, College Station, TX, USA).

Ethical considerations

The questionnaire and an explanation of the study were sent to participants by mail. The recipients were informed that participation was voluntary and that returning the self-administered questionnaire would be interpreted as consent to participate. Ethical approval for the study was obtained from the Ethics Committee at Nihon Fukushi University.

RESULTS

The interaction term between vaccination status and social participation was significantly associated with influenza infection, as was the interaction term between sex and social participation. Thus, all analyses of the groups were stratified by vaccination status and sex. The characteristics of the study sample, stratified by vaccination status and by sex, are shown in Table 1. The vaccinated group was older than the unvaccinated group, and this was true for men and women. In particular, 49.5% of vaccinated men and 32.9% of unvaccinated men were 75 years or older; the respective values were 48.0% and 34.7% for women. Approximately one-third of vaccinated men (29.1%) and vaccinated (33.3%) women participated in 2 or more groups, while less than one-fourth (22.6%) of unvaccinated men participated in 2 or more groups.

A total of 355 cases (5.5%) and 372 cases (4.2%) of influenza infection were observed among vaccinated men and women, respectively, and 136 cases (2.4%) and 124 cases (2.3%) of influenza infection were observed in unvaccinated men and women, respectively. The proportion of respondents with respiratory diseases was higher among vaccinated elders

(7.6% in men and 5.0% in women, P<0.001) than among unvaccinated elders (4.0% in men and 3.4% in women, P<0.001). Vaccinated elders were more likely than unvaccinated elders to live with grandchildren (men: 16.2% vs 11.2%, P<0.001; women: 21.1% vs 13.3%, P<0.001).

Table 2 shows the results of logistic analysis of influenza infection in respondents stratified by influenza vaccination status and sex. Overall, unvaccinated women who participated in 2 or more social activities were more likely to develop influenza than were unvaccinated women who did not participate in such activities (OR, 2.20; 95% confidence interval [CI], 1.47–3.29), after adjustment for age, self-rated health, presence of respiratory disease, living with grandchildren, and socioeconomic status (educational attainment and equivalent income). However, among vaccinated women, social participation in 2 or more activities was not associated with influenza infection after adjustment (OR, 1.06; 95% CI, 0.83-1.36). Social participation was not associated with influenza infection among vaccinated or unvaccinated men. Participation in 1 group was not associated with influenza infection in either group. Presence of respiratory disease was significantly associated with influenza infection among

vaccinated men (OR, 1.94; 95% CI, 1.40–2.71), unvaccinated men (OR, 2.44; 95% CI, 1.28–4.68), and vaccinated women (OR, 1.89; 95% CI, 1.31–2.73). Poor self-rated health was significantly associated with influenza infection in vaccinated (OR, 1.49; 95% CI, 1.15–1.92) and unvaccinated women (OR, 1.80; 95% CI, 1.12–2.87).

Table 1. Characteristics of vaccinated and unvaccinated elders stratified by sex

		Men N=12,231					Women N=14,091				
		Vaccinated N=6,502		Unvaccinated N=5,729			Vaccinated N=8,801		Unvaccinated N=5,290		
Variables		N	%	N	%	P†	N	%	N	%	P†
Age, years	65-69	1,438	(22.1%)	2,067	(36.1%)		1,916	(21.8%)	1,876	(35.5%)	
	70-74	1,845	(28.4%)	1,776	(31.0%)		2,663	(30.3%)	1,578	(29.8%)	
	75-79	1,658	(25.5%)	1,030	(18.0%)		2,163	(24.6%)	989	(18.7%)	
	80-84	1,067	(16.4%)	580	(10.1%)		1,376	(15.6%)	526	(9.9%)	
	85<	494	(7.6%)	276	(4.8%)	**<0.001**	683	(7.8%)	321	(6.1%)	**<0.001**
Participation in social activity, no.	0	3,391	(52.2%)	3,408	(59.5%)		4,058	(46.1%)	2,813	(53.2%)	
	1	1,219	(18.7%)	1,026	(17.9%)		1,812	(20.6%)	974	(18.4%)	
	≥2	1,892	(29.1%)	1,295	(22.6%)	**<0.001**	2,931	(33.3%)	1,503	(28.4%)	**<0.001**
Influenza infection in past year	Not infected	6,147	(94.5%)	5,593	(97.6%)		8,429	(95.8%)	5,166	(97.7%)	
	Infected	355	(5.5%)	136	(2.4%)	**<0.001**	372	(4.2%)	124	(2.3%)	**<0.001**

