National prevalence and determinants of COVID-19 vaccine hesitancy during the initial phase pandemic

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Abstract. – OBJECTIVE: Although previous studies have explored the causes of COVID-19 vaccine hesitancy during the pandemic, there is a lack of generality and reproducibility in these studies. Therefore, we aimed to comprehensively identify the determinants of COVID-19 vaccine hesitancy through a representative nationwide cross-sectional study conducted in South Korea.

SUBJECTS AND METHODS: We used a nationwide, representative, and large-scale dataset from the 2021 Community Health Survey. By analyzing 193,495 participants, we investigated the nationwide incidence of COVID-19 vaccine hesitancy and the various causes thereof.

RESULTS: The national prevalence of COVID-19 vaccine hesitancy was 5.7% (95% CI, 5.5-5.8). COVID-19 vaccine hesitancy was associated with an increased incidence of the following factors: (1) demographic factors including early-middle adulthood [*vs.* late; odds ratio (OR), 1.51; 95% CI, 1.38-1.65] and male sex (*vs.* female sex; OR, 1.08; 95% CI, 1.01-1.14); (2) physically healthy subjects; (3) lower socio-economic status (*vs.* high household income; OR, 1.28; 95% CI, 1.19-1.38); (4) having mental illness (*vs.* normal mental status; OR, 1.25; 95% CI, 1.13-1.38); and (5) unhealthy habits such as current smoking (*vs.* non-smoking; OR, 1.22; 95% CI, 1.13-1.31); and insufficient physical activity (*vs.* sufficient; OR, 1.08; 95% CI, 1.01-1.17). Common reasons for vaccine hesitancy were concerns about side effects (41.34%), health problems (24.60%), and inability to select the type of vaccine (14.13%).

CONCLUSIONS: This representative large-scale nationwide study conducted in South Korea investigated the nationwide prevalence and determinants of vaccine hesitancy. Our results provide useful public health information, especially on novel aspects of vaccination strategies, for policymakers to improve the acceptance of COVID-19 vaccines.

Key Words:
   Public health, Vaccine hesitancy, COVID-19, South Korea, Side effects.

Introduction

Since the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infectious disease in 2019, it has swept across the globe[1,2]. As of December 2022, the cumulative total number of patients with COVID-19 exceeded 650 million across the world, corresponding to around one-tenth of the global population[3]. This pandemic has

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brought not only a danger to public health but also various social and economic crises[4-6]. To minimize the impact of the pandemic on our society, the first goal of governments to contain the further spread of COVID-19 would be to improve the vaccine acceptance rate. In South Korea, where the cumulative total number of patients with COVID-19 exceeded 27 million as of December 2022, the rate of vaccine acceptance was 88.7% by January 2023[1,7]. Of the 10% unvaccinated population, a substantial number of them were vaccine-hesitant people who had been delaying taking or refusing to accept COVID-19 vaccines. Although the safety and efficacy of vaccines have been scientifically proven by numerous experiments[8,9], these people were reluctant to get vaccinated and had doubts regarding vaccine safety and efficacy. The World Health Organization (WHO) declared vaccine hesitancy as one of the top 10 threats to global health in 2019[8]; studies[8] addressing vaccine hesitancy have been reported globally. However, these studies[8] have had several limitations owing to inadequate sample size for representativeness or low-evidence level, including personal and medical risk factors beyond ordinary demographic factors.

Therefore, we conducted a large-scale, population-based, nationwide study in South Korea to investigate the national prevalence of SARS-CoV-2 vaccination hesitancy. We identified comprehensive causative factors covering several aspects (demographic, medical, socioeconomic, psychiatric, and health behavior) and key drivers of COVID-19 vaccination hesitancy.

Subjects and Methods

Data and Study Population

Our study was performed using a nationwide, representative, large-scale dataset from the Community Health Survey 2021[10], which is conducted annually by the Korea Disease Control and Prevention Agency (KDCA) and targeted at adult participants over 19 years old in South Korea. This nationwide survey was conducted with proportional allocation sampling and clustering, multi-stage, and weighting analysis to produce a representative and reliable sampling in South Korea. The participants of the survey were members of selected sample households by probability proportionate and systematic sampling[11]. All records of participants, including personal data, were documented with an assigned investigation number for anonymity and restricted access by the Korean government. Informed consent was obtained from all study participants, and personal identifiable information was not collected. The CHS 2021 data were anonymous, and the study protocol was approved by the Institutional Review of KDCA and Kyung Hee University (KHUH 2022-06-042).

