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Complete List of Authors:	Kwon, David Soonil; Seoul National University College of Medicine Kim, Kyuwoong; Seoul National University College of Medicine, Department of Biomedical Sciences Park, Sang Min; Seoul National University College of Medicine, Department of Biomedical Sciences; Seoul National University Hospital, Seoul National University College of Medicine, Department of Family Medicine
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Factors associated with influenza vaccination coverage among the elderly in South Korea: The Fourth Korean National Health and Nutrition Examination Survey (KNHANES IV)

David Soonil Kwon[a], Kyuwoong Kim[c], Sang Min Park, MD, PhD[b,c, *]

Affiliations:

[a] College of Medicine, Seoul National University, Seoul, South Korea

[b] Department of Family Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea

[c] Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, South Korea

*** Correspondence to:** Sang Min Park, MD, PhD

Department of Family Medicine & Department of Biomedical Sciences, Seoul National University College of Medicine, 28 Yunkeon-dong, Jongro-gu, Seoul 110-744, South Korea

Tel: +82-2-2072-3331 Fax: +82-2-766-3276

E-mail: smpark.snuh@gmail.com

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ABSTRACT

Objective: The annual outbreak of influenza is one of the major causes of both morbidity and mortality among the elderly population around the world. While there is an annual vaccine available to prevent or reduce the incidence of disease, not all older people in Korea choose to be vaccinated. There have been few previous studies to examine the factors influencing influenza vaccination in Korea. Thus this study identifies nationwide factors that affecting influenza vaccination rates in the elderly Koreans.

Methods: We obtained data from the Fourth Korean National Health and Nutrition Examination Survey 2007–2009 (KNHANES IV), a nationwide health survey in Korea. To assess influenza vaccination status we analysed answers to a single question from the survey. From the respondents, we selected 3,567 elderly population aged 65 years or older, to analyse the effects of variables including socio-demographic, health behavioural risk, health status, and psychological factors on vaccination coverage. We identified factors affecting vaccination status using multiple logistic regression analysis.

Results: The rate of influenza vaccination in this elderly population was 75.8%. Overall, the most significant determinants for choosing influenza vaccination were a recent history of health screening (adjusted odds ratio, aOR 2.26, 95% CI: 1.92–2.66) and smoking (aOR 0.78, 95% CI: 0.62–0.98). Other contributing factors were age, household income, marital status, alcohol consumption, physical activity level, a self-reported health status, and a limitation in daily activities. In contrast, psychological factors, including self-perceived quality of life, stress, and depressive mood, did not show close association with vaccination coverage.

Conclusion: To boost influenza vaccination rates in the elderly, an influenza campaign should focus on underrepresented groups, especially smokers. Additionally, promoting routine health screening for the elderly may be an efficiently way to help achieve higher vaccination rates. Our results highlight the need for a new strategy in the vaccination campaign.

Keywords: influenza, vaccination, elderly, factors

STRENGTHS AND IMITATIONS OF THIS STUDY

- There are few studies done regarding factors associated with influenza vaccination coverage among the elderly in Korea
- We used "The Fourth Korean National Health and Nutrition Examination Survey (KNHANES IV)" as database and logistic regression analysis for statistics
- Among several factors identified as associating factors to influenza vaccination, the most "positively" significant factor was "a recent history of health screening"
- Among several factors identified as associating factors to influenza vaccination, the most "negatively" significant factor was "smoking"
- To boost influenza vaccination rates among the elderly, a new vaccination campaign should focus smokers and health screening programs could be a good strategy.
- Those with missing values for any of study variables and respondents who replied "unknown" to any of the study variables were excluded (505 people, 12.4% of the elder sample respondents).
- Exclusion may affect the applicability of our study to the general Korean elderly population.

INTRODUCTION

Influenza is a highly contagious, viral, acute respiratory illness associated with elevated morbidity and mortality particularly, among high-risk individuals, including the elderly and those with underlying chronic diseases.[1-3] The influenza mortality may be underestimated since influenza is not commonly recognised as a cause of mortality in the elderly.[4-6] Even though it is, around 90% of the influenza mortality occurs in people aged 65 years and older.[7] This suggests that the elderly is one of the groups with the highest risk for serious complications in influenza.

Many studies have documented that the influenza vaccination is a safe and cost-effective way of preventing influenza and pneumonia in both the elderly and in children.[8-12] Annual influenza vaccinations have been shown to significantly reduce hospitalisations and mortality in older population.[13, 14] For this reason, the World Health Assembly encourage member states to increase influenza vaccination coverage for high-risk populations to 50% by 2006 and 75% by 2010.[15] Additionally, the United States department of Health and Human Services (HHS) targeted a minimum vaccination rate of 90% for people aged 65 years and older in 2010.[16] In South Korea, the Korea Centres for Disease Control and Prevention (KCDC) clearly recommends that annual influenza vaccinations are encouraged for all people aged 65 or older and aimed to achieve a vaccination coverage greater than 60% for this priority group.[17]

Some authors have reported that the estimated influenza vaccination coverage among the elderly in 2004–05 was 77.2–79.9%.[18, 19] While this result surpassed the KCDC's goal, some discrepancies in coverage rate were observed between different groups within the elderly and thus efforts to achieve better coverage for specific groups, such as those with low-household income, and smokers, are still needed.[17] In other countries, many authors also report that such discrepancies also exist within their population.[20-29] To improve coverage among underrepresented populations, factors hindering vaccination acceptance should be identified and addressed.

Worldwide, acceptance of influenza vaccination across all age groups has been found to be associated with numerous factors, such as gender, age, educational level, marital status, and regency of the last health check-up.[24, 29-39] Similarly, in South Korea, some previous studies have identified vaccination rates being influenced by these same factors.[17-19] However, it appears that few studies have examined the nationwide elderly population of South Korea. Therefore, using the KNHANES IV (the Fourth Korean National Health and Nutrition Examination Survey), our study aimed to find determinants associated with influenza vaccination coverage within the elderly population and to address the limitations of Korea's ongoing vaccination campaign strategy.

METHODS

Study Population

In this study, we used data obtained from the KNHANES IV (2007–2009) conducted by the Korean Centres for Disease Control and Prevention (KCDC). It is a nationwide survey representing the general population of Korea by population-based random sampling of 24,870 individuals across 600 national districts.[21] The survey design includes stratified multistage probability sampling and includes comprehensive information on health status, health behaviour, quality of life and socio-demographics. After gaining informed consent, each survey respondent is interviewed face-to-face in their home by trained interviewers.

From the source population of 24,871 individuals who participated in KNHANES IV, we first excluded the 20,799 individuals who were aged less than 65 years at the time of the survey. We then excluded 211 individuals whose responses to the study variables were missing. Lastly, we excluded 294 individuals who responded "unknown" to any of the study variables. This left a study population of 3,567. (Fig. 1) As the survey data used are publicly available, this study did not require the ethical approval of the Institutional Review Board.

Study Variables

In the survey, influenza vaccination status was indicated by a single question "Have you been vaccinated against influenza during the past 12 months?" and its answer (yes/no) was used as the dependent variable in our study. To identify possible factors associated with the influenza vaccination coverage we categorized survey variables into four groups and we chose potentially relevant variables for each group. (Fig. 2) The four groups and their variables are as follows:

(1) socio-demographics factors (age, sex, educational level, household income, and marital status), (2) health behavioural risk factors (smoking status, alcohol consumption, and physical activity level), (3) health status and accessibility factors (self-reported health status, a history of health screening in the past

2 years, and a limitation in daily activities), and (4) psychological factors (the EuroQoL[40, 41], stress, and self-perceived depressive mood). We studied psychological factors because, although previous studies indicate that mental illness can affect vaccination coverage[42, 43], very few previous papers that studied the determinants of influenza vaccination investigated the effects of different psychological factors.

Statistical Analysis

We used univariate logistic regression to explore which factors of socio-demographics, behavioural risk, health status and accessibility, quality of life, and mental status were associated with an individual's influenza vaccination status. After a univariate logistic regression analysis, we used a multivariate logistic analysis that included variables with a p-value of less than 0.2 in the univariate study. The adjusted odds ratio (aOR) and 95% confidence intervals (95% CI) were calculated to show the strength of each association. A p-value of <0.2 was considered significant. All statistical analyses were performed using Stata 12.0 (Stata Corp., College Station, Texas, USA).[44]

RESULTS

The socio-demographic characteristics of the study population are summarised in Table 1. The population was equally divided into three age groups (65–69, 70–74, and ≥75 years). More females than males participated in the survey (40.7% men, 59.3% women) and around three-quarter of subjects were poorly educated (fewer than 6 years of formal education) (75.7%). Categorising household income into two groups (those earn < 1 million won/month and those earn ≥ 1 million won/month) divided the sample into about two approximately equal groups and more subjects lived without spouse than lived with one. Additionally most people were not current smokers, drank little alcohol, and never exercised. In terms of health status and accessibility, most people reported that they feel unhealthy and most had not undergone a recent health screening. Generally, people had high scores in the EuroQoL Visual Analogue System (VAS) and reported that they frequently felt stressed and had recently felt that their mood had been depressive.

The univariate logistic analysis of factors associated with influenza vaccination status is presented in Table 2. We found that people were more likely to be vaccinated as they aged (70.3% for 65–69 versus 79.3% for ≥75 years) and when they categorized themselves as unhealthy (78.1% for those who reported themselves as unhealthy versus 73.4% for those who reported themselves as healthy). Smokers showed the lowest vaccination coverage with only 69.3% choosing vaccination. In contrast, the group who had recently undergone health screening showed the highest rate of vaccination (81.9%). Individuals who seldom engaged in physical activity showed lower vaccination rates than individuals from other physical activity levels. No significant associations with psychological factors were observed. In the univariate study, the factors that correlated most strongly with vaccination coverage were recent history of health screening (OR 2.11), age (OR 1.61 for ≥75 and 1.57 for 70–74 years old), and moderate physical activity (OR 1.33). While most factors were more or less correlated with vaccination coverage, psychological factors were not strongly associated with vaccination status.