Self-rated health	Good	4,972	(76.5%)	4,494	(78.4%)		6,911	(78.5%)	4,227	(79.9%)	
	Not good	1,328	(20.4%)	1,036	(18.1%)		1,558	(17.7%)	824	(15.6%)	
	Missing	202	(3.1%)	199	(3.5%)	**0.003**	332	(3.8%)	239	(4.5%)	**0.001**
Any respiratory disease	No	6,009	(92.4%)	5,500	(96.0%)		8,357	(95.0%)	5,111	(96.6%)	
	Yes	493	(7.6%)	229	(4.0%)	**<0.001**	444	(5.0%)	179	(3.4%)	**<0.001**
Living with grandchild	No	5,447	(83.8%)	5,088	(88.8%)		6,948	(78.9%)	4,587	(86.7%)	
	Yes	1,055	(16.2%)	641	(11.2%)	**<0.001**	1,853	(21.1%)	703	(13.3%)	**<0.001**
Educational attainment, years	6>	89	(1.4%)	72	(1.3%)		195	(2.2%)	113	(2.1%)	
	6 - 9	2,431	(37.4%)	2,115	(36.9%)		3,847	(43.7%)	2,111	(39.9%)	
	10 - 12	2,271	(34.9%)	1,970	(34.4%)		3,308	(37.6%)	2,045	(38.7%)	
	13<	1,602	(24.6%)	1,446	(25.2%)		1,243	(14.1%)	834	(15.8%)	
	Others	40	(0.6%)	39	(0.7%)		51	(0.6%)	40	(0.8%)	
	Missing	69	(1.1%)	87	(1.5%)	0.296	157	(1.8%)	147	(2.8%)	**<0.001**
Equivalent income (million yen)	Low (-1.99)	2,875	(44.2%)	2,418	(42.2%)		3,595	(40.8%)	2,111	(39.9%)	
	Middle (2-3.99)	2,222	(34.2%)	1,749	(30.5%)		2,421	(27.5%)	1,304	(24.7%)	
	High (4-)	654	(10.1%)	462	(8.1%)		692	(7.9%)	353	(6.7%)	
	Missing	751	(11.6%)	1,100	(19.2%)	**<0.001**	2,093	(23.8%)	1,522	(28.8%)	**<0.001**

† Chi-square test

Table 2. Risk of influenza infection in men and women stratified by influenza vaccination status

Variables		Men				Women			
		Vaccinated		Unvaccinated		Vaccinated		Unvaccinated	
		OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Participation in social activities (no. of groups)	0	Reference		Reference		Reference		Reference	
	1	1.02	(0.76-1.37)	0.94	(0.58-1.53)	1.14	(0.86-1.50)	0.95	(0.54-1.67)
	≥2	1.08	(0.84-1.39)	1.27	(0.85-1.91)	1.06	(0.85-1.36)	**2.20**	**(1.47-3.29)**
Age, years	65-69	Reference		Reference		Reference		Reference	
	70-74	1.15	(0.85-1.56)	0.80	(0.53-1.22)	0.94	(0.74-1.25)	0.39	(0.24-0.63)
	75-79	0.94	(0.68-1.30)	0.98	(0.61-1.58)	0.84	(0.63-1.14)	0.54	(0.32-0.91)
	80-84	0.95	(0.66-1.36)	0.69	(0.35-1.35)	0.54	(0.37-0.80)	0.60	(0.31-1.17)
	85<	0.81	(0.50-1.31)	0.69	(0.27-1.76)	0.62	(0.36-1.06)	-	
Self-rated health	Good	Reference		Reference		Reference		Reference	
	Not good	0.98	(0.74-1.29)	0.80	(0.49-1.31)	**1.49**	**(1.15-1.92)**	**1.80**	**(1.12-2.87)**
	Missing	1.54	(0.92-2.59)	1.41	(0.60-3.29)	1.59	(0.98-2.59)	1.06	(0.38-2.93)
Any	No	Reference		Reference		Reference		Reference	