A total of 229,242 respondents participated in this study. Among the total participants, 35,747 were excluded because of (1) missing height data (n=3,248); (2) missing weight data (n=675); and (3) incomplete or missing personal information (n=31,824). Thus, the final sample consisted of 193,495 participants.

Definition

For the purpose of this study, subjects were divided into two groups, a COVID-19 vaccine acceptance group, and a COVID-19 vaccine hesitant group, as following[9]; (1) COVID-19 vaccine acceptance was defined as participants who reported that they had received the SARS-CoV-2 vaccine; and (2) COVID-19 vaccine hesitancy was defined as those who reported that they were either unwilling or hesitant to take COVID-19 vaccination. This reflected the definition of vaccine hesitancy as declared by the WHO Strategic Advisory Group for Emergencies, which is "a delay in the acceptance of, or refusal of, vaccination despite the availability of vaccination services[12]".

Covariates

The covariates were considered for the following factors; (1) demographic characteristics: age [early to middle adulthood (19 to 64 years), and late adulthood (more than 65 years)], sex, and area of residence (urban and rural)[13]; (2) medical conditions: obesity based on self-reported body mass index, physician-diagnosed hypertension, and diabetes mellitus; (3) socio-economic factors: medical institution accessibility in the neighborhood, mistrust of neighborhood, education levels, recipient of basic livelihood security, monthly income of household (under 4 million KRW, more than 4 million KRW, and unknown) and being involved in economic activity; (4) psychiatric condition: having experienced despair and suicidal thoughts over the past year; and (5) health behavior: current smoking status, level of aerobic physical activity, having received influenza vaccination in the last year, and having undergone national health examination in the last 2 years.

Statistical Analysis

We used this dataset and a complex sample design to ensure the representativeness of the ge-

neral population. Using descriptive statistics, we calculated the weighted and estimated prevalence of COVID-19 vaccine hesitancy[14]. By crossover analysis, baseline characteristics for each group were assessed and compared by mean values with 95% confidence intervals (CIs). Weighted binary logistic regression modeling was used to identify the causes for vaccine hesitancy and to estimate the adjusted relationship between vaccine hesitancy and demographic, medical, socioeconomic, psychiatric, and health-behavioral variables. These estimates are presented as weighted odds ratios (ORs) with 95% CIs. We also calculated the proportions of the participants' reasons for hesitancy and reported them using a bar chart. Data analysis was performed using IBM SPSS Statistics version 26.0, (IBM Corp., Armonk, NY, USA) and Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). Bar charts and forest plots were created using Microsoft Excel and Origin, version 2023 (OriginLab Corporation, Northampton, MA, USA). A two-sided p-value lower than 0.05 considered statistical significance.

Results

Baseline Characteristics

Table I shows baseline characteristics of 193,495 participants (female 50.9%; 95% CI, 50.6 to 51.1 and male 49.1%; 95% CI, 48.9 to 49.4).

COVID-19 Vaccine Acceptance and Hesitancy in 2021

Using the criteria described above, 184,529 respondents were categorized as the vaccine acceptance group (weighted prevalence, 94.3%; 95% CI, 94.2 to 94.5), and 8,966 respondents were categorized as the vaccine-hesitant group (weighted prevalence, 5.7%; 95% CI, 5.5 to 5.8; Figure 1).

Determinants of COVID-19 Vaccine Hesitancy

Table II shows the potential associations between the investigated variables and vaccine hesitancy. In terms of demographics, COVID-19 vaccine hesitancy was significantly associated with the early and middle adulthood age groups (aOR, 1.509; 95% CI, 1.381-1.650) and male sex (aOR, 1.071; 95% CI, 1.009-1.136). Regarding medical conditions, COVID-19 vaccine hesitancy was significantly negatively associated with obesity (aOR, 0.937; 95% CI, 0.880-0.997), hypertension (aOR, 0.661; 95% CI, 0.612-0.714), and diabetes mellitus (aOR, 0.835; 95% CI, 0.753-0.925).