The multivariate logistic regression analysis is presented in Table 3 and shows chosen variables with a p-value less than 0.2 in the univariate study. All factors showed p-values less than 0.2, suggesting that variables were not significantly correlated with each other. The results of the multivariate analysis were generally similar to that of the univariate study, and showed that the factors with the two highest aOR's were age (2.06 for 70–74 years old) and recent history of health screening (2.26). The factor with the lowest aOR was current smoking status (0.78).

DISCUSSION

This study aimed to identify which factors are associated with recent vaccination against influenza within Korea via the results of the representative sample of the Korean population by the KNHANES. The influenza vaccination coverage rate in 2007–2009 among the elderly in Korea was 75.8%. This result is above both the Korea Centre for Disease Control and Prevention (KCDC) goal of 60%[17] and World Health Organisation (WHO) goal of 75% vaccination coverage among the elderly by 2010.[4] However, while the overall vaccination rate among the elderly surpasses these targets, certain populations—such as the younger elderly (70.3% in 65–69 years old), those living alone (74.6%), smokers (69.3%), frequent drinkers (73.5%), those lacking physical activity (74.5%), and those regarding themselves as healthy (73.4%)–showed lower vaccination coverage than the WHO recommends. This indicates an uneven distribution of vaccination coverage within the elderly population.

Socio-demographic factors

Vaccination coverage increased with age, which together with education, household income, and the status of living alone, is a factor that is well known to affect vaccination status. [11, 14, 30, 33, 34] This suggests that future health policies should concentrate on encouraging younger groups to reach the WHO vaccination-rate goal. Living alone reduces vaccination coverage whereas high household income leads to more coverage. It is natural to think that higher education and household wealth ensure not only better social status but also better access to health services. However, for those with high education and high incomes, living alone may reduce their chances of choosing vaccination. Therefore, healthcare professionals should in particular focus on the elderly who live alone.

Health behavioral risks

Smoking and alcohol consumption are again well-studied variables that negatively influence vaccination coverage.[17, 30, 34] In this study smoking was the most negatively influencing factor (aOR 0.78). This

implies that smokers among the elderly are the least protected population even though they are one of the highest-risk groups facing influenza infection. It is possible that smoking may indicate a low interest in personal health and that same disinterest may lead to a lack of interest in vaccination. The same tendency is observed for those who frequently consume alcohol. Therefore, healthcare professionals should encourage such people to think about their health and vaccination.

Health status and accessibility

A history of recent health screening was the factor most positively associated with vaccination (aOR 2.26). In contrast, a self-perception of health was the factor most negatively associated with vaccination (aOR 0.79). Previous studies have clearly demonstrated that vaccination rates can be increased through health screening or recommendations from doctors.[34] Our results suggest that many elderly people who regard themselves as healthy are not motivated to have a vaccination unless they are encouraged to by a visit to a physician. The positive effects of health screening on vaccination coverage may be due to the national health policy to provide free influenza vaccinations to the vulnerable elderly at public health centres.[18] Since the National Cancer Screening Program of the National Cancer Centre in Korea targets the elderly, it is also possible that people who used this service received a recommendation from a physician to accept an influenza vaccine. Thus, healthcare professionals should be reminded that a recommendation from a physician is one of the most successful strategies for improving vaccination coverage among the elderly.

Psychological factors

According to Lorenz et al., the vaccination rate among the mentally ill population is lower than in the general population.[43] This suggested that psychological factors, such as a stressed or depressive mood, might be associated with vaccination coverage. However, in our study, no psychological variables—including being stressed, a depressive mood, or the respondent's perceived quality of life—were

significantly associated with vaccination coverage. Therefore, it is possible that mental health may have a very limited effect on vaccination.

CONCLUTION

Although the influenza vaccination rate among the elderly in Korea reached the WHO target coverage rate, more effort should be made to increase the vaccination rate in underrepresented people, such as those with low household income, those who live alone, smokers, people who frequently consume alcohol, and (in particular) people who have not recently undergone a health screening. For health professionals, this study may help to guide the design of a better strategy to encourage influenza vaccination among the elderly.

CONTRIBUTORSHIP STATEMENT

SMP conceptualised the study. DSK conducted statistical analysis and wrote the first draft of the manuscript. All authors contributed to interpretation of results and revisions of the manuscript.

COMPETING INTERESTS

There are no competing interests

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No additional data are available.

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Table 1. Characteristics of the study population, The Fourth Korean National Health and Nutrition Examination Survey 2007–2009 (n=3,567)

Variable		n	%
Socio-demographics			
Age (years)	65–69	1,326	37.2
	70–74	1,122	31.4
	≥75	1,119	31.4
Gender	Male	1,450	40.7
	Female	2,117	59.3
Education level	Elementary school (≤ 6 years)	2,700	75.7
	More than elementary school	867	24.3
Household income	< 1 million won per month	1,648	46.2
	≥ 1 million won per month	1,919	53.8
Marital status[1]	Living with spouse	2,233	62.6
	Living without spouse	1,334	37.4
Health behavioral risks			
Smoking	Not current or never smoker	3,046	85.4
	Current smoker	521	14.6
Alcohol	Less than once per month or never tried	2,442	68.5
	More than once per month	1,125	31.5
Physical activity level	Never	2,398	67.2
	More than once per week	743	20.8
	Everyday	426	12.0
Health status and accessibility			
Self-reported health status	Unhealthy	1,583	44.4
	Fair	847	23.7
	Healthy	1,137	31.9
History of health screening[2]	No	1,598	44.8
	Yes	1,969	55.2
Limitation in daily activities	No	1,974	55.3
	Yes	1,593	44.7
Psychological factors			
EuroQoL in VAS	≤30	304	8.5
	31-60	1,171	32.8
	≥61	2,092	58.7
Stress	Frequently	2,706	75.9
	Rarely	861	24.1
Depressive mood[3]	Frequently	2,805	78.6
	Rarely	762	21.4

Abbreviations: VAS: visual analogue scale

[1] The term ‘spouse’ refers to an individual who is legally married, or cohabiting, and ‘without spouse’ refers to an individual who is single, divorced, or separated

[2] The health screening refers to national health-care services conducted within 2 years

[3] Depressive mood lasted longer than 2 weeks in a year

Table 2. Factors associated with influenza vaccination status in univariate logistic regression analysis (n=3,567)

Variable	Vaccinated %	Univariate	
		OR (95%CI)	p-value
Socio-demographics			
Age (years)			
65–69	70.3	1.0 (referent)	
70–74	78.8	1.57 (1.30-1.89)	< 0.001
≥75	79.3	1.61 (1.34-1.95)	< 0.001
Gender			
Male	75.0	1.0 (referent)	
Female	76.3	1.07 (0.92-1.25)	0.391
High education[1]	77.9	1.16 (0.97-1.40)	0.101
High household income[2]	76.9	1.14 (0.98-1.33)	0.087
Living alone[3]	74.6	0.90 (0.77-1.06)	0.2
Health behavioral risks			
Current smoking	69.3	0.68 (0.55-0.83)	< 0.001
Frequent drinking[4]	73.5	0.84 (0.71-0.98)	0.032
Physical activity level			
Never	74.5	1.0 (referent)	
More than once per week	79.5	1.33 (1.09-1.63)	0.005
Everyday	76.5	1.11 (0.88-1.42)	0.37
Health status and accessibility			
Self-reported health status			
Unhealthy	78.1	1.0 (referent)	
Fair	74.5	0.82 (0.67-0.99)	0.042
Healthy	73.4	0.77 (0.65-0.92)	0.005
History of health screening[5]	81.9	2.11 (1.81-2.47)	< 0.001
Limitation in daily activities	78.0	1.24 (1.06-1.45)	0.006
Psychological factors			
High EuroQoL: VAS			
≤30	75.7	1.0 (referent)	
31-60	77.1	1.08 (0.81-1.46)	0.592

≥61	75.0	0.97 (0.73-1.28)	0.818
Stressed	74.3	0.90 (0.76-1.08)	0.256
Frequent depressive mood	74.9	0.94 (0.78-1.14)	0.54

Abbreviations: OR: odds ratio, CI: confidence interval, VAS: visual analogue scale

[1] 'Well education' refers to those studied in elementary school

[2] 'High household income' refers to the income more than 1 million won per month

[3] 'Living alone' refers to an individual who is single, divorced, or separated

[4] Frequent drinking is defined by drinking more than once per week

[5] The health screening refers to national health-care services conducted within 2 years

[6] Depressive mood lasted longer than 2 weeks in a year

Table 3. Factors associated with influenza vaccination status in multivariate logistic regression analysis (n=3,567).