respiratory disease	Yes	**1.94**	**(1.40-2.71)**	**2.44**	**(1.28-4.68)**	**1.89**	**(1.31-2.73)**	1.14	(0.45-2.87)
Living with grandchild	No	Reference		Reference		Reference		Reference	
	Yes	1.21	(0.92-1.60)	1.56	(0.97-2.49)	0.98	(0.71-1.28)	0.91	(0.51-1.61)
Educational attainment, years	6>	Reference		Reference		Reference		Reference	
	6 - 9	0.87	(0.37-2.04)	0.38	(0.11-1.29)	0.90	(0.44-1.89)	1.30	(0.17-9.76)
	10 - 12	0.73	(0.31-1.75)	0.58	(0.17-1.96)	0.77	(0.38-1.64)	1.20	(0.16-9.14)
	13<	0.80	(0.33-1.91)	0.39	(0.11-1.36)	0.74	(0.37-1.64)	1.03	(0.13-8.14)
	Others	1.20	(0.28-5.11)	1.07	(0.17-6.86)	0.75	(0.19-3.68)	1.86	(0.11-31.34)
	Missing	0.84	(0.23-3.14)	0.26	(0.03-2.57)	1.09	(0.39-3.01)	0.57	(0.03-9.36)
Equivalent income (million yen)	Low (-199)	Reference		Reference		Reference		Reference	
	Middle (200-399)	0.87	(0.68-1.12)	0.87	(0.58-1.31)	1.09	(0.84-1.41)	1.09	(0.72-1.67)
	High (400-)	0.67	(0.43-1.03)	1.17	(0.65-2.11)	0.79	(0.53-1.25)	0.58	(0.25-1.39)
	Missing	0.66	(0.84-1.62)	0.66	(0.39-1.12)	0.94	(0.71-1.24)	0.62	(0.37-1.03)
Constant		0.07	(0.03-0.16)	0.06	(0.02-0.19)	0.05	(0.02-0.12)	0.02	(0-0.19)

Each social participation was not associated with influenza infection among vaccinated elderly men or women (Fig. 1 and 2). Among unvaccinated elders (Fig. 3 and 4), only men who participated in a leisure activity group had a significantly decreased risk of influenza infection (OR,0.56; 95% CI,–0.33-0.94; Fig. 3).

DISCUSSION

In this study, risk of influenza infection was higher for unvaccinated elders, particularly women, than for vaccinated Japanese elders. This suggests that influenza vaccination is effective in preventing influenza infection among active older adults and highlights the urgent need for additional efforts to promote influenza vaccination among socially active elders, especially women.

In an analysis of upper respiratory tract viruses, such as rhinovirus, in a quarantine setting, Cohen *et al.* found that for unknown reasons individuals with diverse social networks had greater resistance to upper respiratory illnesses.[29] It is hypothesized that certain immune mechanism operates as pathways and that behavior affects release of cytokines in nasal passages. Similarly, establishing a social network through group activities might prevent viral infection. However, frequent contact with infected persons could result in infection even among people with robust social networks. In our study, the risk of influenza infection was not higher among vaccinated elders when the likelihood of contact increased. When available, vaccines might help prevent transmission of infectious

respiratory agents other than influenza virus, as is the case for the pneumococcal vaccine.[30] However, when no vaccine is available, non-pharmaceutical interventions such as respiratory hygiene and cough etiquette[31 32] may be effective preventive measures. Future studies should investigate infections other than influenza.