In socio-economic status, COVID-19 vaccine hesitancy was significantly associated with poor medical institution accessibility in neighborhood (aOR, 1.318; 95% CI, 233 to 1.406), mistrust of neighborhood (aOR, 1.423; 95% CI, 1.343 to 1.508), recipient of basic livelihood security (aOR, 1.315; 95% CI, 1.155 to 1.498), lower monthly household income (aOR, 1.282; 95% CI, 1.191 to 1.380), and not being involved in economic activity (aOR, 1.848; 95% CI, 1.738 to 1.965).

Regarding psychiatric disorders, COVID-19 vaccine hesitancy was significantly associated with experiences of sadness and despair in the past 1 year (aOR, 1.252; 95% CI, 1.133-1.383) and suicidal thoughts in the past 1 year (aOR, 1.257; 95% CI, 1.137-1.390).

Regarding health aspects, COVID-19 vaccine hesitancy was significantly associated with current smoking habits (aOR, 1.216; 95% CI, 1.129-1.310). Insufficient aerobic physical activity (aOR, 1.080; 95% CI, 1.001-1.165), no influenza vaccination in the previous 1 year (aOR, 2.985; 95% CI, 2.778-3.205), and not undergoing national health examination in the last 2 years (aOR, 1.949; 95% CI, 1.838-2.061; Figure 3).

Reasons Causing Hesitancy of COVID-19 Vaccination

The reasons for hesitancy in accepting the COVID-19 vaccine are shown in Figure 2. The most common reasons for vaccine hesitancy were concerns about side effects after vaccination [41.34% (3,707/8,966)], health problems [24.59% (2,205/8,966)], and inability to select the type of vaccine [14.13% (1,267/8,966)].

Discussion

Key Findings

To the best of our knowledge, this is the first large-scale study (n=193,495) to investigate the demographic, medical, socioeconomic, psychiatric, and health behavior risk factors among persons with vaccine hesitancy in South Korea. This study aimed to identify and analyze the determinants of vaccine hesitancy. The national prevalence of vaccine hesitancy was 5.7% (95% CI, 5.5-5.8). COVID-19 vaccine hesitancy was associated with certain demographic characteristics (younger age and male sex), physically healthy subjects, lower socioeconomic status, mental illness, and poor health behaviors such as current smoking habits and insufficient physical activity.

Table I. Baseline characteristic of included participants in Community Health Survey (total n=193,495).