Variable	Vaccinated %	Multivariate	
		aOR (95%CI)	p-value
Socio-demographics			
Age (years)			
65–69	70.3	1.0 (referent)	
70–74	78.8	1.79 (1.48-2.17)	< 0.001
≥75	79.3	2.06 (1.68-2.52)	< 0.001
High education[1]	77.9	1.27 (1.03-1.57)	0.025
High household income[2]	76.9	1.13 (0.96-1.33)	0.143
Living alone[3]	74.6	0.82 (0.68-1.00)	0.045
Health behavioral risks			
Current smoking	69.3	0.78 (0.62-0.98)	0.03
Frequent drinking[4]	73.5	0.86 (0.72-1.04)	0.124
Physical activity level			
Never	74.5	1.0 (referent)	
More than once per week	79.5	1.29 (1.05-1.59)	0.017
Health status and accessibility			
Self-reported health status			
Unhealthy	78.1	1.0 (referent)	
Fair	74.5	0.85 (0.68-1.06)	0.144
Healthy	73.4	0.79 (0.64-0.97)	0.025
History of health screening[5]	81.9	2.26 (1.92-2.66)	< 0.001
Limitation in daily activities	78.0	1.18 (0.99-1.41)	0.072

Abbreviations: aOR: adjusted odds ratio, CI: confidence interval, VAS: visual analogue scale

[1] 'High education' refers to those studied in elementary school

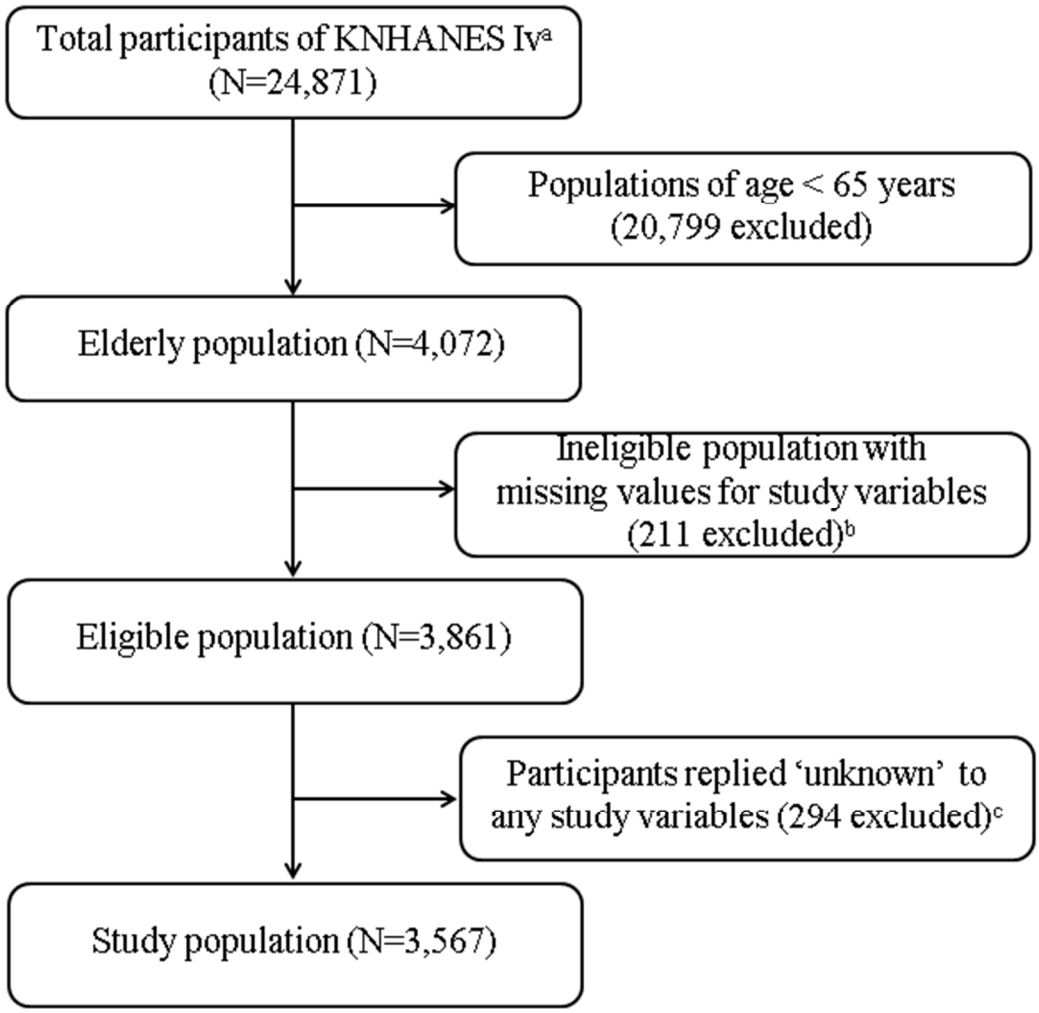
[2] 'High household income' refers to the income more than 1 million won per month

[3] 'Living alone' refers to an individual who is single, divorced, or separated

[4] Frequent drinking is defined by drinking more than once per week

[5] The health screening refers to national health-care services conducted within 2 years

Figure 1. The study population framework

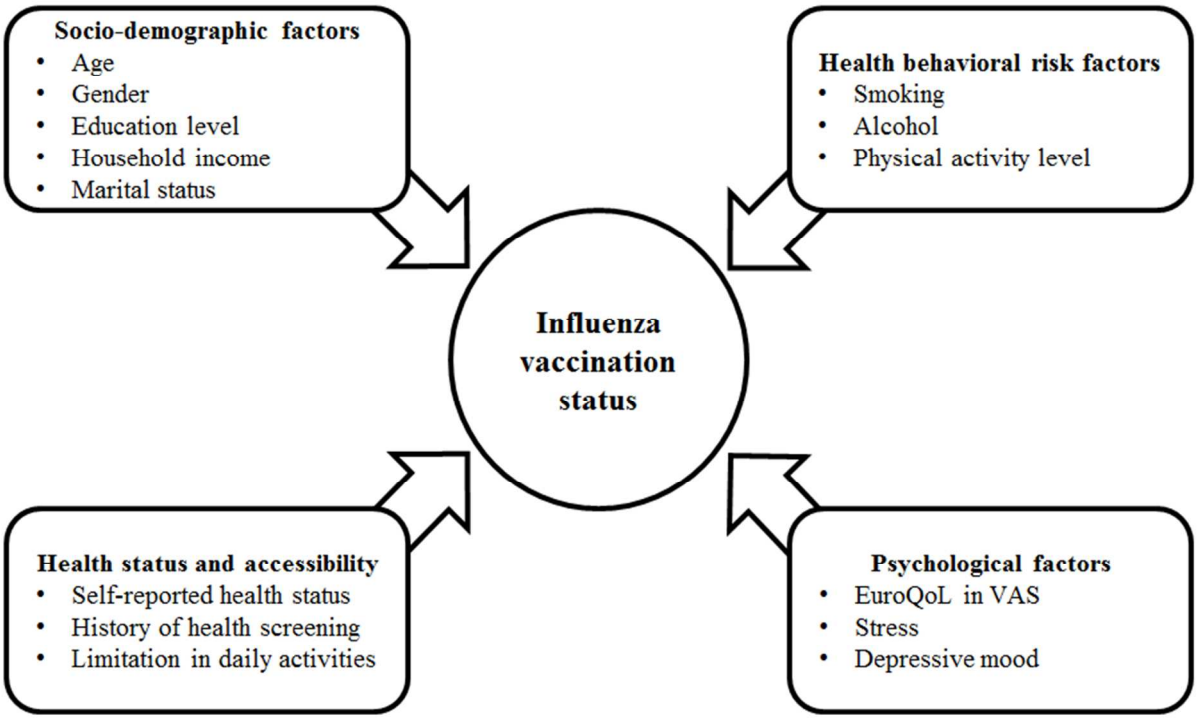


a The Fourth Korean National Health and Nutrition Examination Survey 2007–2009

b The number of non-responders for vaccination status was zero.

c The number of responders for vaccination status as "unknown" was zero.

Figure 2. Categorization of the study variables in this study



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 **[Within the title page 1 and method section of the abstract page 2]**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **[See results section of abstract page 2]**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **[page 4]**
Objectives	3	State specific objectives, including any prespecified hypotheses **[page 5]**
Methods		
Study design	4	Present key elements of study design early in the paper **[Methods page 6]**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **[page 6-7]**
Participants	6	(*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 **[page 6]**
		(*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	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **[page 6-7]**
Data sources/ measurement	8*	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 **[page 6]**
Bias	9	Describe any efforts to address potential sources of bias **[page 3]**
Study size	10	Explain how the study size was arrived at **[page 6 and Figure 1]**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **[page 6 and Figure 2]**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **[page 7]**
		(*b*) Describe any methods used to examine subgroups and interactions **[page 6-7]**
		(*c*) Explain how missing data were addressed **[N/A]**
		(*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 **[page 6 and Figure 1]**
		(*e*) Describe any sensitivity analyses **[N/A]**

Continued on next page

Results		
Participants	13*	(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 **[page 6 and Figure 1 page 24]**
		(b) Give reasons for non-participation at each stage **[page 6 and Figure 1]**
		(c) Consider use of a flow diagram **[Figure 1]**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **[Page 8 and Table 1]**
		(b) Indicate number of participants with missing data for each variable of interest **[Figure 1]**
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) **[]**
Outcome data	15*	*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 **[Table 2,3]**
Main results	16	(*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 **[Page 8-9 and Table 2,3]**
		(*b*) Report category boundaries when continuous variables were categorized **[Table 1,2,3]**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **[N/A]**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **[N/A]**
Discussion		
Key results	18	Summarise key results with reference to study objectives **[Page 8 and Table 1,2,3]**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **[Page 2]**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **[Page 10-13]**
Generalisability	21	Discuss the generalisability (external validity) of the study results **[Page 2 and 13]**
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 **[N/A]**

*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.

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Factors associated with influenza vaccination coverage among the elderly in South Korea: The Fourth Korean National Health and Nutrition Examination Survey (KNHANES IV)

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Factors associated with influenza vaccination coverage among the elderly in South Korea: The Fourth Korean National Health and Nutrition Examination Survey (KNHANES IV)

David Soonil Kwon[a], Kyuwoong Kim[c], Sang Min Park, MD, PhD[b,c, *]

Affiliations:

[a] Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea

[b] Department of Family Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea

[c] Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, South Korea

*** Correspondence to:** Sang Min Park, MD, PhD

Department of Family Medicine & Department of Biomedical Sciences, Seoul National University College of Medicine, 28 Yunkeon-dong, Jongro-gu, Seoul 110-744, South Korea

Tel: +82-2-2072-3331 Fax: +82-2-766-3276

E-mail: smpark.snuh@gmail.com

Disclosure of Conflicts of Interest: None reported.

ABSTRACT

Objective: The annual outbreak of influenza is one of the major causes of both morbidity and mortality among the elderly population around the world. While there is an annual vaccine available to prevent or reduce the incidence of disease, not all older people in Korea choose to be vaccinated. There have been few previous studies to examine the factors influencing influenza vaccination in Korea. Thus this study identifies nationwide factors that affect influenza vaccination rates in elderly Koreans.