In this study, participation in social activities did not increase the risk of influenza infection among vaccinated elders, even after adjustment for confounding factors. In general, influenza vaccines provide protection against influenza infection.[21 33] Several previous studies reported that vaccination reduced hospitalizations and deaths in older adults.[34-36] Our results confirm the effectiveness of influenza vaccines, but only in women. Protection is sometimes greatly reduced or absent, especially in older adults.[22] This study is one of the few that have confirmed the effectiveness of influenza vaccination in older adults.

Respondents were stratified by vaccination status because it may modify the association between social participation and influenza infection. Older people who participate in 2 or more groups are more likely to be vaccinated than are those who do not participate in such activities. It is

believed that elders who participate in social activities have good access to health information, including how and where they can receive influenza vaccinations.[20 37 38] Gathering for any group activity means sharing information in participant interests, such as health information, even when the aim of the activity may not be directly related to such interests. In addition, socially active persons have better medical access, which includes vaccinations and consultation with physicians.[20] This suggests that social persons who participate in groups are more likely than nonsocial persons to see a doctor when they develop a fever, especially in Japan, where medical resources are accessible to the entire population.

We also stratified respondents by sex. Evidence indicates that antibody responses after vaccination are stronger for women than for men.[39] Such differences in response were observed for various vaccines, including influenza vaccine.[40 41] This could explain the sex differences observed in this study. Behavioral differences between men and women may also have a role. Women tend to talk more than men during social activities. The risk of influenza infection was higher in unvaccinated women who participated in 2 or more groups.

The risk of influenza infection varied in relation to the type of social activity and by sex, but most activities did not significantly increase infection risk in vaccinated or unvaccinated elders. Only participation in a leisure activity group was associated with decreased risk for infection, among unvaccinated men, perhaps because such groups have less opportunities for close contact.[23] However, reason why a significant association was observed only in unvaccinated men was unclear. One reason for the lack of a significant association with most activities was larger effect of number of participation rather than type of social activity. Transmission of the influenza virus between humans is mainly by respiratory droplets, although airborne transmission is possible.[42 43] Thus, activities with fewer opportunities for conversation and direct contact have less infection risk. Similarly, the risk of transmission is higher for larger groups.[43 44] In our study, group size and number of people gathered were unknown. Future studies should investigate why infection risk varies by group type and sex.

Our study has several limitations. First, because it is cross-sectional, causality cannot be inferred. A longitudinal study or randomized controlled

trial is needed in order to prove a causal relationship between social participation and influenza infection. Second, diagnosis of influenza infection was based on self-reports rather than on the results of laboratory testing. However, in Japan, commercial rapid diagnostic test kits are commonly used in clinical settings such as outpatient clinics. These kits have high sensitivity and specificity in the diagnosis of influenza infection.[45 46] In addition, medical access is good because of the universal health insurance system in Japan.[47] Older adults with an influenza-like illness in Japan are generally tested with rapid diagnostic tests.[45 48] Third, vaccination history was self-reported. Fourth, previous influenza infection was not assessed.

In conclusion, social participation increased the risk of influenza infection among unvaccinated elders, particularly women, which suggests that additional efforts are needed in order to encourage influenza vaccination among socially active elders.

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CONTRIBUTORSHIP STATEMENT

All authors meet ICMJE criteria for authorship. YS and TK contributed to the study design. YS performed statistical analysis and drafted the manuscript. TK advised on data analysis and interpretation. RS, KK, and TK revised the manuscript. KK is the principal investigator of the JAGES project. AT helped to develop the idea of the study. All authors read and approved the final manuscript.

DECLARATION OF COMPETING INTERESTS

We have read and understand BMJ policy on declaration of interests and declare that we have no competing interests.

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DATA SHARING STATEMENT

No additional data available.

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Figure legends

Figure 1. Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among vaccinated men.

Logistic regression was adjusted for age, number of participating groups, self-rated health, respiratory disease, living with grandchildren, and socioeconomic status.

Figure 2. Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among vaccinated women.

Logistic regression was adjusted for possible confounders.

Figure 3. Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among unvaccinated men.

Logistic regression was adjusted for possible confounders.

Figure 4. Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among unvaccinated women.

Logistic regression was adjusted for possible confounders.

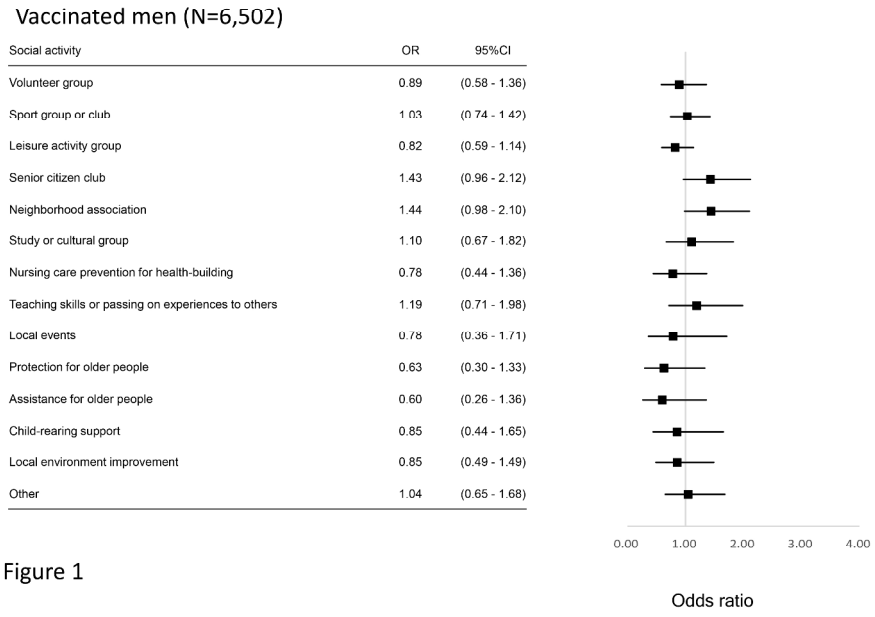

Figure 1

Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among vaccinated men.
Logistic regression was adjusted for age, number of participating groups, self-rated health, respiratory disease, living with grandchildren, and socioeconomic status.

355x266mm (300 x 300 DPI)

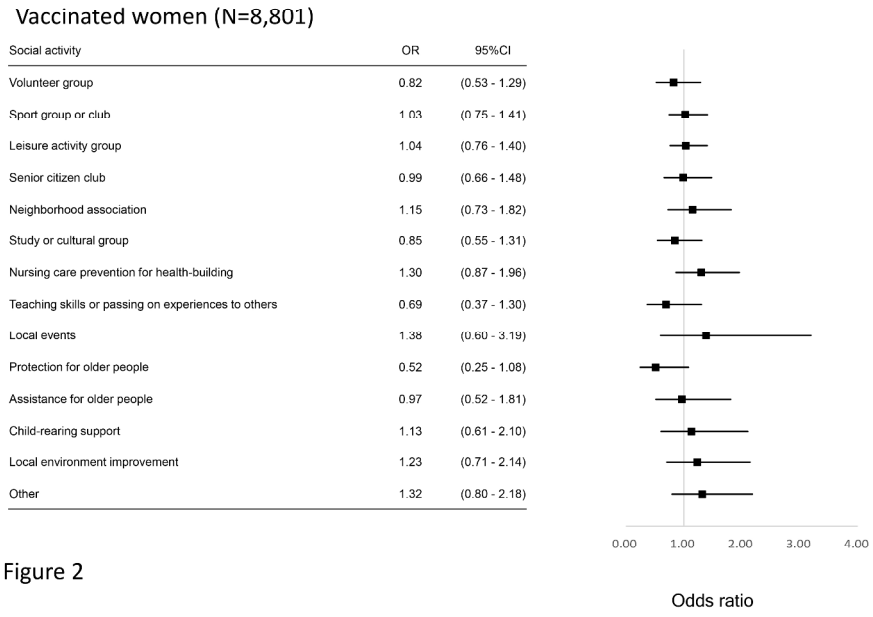

Figure 2

Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among vaccinated women.
Logistic regression was adjusted for possible confounders.