Methods: We obtained data from the Fourth Korean National Health and Nutrition Examination Survey 2007–2009 (KNHANES IV), a nationwide health survey in Korea. To assess influenza vaccination status we analysed answers to a single question from the survey. From the respondents, we selected 3,567 elderly population aged 65 years or older, to analyse the effects of variables including socio-demographic, health behavioural risk, health status, and psychological factors on vaccination coverage. We identified factors that affect vaccination status using multiple logistic regression analysis.

Results: The rate of influenza vaccination in this elderly population was 75.8%. Overall, the most significant determinants for choosing influenza vaccination were a recent history of health screening (adjusted odds ratio, aOR 2.26, 95% CI: 1.92–2.66) and smoking (aOR 0.78, 95% CI: 0.62–0.98). Other contributing factors were age, household income, marital status, alcohol consumption, physical activity level, a self-reported health status, and a limitation in daily activities. In contrast, psychological factors, including self-perceived quality of life, stress, and depressive mood, did not show close association with vaccination coverage.

Conclusion: To boost influenza vaccination rates in the elderly, an influenza campaign should focus on underrepresented groups, especially smokers. Additionally, promoting routine health screening for the elderly may be an efficient way to help achieve higher vaccination rates. Our results highlight the need for a new strategy in the vaccination campaign.

Keywords: influenza, vaccination, elderly, factors

STRENGTHS AND LIMITATIONS

- Cross-sectional study with a sample size of 3,567 collected from a national health survey.
- Assessment of nationwide factors associated with influenza vaccination in elderly population.
- Main limitations include a possible recall bias and having no further verification of vaccination status.

INTRODUCTION

Influenza is a highly contagious, viral, acute respiratory illness associated with elevated morbidity and mortality particularly, among high-risk individuals, including the elderly and those with underlying chronic diseases.[1-3] The influenza mortality may be underestimated since influenza is not commonly recognised as a cause of mortality in the elderly.[4-6] Even though it is, around 90% of the influenza mortality occurs in people aged 65 years and older.[7] This suggests that the elderly is one of the groups with the highest risk for serious complications in influenza.

Many studies have documented that the influenza vaccination is a safe and cost-effective way of preventing influenza and pneumonia in both the elderly and in children.[8-12] Annual influenza vaccinations have been shown to significantly reduce hospitalisations and mortality in older population.[13, 14] For this reason, the World Health Assembly encourage member states to increase influenza vaccination coverage for high-risk populations to 50% by 2006 and 75% by 2010.[15] Additionally, the United States department of Health and Human Services (HHS) targeted a minimum vaccination rate of 90% for people aged 65 years and older in 2010.[16] In South Korea, the Korea Centres for Disease Control and Prevention (KCDC) clearly recommends that annual influenza vaccinations are encouraged for all people aged 65 or older and aimed to achieve a vaccination coverage greater than 60% for this priority group.[17]

Some authors have reported that the estimated influenza vaccination coverage among the elderly in 2004–05 was 77.2–79.9%.[18, 19] While this result surpassed the KCDC's goal, some discrepancies in coverage rate were observed between different groups within the elderly and thus efforts to achieve better coverage for specific groups, such as those with low-household income, and smokers, are still needed.[17] In other countries, many authors also report that such discrepancies also exist within their population.[20-29] To improve coverage among underrepresented populations, factors hindering vaccination acceptance should be identified and addressed.

Worldwide, acceptance of influenza vaccination across all age groups has been found to be associated with numerous factors, such as gender, age, educational level, marital status, and regency of the last health check-up.[24, 29-39] Similarly, in South Korea, some previous studies have identified vaccination rates being influenced by these same factors.[17-19] However, it appears that few studies have examined the nationwide elderly population of South Korea. Therefore, using the KNHANES IV (the Fourth Korean National Health and Nutrition Examination Survey), our study aimed to find determinants associated with influenza vaccination coverage within the elderly population and to address the limitations of Korea's ongoing vaccination campaign strategy.

METHODS

Study Population

In this study, we used data obtained from the KNHANES IV (2007–2009) conducted by the Korean Centres for Disease Control and Prevention (KCDC). It is a nationwide survey representing the general population of Korea by population-based random sampling of 24,870 individuals across 600 national districts. For constructing the study sample in KNHANES IV, they carefully chose multiple households that represent their district via systematic sampling. And those chosen households received an informed consent. Any family member from the chosen household was invited to interviewers and the survey was done. Since this requires respondents to visit the interviewers during daytime, there might be a significant gender bias since housewives are easier to visit the interviewers. This gender bias has been shown in Table 1 (Male 40.7% vs. female 59.3%). The gender bias suggests women have more feasibility to participate in this survey.

The survey design includes stratified multistage probability sampling and includes comprehensive information on health status, health behaviour, quality of life and socio-demographics. After gaining informed consent, each survey respondent is interviewed face-to-face in their home by trained interviewers.

From the source population of 24,871 individuals who participated in KNHANES IV, we first excluded the 20,799 individuals who were aged less than 65 years at the time of the survey. We then excluded 211 individuals whose responses to the study variables were missing. Lastly, we excluded 294 individuals who responded “unknown” to any of the study variables. This left a study population of 3,567. (Fig. 1) As the survey data used are publicly available, this study did not require the ethical approval of the Institutional Review Board.

Study Variables

In the survey, influenza vaccination status was indicated by a single question "Have you been vaccinated against influenza during the past 12 months?" and its answer (yes/no) was used as the dependent variable in our study. To identify possible factors associated with the influenza vaccination coverage we categorized survey variables into four groups and we chose potentially relevant variables for each group. (Fig. 2) The four groups and their variables are as follows:

(1) socio-demographics factors (age, sex, educational level, household income, and marital status), (2) health behavioural risk factors (smoking status, alcohol consumption, and physical activity level), (3) health status and accessibility factors (self-reported health status, a history of health screening in the past 2 years, and a limitation in daily activities), and (4) psychological factors (the EuroQoL[40, 41], stress, and self-perceived depressive mood). We studied psychological factors because, although previous studies indicate that mental illness can affect vaccination coverage[42, 43], very few previous papers that studied the determinants of influenza vaccination investigated the effects of different psychological factors.

Statistical Analysis

We used univariate logistic regression to explore which factors of socio-demographics, behavioural risk, health status and accessibility, quality of life, and mental status were associated with an individual's influenza vaccination status. After a univariate logistic regression analysis, we used a multiple logistic analysis .The adjusted odds ratio (aOR) and 95% confidence intervals (95% CI) were calculated to show the strength of each association. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using Stata 12.0 (Stata Corp., College Station, Texas, USA).[44]

RESULTS

The socio-demographic characteristics of the study population are summarised in Table 1. The population was equally divided into three age groups (65–69, 70–74, and ≥75 years). More females than males participated in the survey (40.7% men, 59.3% women) and around three-quarter of subjects were poorly educated (fewer than 6 years of formal education) (75.7%). Categorising household income into two groups (those earn < 1,000 USD/month and those earn ≥ 1,000 USD/month) divided the sample into about two approximately equal groups and more subjects lived without spouse than lived with one. Additionally most people were not current smokers, drank little alcohol, and never exercised. In terms of health status and accessibility, most people reported that they feel unhealthy and most had not undergone a recent health screening. Generally, people had high scores in the EuroQoL Visual Analogue System (VAS) and reported that they frequently felt stressed and had recently felt that their mood had been depressive.

The univariate logistic analysis of factors associated with influenza vaccination status is presented in Table 2. We found that people were more likely to be vaccinated as they aged (70.3% for 65–69 versus 79.3% for ≥75 years) and when they categorized themselves as unhealthy (78.1% for those who reported themselves as unhealthy versus 73.4% for those who reported themselves as healthy). Smokers showed the lowest vaccination coverage with only 69.3% choosing vaccination. In contrast, the group who had recently undergone health screening showed the highest rate of vaccination (81.9%). Individuals who seldom engaged in physical activity showed lower vaccination rates than individuals from other physical activity levels. No significant associations with psychological factors were observed. In the univariate study, the factors that correlated most strongly with vaccination coverage were recent history of health screening (Vaccinated Percentage 81.9%, OR 2.11, 95% CI: 1.81-2.47), age (Vaccinated Percentage 79.3%, OR 1.61, 95% CI: 1.34-1.95 for ≥75 and Vaccinated Percentage 78.8%, OR 1.57, 95% CI: 1.30-1.89 for 70–74 years old), and moderate physical activity (Vaccinated Percentage 79.5%, OR 1.33, 95% CI:1.09-1.63).

The multiple logistic regression analysis is presented in Table 3. The results of the multiple logistic regression analysis were generally similar to that of the univariate study, and showed that the factors with the two highest aOR's were age (2.06, 95% CI: 1.68-2.52 for 70–74 years old) and recent history of health screening (2.26, 95% CI: 1.92-2.66). The factor with the lowest aOR was current smoking status (0.78, 95% CI: 0.62-0.98).

DISCUSSION

This study aimed to identify which factors are associated with recent vaccination against influenza within Korea via the results of the representative sample of the Korean population by the KNHANES. The influenza vaccination coverage rate in 2007–2009 among elderly Koreans was 75.8%. This result is above both the Korea Centre for Disease Control and Prevention (KCDC) goal of 60%[17] and World Health Organisation (WHO) goal of 75% vaccination coverage among the elderly by 2010.[4] However, while the overall vaccination rate among the elderly surpasses these targets, certain populations—such as the younger elderly (70.3% in 65–69 years old), those living alone (74.6%), smokers (69.3%), frequent drinkers (73.5%), those lacking physical activity (74.5%), and those regarding themselves as healthy (73.4%)–showed lower vaccination coverage than the WHO recommends. This indicates an uneven distribution of vaccination coverage within the elderly population.

Socio-demographic factors

Vaccination coverage increased with age, which together with education, household income, and the status of living alone, is a factor that is well known to affect vaccination status. [11, 14, 30, 33, 34] This suggests that future health policies should concentrate on encouraging younger groups to reach the WHO vaccination-rate goal. Living alone reduces vaccination coverage whereas high household income leads to more coverage. It is natural to think that higher education and household wealth ensure not only better social status but also better access to health services. However, for those with high education and high incomes, living alone may reduce their chances of choosing vaccination. Therefore, healthcare professionals should in particular focus on the elderly who live alone.