355x266mm (300 x 300 DPI)

Unvaccinated men (N=5,729)

Social activity	OR	95%CI
Volunteer group	1.16	(0.59 - 2.26)
Sport group or club	1.55	(0.95 - 2.54)
Leisure activity group	0.56	(0.33 - 0.94)
Senior citizen club	1.10	(0.54 - 2.24)
Neighborhood association	0.71	(0.36 - 1.40)
Study or cultural group	0.99	(0.45 - 2.20)
Nursing care prevention for health-building	1.04	(0.43 - 2.51)
Teaching skills or passing on experiences to others	1.14	(0.54 - 2.43)
Local events	1.13	(0.42 - 3.08)
Protection for older people	1.18	(0.42 - 3.28)
Assistance for older people	1.52	(0.55 - 4.20)
Child-rearing support	0.82	(0.29 - 2.31)
Local environment improvement	0.95	(0.43 - 2.10)
Other	0.83	(0.40 - 1.71)

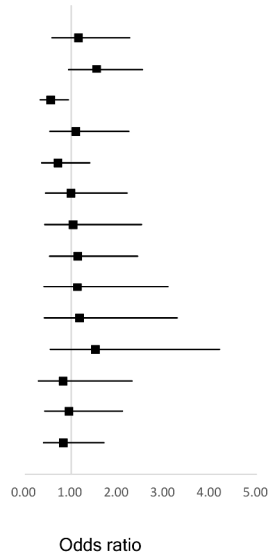

Figure 3

Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among unvaccinated men.
Logistic regression was adjusted for possible confounders.

355x266mm (300 x 300 DPI)

Unvaccinated women (N=5,290)

Social activity	OR	95%CI
Volunteer group	0.65	(0.31 - 1.36)
Sport group or club	0.93	(0.55 - 1.55)
Leisure activity group	1.11	(0.69 - 1.81)
Senior citizen club	1.74	(0.91 - 3.31)
Neighborhood association	1.07	(0.54 - 2.14)
Study or cultural group	0.78	(0.39 - 1.54)
Nursing care prevention for health-building	1.19	(0.60 - 2.36)
Teaching skills or passing on experiences to others	0.44	(0.18 - 1.09)
Local events	0.69	(0.19 - 2.47)
Protection for older people	1.13	(0.48 - 2.62)
Assistance for older people	1.53	(0.69 - 3.39)
Child-rearing support	0.64	(0.24 - 1.69)
Local environment improvement	0.84	(0.34 - 2.07)
Other	1.23	(0.61 - 2.46)

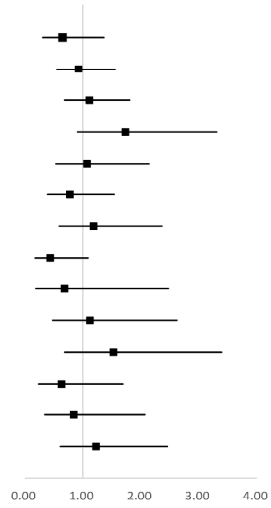

Figure 4

Odds ratios (ORs) for influenza infection in relation to participation in specific social activities among unvaccinated women.
Logistic regression was adjusted for possible confounders.

355x266mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1✓	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
	P3-4	(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2✓ P6-7	Explain the scientific background and rationale for the investigation being reported
Objectives	3✓ P7-8	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4✓ P9	Present key elements of study design early in the paper
Setting	5✓ P8-9	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6✓ P9	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7✓ P9-11	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*✓ P9-11	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9✓ P10	Describe any efforts to address potential sources of bias
Study size	10✓ P9	Explain how the study size was arrived at
Quantitative variables	11✓ P9-11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12✓ P12-13i	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*✓ P14	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*✓ P14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*✓ P14	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16✓ P14-15	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17✓ P23	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18✓ P24	Summarise key results with reference to study objectives
Limitations	19✓ P28-29	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20✓ P24-27	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21✓ P25	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.