Health behavioral risks

In this study smoking was the most negatively influencing factor (aOR 0.78, 95% CI: 0.62-0.98). Smoking and alcohol consumption are again well-studied variables that negatively influence vaccination

coverage. [17, 30, 34] This implies that smokers among the elderly are the least protected population even though they are one of the highest-risk groups facing influenza infection. In theory, smokers naturally could have more pulmonary complications than non-smokers such as Chronic Obstructive Pulmonary Disease (COPD), lung cancer, or pneumonia. And it is legitimate to think the people with more comorbidities have a higher chance to visit hospitals and receive vaccination recommendations. But our study showed an opposite result. The same tendency is observed for those who frequently consume alcohol. Therefore, healthcare professionals should encourage such people to get vaccinations.

Health status and accessibility

A history of recent health screening was the factor most positively associated with vaccination (aOR 2.26, 95% CI: 1.68-2.52). In contrast, a self-perception of health was the factor most negatively associated with vaccination (aOR 0.79, 95% CI: 0.64-0.97). Previous studies have clearly demonstrated that vaccination rates can be increased through health screening or recommendations from doctors [34]. Our results suggest that many elderly people who regard themselves as healthy are not motivated to have a vaccination unless they are encouraged to by a visit to a physician. The positive effects of health screening on vaccination coverage may be due to the national health policy to provide free influenza vaccinations to the vulnerable elderly at public health centres [18]. Since the National Cancer Screening Program of the National Cancer Centre in Korea targets the elderly, it is also possible that people who used this service received a recommendation from a physician to accept an influenza vaccine. Thus, healthcare professionals should be reminded that a recommendation from a physician is one of the most successful strategies for improving vaccination coverage among the elderly.

We thought further major possible factors that could influence vaccination status include the distance between respondent's residence and the nearest medical centre. It is because the distance to get to hospitals influences the hospital accessibility. Since we found the most important factor regarding to the

vaccination rate was the recent history of health screening, the shorter distance to get to medical centres possibly affects to the higher vaccination rate. Unfortunately, the distance between respondent's residence and the nearest medical centre was not included in the survey and we couldn't evaluate on this.

Psychological factors

According to Lorenz et al., the vaccination rate among the mentally ill population is lower than in the general population [43]. This suggested that psychological factors, such as a stressed or depressive mood, might be associated with vaccination coverage. In our study, no psychological variables—including being stressed, a depressive mood, or the respondent's perceived quality of life—were significantly associated with vaccination coverage. This discrepancy might be due to a cultural difference between study sites, the willingness of respondents to report mental illness, limitations of sample size among the non-vaccinated population, or other factors not considered in the multivariable model.

LIMITATIONS

In our study, there are some following limitations. Firstly, some respondents of KHNANES IV were interviewed during summer and this might lead to a recall bias since most vaccination campaign generally conducted during a couple of months in autumn. The respondent who had vaccination in the last autumn possibly forgot their vaccination status at the time of the survey if this time gap increases. Therefore, the vaccination rate possibly be underestimated. Also, the collinearity between presumed independent variables were not examined thoroughly. And this might undermine the integrity of the result.

CONCLUSION

Although the influenza vaccination rate in elderly Koreans reached the WHO target coverage rate, more effort should be made to increase the vaccination rate in underrepresented people, such as those with low household income, those who live alone, smokers, people who frequently consume alcohol, and (in particular) people who have not recently undergone a health screening. For health professionals, this study may help to guide the design of a better strategy to encourage influenza vaccination among the elderly.

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CONTRIBUTORSHIP STATEMENT

Substantial contributions to the study design: Sang Min Park

Analysis of data: David Soonil Kwon

Interpretation of data for the work: All authors

Drafting the work or revising it critically for important intellectual content: All authors

Final approval of the version to be published: Sang Min Park

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately resolved: All authors

COMPETING INTERESTS

None to declare.

FUNDING

This study has no funding to report.

DATA SHARING STATEMENT

No additional data available.

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Table 1. Characteristics of the study population, The Fourth Korean National Health and Nutrition Examination Survey 2007–2009 (n=3,567)

Variable		n	%
Socio-demographics			
Age (years)	65–69	1,326	37.2
	70–74	1,122	31.4
	≥75	1,119	31.4
Gender	Male	1,450	40.7
	Female	2,117	59.3
Education level	Elementary school (≤ 6 years)	2,700	75.7
	More than elementary school	867	24.3
Household income[1]	< 1,000 USD per month	1,648	46.2
	≥ 1,000 USD per month	1,919	53.8
Marital status[2]	Living with spouse	2,233	62.6
	Living without spouse	1,334	37.4
Health behavioral risks			
Smoking	Not current or never smoker	3,046	85.4
	Current smoker	521	14.6
Alcohol	Less than once per month or never tried	2,442	68.5
	More than once per month	1,125	31.5
Physical activity level	Never	2,398	67.2
	More than once per week	743	20.8
	Everyday	426	12.0
Health status and accessibility			
Self-reported health status	Unhealthy	1,583	44.4
	Fair	847	23.7
	Healthy	1,137	31.9
History of health screening[3]	No	1,598	44.8
	Yes	1,969	55.2
Limitation in daily activities	No	1,974	55.3
	Yes	1,593	44.7
Psychological factors			
EuroQoL in VAS	≤30	304	8.5
	31-60	1,171	32.8
	≥61	2,092	58.7
Stress	Frequently	2,706	75.9
	Rarely	861	24.1
Depressive mood[4]	Frequently	2,805	78.6
	Rarely	762	21.4

Abbreviations: VAS: visual analogue scale

[1] 1,000 U.S Dollar=1 Million Korean Won (1USD=1,000 KRW)

[2] The term 'spouse' refers to an individual who is legally married, or cohabiting, and 'without spouse' refers to an individual who is single, divorced, or separated

[3] The health screening refers to national health-care services conducted within 2 years

[4] Depressive mood lasted longer than 2 weeks in a year

Table 2. Factors associated with influenza vaccination status in univariate logistic regression analysis (n=3,567)

Variable	Vaccinated %	Univariate	
		OR (95%CI)	p-value
Socio-demographics			
Age (years)			
65–69	70.3	1.0 (referent)	
70–74	78.8	1.57 (1.30-1.89)	< 0.001
≥75	79.3	1.61 (1.34-1.95)	< 0.001
Gender			
Male	75.0	1.0 (referent)	
Female	76.3	1.07 (0.92-1.25)	0.391
High education[1]	77.9	1.16 (0.97-1.40)	0.101
High household income[2]	76.9	1.14 (0.98-1.33)	0.087
Living alone[3]	74.6	0.90 (0.77-1.06)	0.2
Health behavioral risks			
Current smoking	69.3	0.68 (0.55-0.83)	< 0.001
Frequent drinking[4]	73.5	0.84 (0.71-0.98)	0.032
Physical activity level			
Never	74.5	1.0 (referent)	
More than once per week	79.5	1.33 (1.09-1.63)	0.005
Everyday	76.5	1.11 (0.88-1.42)	0.37
Health status and accessibility			
Self-reported health status			
Unhealthy	78.1	1.0 (referent)	
Fair	74.5	0.82 (0.67-0.99)	0.042
Healthy	73.4	0.77 (0.65-0.92)	0.005
History of health screening[5]	81.9	2.11 (1.81-2.47)	< 0.001
Limitation in daily activities	78.0	1.24 (1.06-1.45)	0.006
Psychological factors			
High EuroQoL: VAS			
≤30	75.7	1.0 (referent)	
31-60	77.1	1.08 (0.81-1.46)	0.592

≥61	75.0	0.97 (0.73-1.28)	0.818
Stressed	74.3	0.90 (0.76-1.08)	0.256
Frequent depressive mood	74.9	0.94 (0.78-1.14)	0.54

Abbreviations: OR: odds ratio, CI: confidence interval, VAS: visual analogue scale

[1] 'Well education' refers to those studied in elementary school

[2] 'High household income' refers to the income more than 1 million won per month

[3] 'Living alone' refers to an individual who is single, divorced, or separated

[4] Frequent drinking is defined by drinking more than once per week

[5] The health screening refers to national health-care services conducted within 2 years

[6] Depressive mood lasted longer than 2 weeks in a year

Table 3. Factors associated with influenza vaccination status in multiple logistic regression analysis (n=3,567).

Variable	Vaccinated %	Multiple	
		aOR (95%CI)	p-value
Socio-demographics			
Age (years)			
65–69	70.3	1.0 (referent)	
70–74	78.8	1.79 (1.48-2.17)	< 0.001
≥75	79.3	2.06 (1.68-2.52)	< 0.001
High education[1]	77.9	1.27 (1.03-1.57)	0.025
High household income[2]	76.9	1.13 (0.96-1.33)	0.143
Living alone[3]	74.6	0.82 (0.68-1.00)	0.045
Health behavioral risks			
Current smoking	69.3	0.78 (0.62-0.98)	0.03
Frequent drinking[4]	73.5	0.86 (0.72-1.04)	0.124
Physical activity level			
Never	74.5	1.0 (referent)	
More than once per week	79.5	1.29 (1.05-1.59)	0.017
Health status and accessibility			
Self-reported health status			
Unhealthy	78.1	1.0 (referent)	
Fair	74.5	0.85 (0.68-1.06)	0.144
Healthy	73.4	0.79 (0.64-0.97)	0.025
History of health screening[5]	81.9	2.26 (1.92-2.66)	< 0.001
Limitation in daily activities	78.0	1.18 (0.99-1.41)	0.072

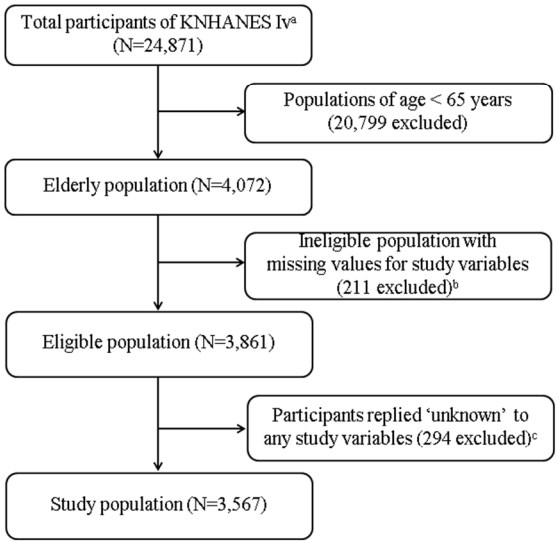
Abbreviations: aOR: adjusted odds ratio, CI: confidence interval, VAS: visual analogue scale

[1] 'High education' refers to those studied in elementary school

[2] 'High household income' refers to the income more than 1 million won per month

[3] 'Living alone' refers to an individual who is single, divorced, or separated

Figure 1. The study population framework



a The Fourth Korean National Health and Nutrition Examination Survey 2007–2009

b The number of non-responders for vaccination status was zero.

c The number of responders for vaccination status as "unknown" was zero.

Figure 1.The study population framework

209x297mm (300 x 300 DPI)

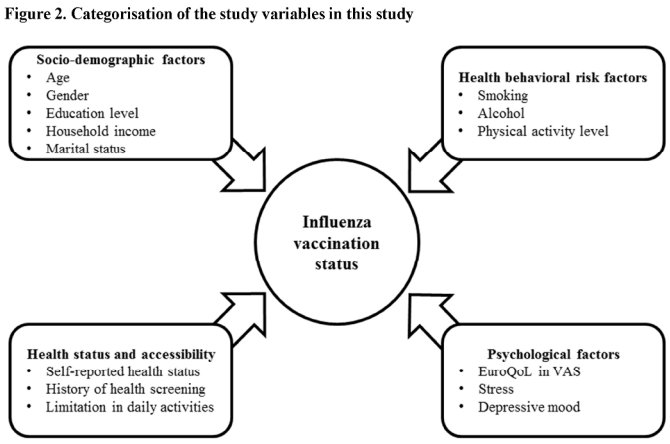


Figure 2. Categorisation of the study variables in this study

215x279mm (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 **[Within the title page 1 and method section of the abstract page 2]**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **[See results section of abstract page 2]**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **[page 4]**
Objectives	3	State specific objectives, including any prespecified hypotheses **[page 5]**
Methods		
Study design	4	Present key elements of study design early in the paper **[Methods page 6]**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **[page 6-7]**
Participants	6	(*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 **[page 6]**
		(*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	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **[page 6-7]**
Data sources/ measurement	8*	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 **[page 6]**
Bias	9	Describe any efforts to address potential sources of bias **[page 3]**
Study size	10	Explain how the study size was arrived at **[page 6 and Figure 1]**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **[page 6 and Figure 2]**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **[page 7]**
		(*b*) Describe any methods used to examine subgroups and interactions **[page 6-7]**
		(*c*) Explain how missing data were addressed **[N/A]**
		(*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 **[page 6 and Figure 1]**
		(*e*) Describe any sensitivity analyses **[N/A]**

Continued on next page

Results		
Participants	13*	(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 **[page 6 and Figure 1 page 24]**
		(b) Give reasons for non-participation at each stage **[page 6 and Figure 1]**
		(c) Consider use of a flow diagram **[Figure 1]**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **[Page 8 and Table 1]**
		(b) Indicate number of participants with missing data for each variable of interest **[Figure 1]**
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) **[]**
Outcome data	15*	*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 **[Table 2,3]**
Main results	16	(*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 **[Page 8-9 and Table 2,3]**
		(*b*) Report category boundaries when continuous variables were categorized **[Table 1,2,3]**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **[N/A]**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **[N/A]**
Discussion		
Key results	18	Summarise key results with reference to study objectives **[Page 8 and Table 1,2,3]**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **[Page 2]**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **[Page 10-13]**
Generalisability	21	Discuss the generalisability (external validity) of the study results **[Page 2 and 13]**
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 **[N/A]**

*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.

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Factors associated with influenza vaccination coverage among the elderly in South Korea: The Fourth Korean National Health and Nutrition Examination Survey (KNHANES IV)

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Factors associated with influenza vaccination coverage among the elderly in South Korea: The Fourth Korean National Health and Nutrition Examination Survey (KNHANES IV)

David Soonil Kwon[1], Kyuwoong Kim[2], Sang Min Park[2,3] *

Affiliations:

[1] Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea

[2] Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, South Korea

[3] Department of Family Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea

*** Correspondence to:** Sang Min Park, MD, MPH, PhD

Department of Family Medicine & Department of Biomedical Sciences, Seoul National University College of Medicine, 28 Yunkeon-dong, Jongro-gu, Seoul 110-744, South Korea

Tel: +82-2-2072-3331 Fax: +82-2-766-3276

E-mail: smpark.snuh@gmail.com

Disclosure of Conflicts of Interest: None reported.

ABSTRACT

Objective: The annual outbreak of influenza is one of the major causes of both morbidity and mortality among the elderly population around the world. While there is an annual vaccine available to prevent or reduce the incidence of disease, not all older people in Korea choose to be vaccinated. There have been few previous studies to examine the factors influencing influenza vaccination in Korea. Thus this study identifies nationwide factors that affect influenza vaccination rates in elderly Koreans.

Methods: We obtained data from the Fourth Korean National Health and Nutrition Examination Survey 2007–2009 (KNHANES IV), a nationwide health survey in Korea. To assess influenza vaccination status we analyzed answers to a single question from the survey. From the respondents, we selected 3,567 elderly population aged 65 years or older, to analyse the effects of variables including socio-demographic, health behavioural risk, health status, and psychological factors on vaccination coverage. We identified factors that affect vaccination status using a multiple logistic regression analysis.

Results: The rate of influenza vaccination in this elderly population was 75.8%. Overall, the most significant determinants for choosing influenza vaccination were a recent history of health screening (adjusted odds ratio, aOR 2.26, 95% CI: 1.92–2.66) and smoking (aOR 0.78, 95% CI: 0.62–0.98). Other contributing factors were age, household income, marital status, alcohol consumption, physical activity level, a self-reported health status, and a limitation in daily activities. In contrast, psychological factors, including self-perceived quality of life, stress, and depressive mood, did not show close association with vaccination coverage.

Conclusion: To boost influenza vaccination rates in the elderly, an influenza campaign should focus on underrepresented groups, especially smokers. Additionally, promoting routine health screening for the elderly may be an efficient way to help achieve higher vaccination rates. Our results highlight the need for a new strategy for the vaccination campaign.

Keywords: influenza, vaccination, elderly, factors

STRENGTHS AND LIMITATIONS

- The results of this study highlight potential factors associated with under-vaccination among the elderly, which has an important public health implication for improving vaccinations rates.
- Cross-sectional study with a sample size of 3,567 collected from a national health survey.
- Assessment of nationwide factors associated with influenza vaccination in elderly population.
- Main limitations include a possible recall bias and having no further verification of vaccination status.
- The generalisability of the study results might be limited due to the gender bias among the participants.

INTRODUCTION

Influenza is a highly contagious, viral, acute respiratory illness associated with elevated morbidity and mortality, particularly among high-risk individuals, including the elderly and those with underlying chronic diseases.[1-3] The influenza mortality may be underestimated since influenza is not commonly recognised as a cause of mortality in the elderly.[4-6] Despite this, around 90% of the influenza mortality occurs in people aged 65 years and older.[7] This suggests that the elderly is one of the groups with the highest risk for serious complications in influenza.

Many studies have documented that the influenza vaccination is a safe and cost-effective way of preventing influenza and pneumonia in both the elderly and in children.[8-12] Annual influenza vaccinations have been shown to significantly reduce hospitalisations and mortality in older population.[13, 14] For this reason, the World Health Assembly encourage member states to increase influenza vaccination coverage for high-risk populations to 50% by 2006 and 75% by 2010.[15] Additionally, the United States department of Health and Human Services (HHS) targeted a minimum vaccination rate of 90% for people aged 65 years and older in 2010.[16] In South Korea, the Korea Centres for Disease Control and Prevention (KCDC) clearly recommends that annual influenza vaccinations are encouraged for all people aged 65 or older and aimed to achieve a vaccination coverage greater than 60% for this priority group.[17]

Some authors have reported that the estimated influenza vaccination coverage among the elderly in 2004–05 was 77.2–79.9%.[18, 19] While this result surpassed the KCDC's goal, some discrepancies in coverage rate were observed between different groups within the elderly and thus efforts to achieve better coverage for specific groups, such as those with low household income, and smokers, are still needed.[17] In other countries, many authors also report that such discrepancies also exist within their populations.[20-29] To improve coverage among underrepresented populations, factors hindering vaccination acceptance should be identified and addressed.

Worldwide, acceptance of influenza vaccination across all age groups has been found to be associated with numerous factors, such as gender, age, educational level, marital status, and recency of the last health check-up. [24, 29-39] Similarly, in South Korea, some previous studies have identified vaccination rates being influenced by these same factors. [17-19] However, it appears that few studies have examined the nationwide elderly population of South Korea. Therefore, using the KNHANES IV (the Fourth Korean National Health and Nutrition Examination Survey), our study aimed to find determinants associated with influenza vaccination coverage within the elderly population and to address the limitations of Korea's ongoing vaccination campaign strategy.

METHODS

Study Population

In this study, we used data obtained from the KNHANES IV (2007–2009) conducted by the Korean Centres for Disease Control and Prevention (KCDC). It is a nationwide survey representing the general population of Korea by population-based random sampling of 24,870 individuals across 600 national districts. For constructing the study sample in KNHANES IV, they carefully chose multiple households that represent their district via systematic sampling. And those chosen households received an informed consent. The overall response rate of the KNAHANES IV was 78.4%. The survey design includes stratified multistage probability sampling and includes comprehensive information on health status, health behaviour, quality of life and socio-demographics. After gaining informed consent, each survey respondent is interviewed face-to-face in their home by trained interviewers. From the source population of 24,871 individuals who participated in KNHANES IV, we first excluded the 20,799 individuals who were aged less than 65 years at the time of the survey. We then excluded 211 individuals whose responses to the study variables were missing. Lastly, we excluded 294 individuals who responded "unknown" to any of the study variables. This left a study population of 3,567. (Fig. 1) As the survey data used are publicly available, this study did not require the ethical approval of the Institutional Review Board.

Study Variables

In the survey, influenza vaccination status was indicated by a single question "Have you been vaccinated against influenza during the past 12 months?" and its answer (yes/no) was used as the dependent variable in our study. To identify possible factors associated with the influenza vaccination coverage we categorized survey variables into four groups and we chose potentially relevant variables for each group. (Fig. 2) The four groups and their variables are as follows:

(1) socio-demographics factors (age, sex, educational level, household income, and marital status), (2) health behavioural risk factors (smoking status, alcohol consumption, and physical activity level), (3)

health status and accessibility factors (self-reported health status, a history of health screening in the past 2 years, and a limitation in daily activities), and (4) psychological factors (the EuroQoL[40, 41], stress, and self-perceived depressive mood). We studied psychological factors because, although previous studies indicate that mental illness can affect vaccination coverage[42, 43], very few previous papers that studied the determinants of influenza vaccination investigated the effects of different psychological factors.

Statistical Analysis

We used univariate logistic regression to explore which factors of socio-demographics, behavioural risk, health status and accessibility, quality of life, and mental status were associated with an individual's influenza vaccination status. After a univariate logistic regression analysis, we used a multiple logistic analysis. The adjusted odds ratio (aOR) and 95% confidence intervals (95% CI) were calculated to show the strength of each association. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using Stata 12.0 (Stata Corp., College Station, Texas, USA). [44]

RESULTS

The socio-demographic characteristics of the study population are summarised in Table 1. The population was equally divided into three age groups (65–69, 70–74, and ≥75 years). More females than males participated in the survey (40.7% men, 59.3% women) and around three-quarters of the subjects were poorly educated (fewer than 6 years of formal education) (75.7%). Categorising household income into two groups (those earn < 1,000 USD/month and those earn ≥ 1,000 USD/month) divided the sample into about two approximately equal groups and more subjects lived without spouse (62.6%) than lived with one (37.4%). Additionally, most people were not current smokers (85.4%), drank little alcohol (68.5%), and never exercised (67.2%). In terms of health status and accessibility, most people reported that they

feel unhealthy (44.4%) and most had undergone a recent health screening (55.2%). Generally, people had high scores (58.7% with ≥61) in the EuroQoL Visual Analogue System (VAS) and reported that they frequently felt stressed (75.9%) and had recently felt that their mood had been depressive (78.6%). The univariate logistic analysis of factors associated with influenza vaccination status is presented in Table 2. We found that people were more likely to be vaccinated as they aged (70.3% for 65–69 versus 79.3% for ≥75 years) and when they categorized themselves as unhealthy (78.1% for those who reported themselves as unhealthy versus 73.4% for those who reported themselves as healthy). Smokers showed the lowest vaccination coverage with only 69.3% choosing vaccination. In contrast, the group who had recently undergone health screening showed the highest rate of vaccination (81.9%). Individuals who seldom engaged in physical activity showed lower vaccination rates than individuals from other physical activity levels. No significant associations with psychological factors were observed. In the univariate study, the factors that correlated most strongly with vaccination coverage were recent history of health screening (Vaccinated Percentage 81.9%, OR 2.11, 95% CI: 1.81-2.47), age (Vaccinated Percentage 79.3%, OR 1.61, 95% CI: 1.34-1.95 for ≥75 and Vaccinated Percentage 78.8%, OR 1.57, 95% CI: 1.30-1.89 for 70–74 years old), and moderate physical activity (Vaccinated Percentage 79.5%, OR 1.33, 95% CI:1.09-1.63). The multiple logistic regression analysis is presented in Table 3. The results of the multiple logistic regression analysis were generally similar to that of the univariate study, and showed that the factors with the two highest aOR's were age (2.06, 95% CI: 1.68-2.52 for 70–74 years old) and recent history of health screening (2.26, 95% CI: 1.92-2.66). The factor with the lowest aOR was current smoking status (0.78, 95% CI: 0.62-0.98).

DISCUSSION

This study aimed to identify which factors are associated with recent vaccination against influenza within Korea via the results of the representative sample of the Korean population by the KNHANES. The influenza vaccination coverage rate in 2007–2009 among elderly Koreans was 75.8%. This result is above both the Korea Centre for Disease Control and Prevention (KCDC) goal of 60%[17] and World Health Organisation (WHO) goal of 75% vaccination coverage among the elderly by 2010.[4] However, while the overall vaccination rate among the elderly surpasses these targets, certain populations—such as the younger elderly (70.3% in 65–69 years old), those living alone (74.6%), smokers (69.3%), frequent drinkers (73.5%), those lacking physical activity (74.5%), and those regarding themselves as healthy (73.4%)–showed lower vaccination coverage than the WHO recommends. This indicates an uneven distribution of vaccination coverage within the elderly population.

Socio-demographic factors

Well known factors that affect increased vaccination coverage are older age, higher education, higher household income, and living alone. [11, 14, 30, 33, 34] This suggests that future health policies should concentrate on encouraging younger groups to reach the WHO vaccination-rate goal. Living alone reduces vaccination coverage whereas high household income leads to more coverage. It is common to think that higher education and household wealth ensure not only improved social status but also greater access to health services. However, for those with high education and high incomes, living alone may reduce their chances of choosing vaccination. Therefore, healthcare professionals should in particular focus on the elderly who live alone.

Health behavioral risks

In this study smoking was the most negatively influencing factor (aOR 0.78, 95% CI: 0.62-0.98). Smoking and alcohol consumption are again well-studied variables that negatively influence vaccination

coverage. [17, 30, 34] This implies that smokers among the elderly are the least protected population even though they are one of the highest-risk groups facing influenza infection. In theory, smokers naturally could have more pulmonary complications than non-smokers such as Chronic Obstructive Pulmonary Disease (COPD), lung cancer, or pneumonia [45, 46, 47]. It is plausible that people with more comorbidities have a higher chance of visiting hospitals and receiving vaccination recommendations. But our study showed an opposite result–the same tendency is observed for those who frequently consume alcohol. Therefore, healthcare professionals should encourage such people to get vaccinations.

Health status and accessibility

A history of recent health screening was the factor most positively associated with vaccination (aOR 2.26, 95% CI: 1.68-2.52). In contrast, a self-perception of better health was the factor most negatively associated with vaccination (aOR 0.79, 95% CI: 0.64-0.97). Previous studies have clearly demonstrated that vaccination rates can be increased through health screening or recommendations from doctors [34]. Our results suggest that many elderly people who regard themselves as healthy are not motivated to have a vaccination unless they are encouraged to visit to a physician. The positive effects of health screening on vaccination coverage may be due to the national health policy that provides free influenza vaccinations to the vulnerable elderly at public health centres [18]. Since the National Cancer Screening Program of the National Cancer Centre in Korea targets the elderly, it is also possible that people who used this service received a recommendation from a physician to accept an influenza vaccine. Thus, healthcare professionals should be reminded that a recommendation from a physician is one of the most successful strategies for improving vaccination coverage among the elderly.

Psychological factors

According to Lorenz et al., the vaccination rate among the mentally ill population is lower than in the general population [43]. This suggests that psychological factors, such as a stressed or depressive mood,

may be associated with vaccination coverage. In our study, no psychological variables—including being stressed, a depressive mood, or the respondent's perceived quality of life—were significantly associated with vaccination coverage. This discrepancy might be due to a cultural difference between study sites, the willingness of respondents to report mental illness, limitations of sample size among the non-vaccinated population, or other factors not considered in the multivariable model.

LIMITATIONS

This study had several limitations. First, some respondents of KHNANES IV were interviewed during the summer and this may have led to a recall bias since most vaccination campaigns are generally conducted during a couple of months in autumn. For example, if a respondent had a vaccination last autumn it is possible he or she forgot their vaccination status at the time of the survey. Therefore, the vaccination rate is potentially underestimated. Second, there might be a significant gender bias (Male: 40.7% vs. Female 59.3%) because it was easier for housewives to visit the interviewers compared to other family members who were all invited to complete the survey during the daytime. The gender bias suggests that women were more likely to participate in this survey. Third, the collinearity between presumed independent variables(socio-demographics factors, health behavioural risk factors, health status and accessibility factors, and psychological factors) was not examined thoroughly, and possible dependency between variables may have undermined the integrity of the result.

CONCLUSION

Although the influenza vaccination rate in elderly Koreans reached the WHO target coverage rate, more should be done to increase the vaccination rate for underrepresented populations, such as those with low household income, those who live alone, smokers, people who frequently consume alcohol, and in particular, people who have not recently undergone a health screening. The results of this study may help to guide health professionals in their design of a better strategy to encourage influenza vaccination among the elderly.

ACKNOWLEDGEMENT

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CONTRIBUTORSHIP STATEMENT

Substantial contributions to the study design: Sang Min Park

Analysis of data: David Soonil Kwon

Interpretation of data for the work: All authors

Drafting the work or revising it critically for important intellectual content: All authors

Final approval of the version to be published: Sang Min Park

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately resolved: All authors

COMPETING INTERESTS

None to declare.

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DATA SHARING STATEMENT

No additional data available.

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Table 1. Characteristics of the study population, The Fourth Korean National Health and Nutrition Examination Survey 2007–2009 (n=3,567)

Variable		n	%
Socio-demographics			
Age (years)	65–69	1,326	37.2
	70–74	1,122	31.4
	≥75	1,119	31.4
Gender	Male	1,450	40.7
	Female	2,117	59.3
Education level	Elementary school (≤ 6 years)	2,700	75.7
	More than elementary school	867	24.3
Household income[1]	< 1,000 USD per month	1,648	46.2
	≥ 1,000 USD per month	1,919	53.8
Marital status[2]	Living with spouse	2,233	62.6
	Living without spouse	1,334	37.4
Health behavioral risks			
Smoking	Not current or never smoker	3,046	85.4
	Current smoker	521	14.6
Alcohol	Less than once per month or never tried	2,442	68.5
	More than once per month	1,125	31.5
Physical activity level	Never	2,398	67.2
	More than once per week	743	20.8
	Everyday	426	12.0
Health status and accessibility			
Self-reported health status	Unhealthy	1,583	44.4
	Fair	847	23.7
	Healthy	1,137	31.9
History of health screening[3]	No	1,598	44.8
	Yes	1,969	55.2
Limitation in daily activities	No	1,974	55.3
	Yes	1,593	44.7
Psychological factors			
EuroQoL in VAS	≤30	304	8.5
	31-60	1,171	32.8
	≥61	2,092	58.7
Stress	Frequently	2,706	75.9
	Rarely	861	24.1
Depressive mood[4]	Frequently	2,805	78.6
	Rarely	762	21.4

Abbreviations: VAS: visual analogue scale

[1] 1,000 U.S Dollar=1 Million Korean Won (1USD=1,000 KRW)

[2] The term 'spouse' refers to an individual who is legally married, or cohabiting, and 'without spouse' refers to an individual who is single, divorced, or separated

[3] The health screening refers to national health-care services conducted within 2 years

[4] Depressive mood lasted longer than 2 weeks in a year

Table 2. Factors associated with influenza vaccination status in univariate logistic regression analysis (n=3,567)

Variable	Vaccinated %	Univariate	
		OR (95%CI)	p-value
Socio-demographics			
Age (years)			
65–69	70.3	1.0 (referent)	
70–74	78.8	1.57 (1.30-1.89)	< 0.001
≥75	79.3	1.61 (1.34-1.95)	< 0.001
Gender			
Male	75.0	1.0 (referent)	
Female	76.3	1.07 (0.92-1.25)	0.391
High education[1]	77.9	1.16 (0.97-1.40)	0.101
High household income[2]	76.9	1.14 (0.98-1.33)	0.087
Living alone[3]	74.6	0.90 (0.77-1.06)	0.2
Health behavioral risks			
Current smoking	69.3	0.68 (0.55-0.83)	< 0.001
Frequent drinking[4]	73.5	0.84 (0.71-0.98)	0.032
Physical activity level			
Never	74.5	1.0 (referent)	
More than once per week	79.5	1.33 (1.09-1.63)	0.005
Everyday	76.5	1.11 (0.88-1.42)	0.37
Health status and accessibility			
Self-reported health status			
Unhealthy	78.1	1.0 (referent)	
Fair	74.5	0.82 (0.67-0.99)	0.042
Healthy	73.4	0.77 (0.65-0.92)	0.005
History of health screening[5]	81.9	2.11 (1.81-2.47)	< 0.001
Limitation in daily activities	78.0	1.24 (1.06-1.45)	0.006
Psychological factors			
High EuroQoL: VAS			
≤30	75.7	1.0 (referent)	
31-60	77.1	1.08 (0.81-1.46)	0.592

≥61	75.0	0.97 (0.73-1.28)	0.818
Stressed	74.3	0.90 (0.76-1.08)	0.256
Frequent depressive mood	74.9	0.94 (0.78-1.14)	0.54

Abbreviations: OR: odds ratio, CI: confidence interval, VAS: visual analogue scale

[1] 'Well education' refers to those studied in elementary school

[2] 'High household income' refers to the income more than 1 million won per month

[3] 'Living alone' refers to an individual who is single, divorced, or separated

[4] Frequent drinking is defined by drinking more than once per week

[5] The health screening refers to national health-care services conducted within 2 years

[6] Depressive mood lasted longer than 2 weeks in a year

Table 3. Factors associated with influenza vaccination status in multiple logistic regression analysis (n=3,567).

Variable	Vaccinated %	Multiple	
		aOR (95%CI)	p-value
Socio-demographics			
Age (years)			
65–69	70.3	1.0 (referent)	
70–74	78.8	1.79 (1.48-2.17)	< 0.001
≥75	79.3	2.06 (1.68-2.52)	< 0.001
High education[1]	77.9	1.27 (1.03-1.57)	0.025
High household income[2]	76.9	1.13 (0.96-1.33)	0.143
Living alone[3]	74.6	0.82 (0.68-1.00)	0.045
Health behavioral risks			
Current smoking	69.3	0.78 (0.62-0.98)	0.03
Frequent drinking[4]	73.5	0.86 (0.72-1.04)	0.124
Physical activity level			
Never	74.5	1.0 (referent)	
More than once per week	79.5	1.29 (1.05-1.59)	0.017
Health status and accessibility			
Self-reported health status			
Unhealthy	78.1	1.0 (referent)	
Fair	74.5	0.85 (0.68-1.06)	0.144
Healthy	73.4	0.79 (0.64-0.97)	0.025
History of health screening[5]	81.9	2.26 (1.92-2.66)	< 0.001
Limitation in daily activities	78.0	1.18 (0.99-1.41)	0.072

Abbreviations: aOR: adjusted odds ratio, CI: confidence interval, VAS: visual analogue scale

[1] 'High education' refers to those studied in elementary school

[2] 'High household income' refers to the income more than 1 million won per month

[3] 'Living alone' refers to an individual who is single, divorced, or separated

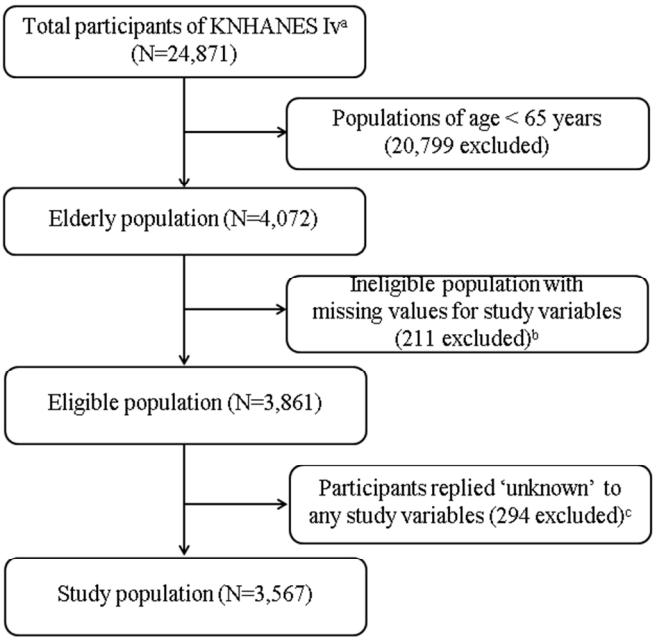
Figure 1. The study population framework

[a] The Fourth Korean National Health and Nutrition Examination Survey 2007-2009

[b] The number of non-responders for vaccination status was zero

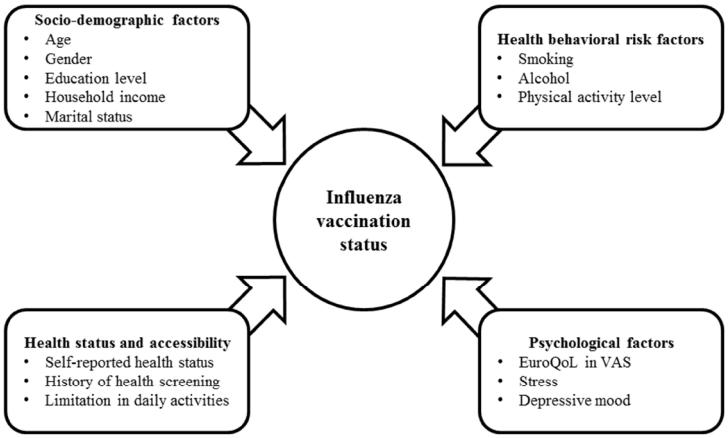
[c] The number of responders for vaccination status as “unknown” was zero

Figure 2. Categorisation of the study variables in this study



selection process for the study population

209x137mm (300 x 300 DPI)



study variables used in this study grouped by categories

212x126mm (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 **[Within the title page 1 and method section of the abstract page 2]**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **[See results section of abstract page 2]**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **[page 4]**
Objectives	3	State specific objectives, including any prespecified hypotheses **[page 5]**
Methods		
Study design	4	Present key elements of study design early in the paper **[Methods page 6]**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **[page 6-7]**
Participants	6	(*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 **[page 6]**
		(*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	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **[page 6-7]**
Data sources/ measurement	8*	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 **[page 6]**
Bias	9	Describe any efforts to address potential sources of bias **[page 3]**
Study size	10	Explain how the study size was arrived at **[page 6 and Figure 1]**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **[page 6 and Figure 2]**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **[page 7]**
		(*b*) Describe any methods used to examine subgroups and interactions **[page 6-7]**
		(*c*) Explain how missing data were addressed **[N/A]**
		(*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 **[page 6 and Figure 1]**
		(*e*) Describe any sensitivity analyses **[N/A]**

Continued on next page

Results		
Participants	13*	(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 **[page 6 and Figure 1 page 24]**
		(b) Give reasons for non-participation at each stage **[page 6 and Figure 1]**
		(c) Consider use of a flow diagram **[Figure 1]**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **[Page 8 and Table 1]**
		(b) Indicate number of participants with missing data for each variable of interest **[Figure 1]**
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) **[]**
Outcome data	15*	*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 **[Table 2,3]**
Main results	16	(*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 **[Page 8-9 and Table 2,3]**
		(*b*) Report category boundaries when continuous variables were categorized **[Table 1,2,3]**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **[N/A]**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **[N/A]**
Discussion		
Key results	18	Summarise key results with reference to study objectives **[Page 8 and Table 1,2,3]**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **[Page 2]**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **[Page 10-13]**
Generalisability	21	Discuss the generalisability (external validity) of the study results **[Page 2 and 13]**
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 **[N/A]**

*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.