| Risk factors	Co-variates	Weighted % (95% CI)		
		Total	COVID-19 vaccine acceptance	COVID-19 vaccine hesitancy
Demographic	Number (n)	193,495	184,529	8,966
	Number (%)	100.0	94.3 (94.2 to 94.5)	5.7 (5.5 to 5.8)
	Age, years (%)			
	Early and middle adulthood (19 to 64)	75.8 (75.5 to 76.0)	75.1 (74.8 to 75.4)	87.2 (88.5 to 87.8)
	Late adulthood (≥65)	24.2 (24.0 to 24.5)	24.9 (24.6 to 25.2)	12.8 (12.2 to 13.5)
	Sex			
	Male	49.1 (48.9 to 49.4)	49.0 (48.8 to 49.2)	51.3 (50.3 to 52.3)
	Female	50.9 (50.6 to 51.1)	51.0 (50.8 to 51.2)	48.7 (47.7 to 49.7)
	Area of residence			
	Urban	69.9 (69.7 to 70.2)	69.9 (69.6 to 70.2)	70.4 (69.8 to 71.0)
	Rural	30.1 (29.8 to 30.3)	30.1 (29.8 to 30.4)	29.6 (29.0 to 30.2)
Medical Conditions	Obesity*			
	No	69.6 (69.3 to 69.9)	69.5 (69.2 to 69.8)	71.4 (70.5 to 72.4)
	Yes	30.4 (30.1 to 30.7)	30.5 (30.2 to 30.8)	28.6 (27.6 to 29.5)
	Hypertension			
	No	75.3 (75.1 to 75.6)	74.7 (74.4 to 74.9)	86.5 (85.8 to 87.1)
	Yes	24.7 (24.4 to 24.9)	25.3 (25.1 to 25.6)	13.5 (12.9 to 14.2)
	Diabetes mellitus			
	No	89.3 (89.2 to 89.5)	89.1 (88.9 to 89.3)	93.5 (93.0 to 94.0)
	Yes	10.7 (10.5 to 10.8)	10.9 (19.7 to 11.1)	6.5 (5.0 to 7.0)
Socio-economic	Poor accessibility of medical institution in neighborhood			
	No	80.9 (80.6 to 81.2)	81.3 (81.0 to 81.5)	75.1 (74.2 to 76.0)
	Yes	19.1 (18.8 to 19.4)	18.7 (18.5 to 19.0)	24.9 (24.0 to 25.8)
	Mistrust of the neighborhood			
	No	62.9 (62.5 to 63.2)	63.7 (63.3 to 64.0)	49.2 (48.1 to 50.3)
	Yes	37.1 (36.8 to 37.5)	36.3 (36.0 to 36.7)	50.8 (49.7 to 51.9)
	University and higher as the highest level of education			
	No	63.1 (62.7 to 63.4))	63.3 (63.0 to 63.7)	58.9 (57.8 to 60.0)
	Yes	36.9 (36.6 to 37.3)	36.7 (36.3 to 37.0)	41.1 (40.0 to 42.2)
	Recipient of basic livelihood security			
	No	96.4 (96.3 to 96.6)	96.6 (96.4 to 96.7)	94.3 (93.8 to 94.8)
	Yes	3.6 (3.4 to 3.7)	3.4 (3.3 to 3.6)	5.7 (5.2 to 6.2)
	Monthly income of household			
	Under 4 million KRW	42.5 (42.1 to 42.9)	42.3 (41.8 to 42.7)	46.4 (45.2 to 47.5)
	More than 4 million KRW	38.4 (38.0 to 38.8)	38.6 (38.2 to 39.1)	34.7 (33.5 to 35.8)
	Unknown	19.1 (18.7 to 19.5)	19.1 (18.7 to 19.5)	19.0 (18.0 to 19.9)
	Not being involved in economic activity			
	No	63.5 (63.2 to 63.8)	64.1 (63.8 to 64.4)	53.7 (52.7 to 54.8)
	Yes	36.5 (36.2 to 36.8)	35.9 (35.6 to 36.2)	46.3 (45.2 to 47.3)
Psychiatric conditions	Experience of sadness and despair over the past year			
	No	92.9 (92.7 to 93.0)	93.1 (92.9 to 93.3)	89.5 (88.8 to 90.0)
	Yes	7.1 (7.0 to 7.3)	6.9 (6.7 to 7.1)	10.5 (10.0 to 11.2)
	Suicidal thoughts over the past year			
	No	93.6 (93.4 to 93.7)	93.8 (93.6 to 93.9)	90.0 (89.4 to 90.6)
	Yes	6.4 (6.3 to 6.6)	6.2 (6.1 to 6.4)	10.0 (9.4 to 10.6)
Health behavior	Current smoking status			
	Nonsmoker	83.5 (83.3 to 83.7)	83.9 (83.7 to 84.1)	77.3 (76.4 to 78.1)
	Smoker	16.5 (16.3 to 16.7)	16.1 (15.9 to 16.3)	22.7 (21.9 to 23.6)
	Insufficient aerobic physical activity**			
	No	18.1 (17.9 to 18.4)	18.1 (17.9 to 18.4)	18.2 (17.4 to 19.1)
	Yes	81.9 (81.6 to 82.1)	81.9 (81.6 to 82.1)	81.8 (80.9 to 82.6)

(Table continued)

Table I *(continued).* Baseline characteristic of included participants in Community Health Survey (total n=193,495).

Risk factors	Co-variates	Weighted % (95% CI)		
		Total	COVID-19 vaccine acceptance	COVID-19 vaccine hesitancy
	No influenza vaccination in the last year			
	No	56.4 (56.1 to 56.7)	58.2 (57.8 to 58.5)	26.8 (25.8 to 27.8)
	Yes	43.6 (43.3 to 43.9)	41.8 (41.5 to 42.2)	73.2 (72.2 to 74.2)
	Did not receive national health examination in the last 2 years			
	No	76.2 (75.9 to 76.4)	77.5 (77.2 to 77.7)	54.2 (53.2 to 55.3)
	Yes	23.8 (23.6 to 24.1)	22.5 (22.3 to 22.8)	45.8 (44.7 to 46.8)

*Obesity status was determined based on body mass index calculated using body height, weight, sex, and age in reference to the 2017 Korean National Growth Body Mass Index-for-age Charts. **Sufficiency of aerobic physical activity is calculated by metabolic equivalent of task score and considered to meet World Health Organization physical activity guidelines.
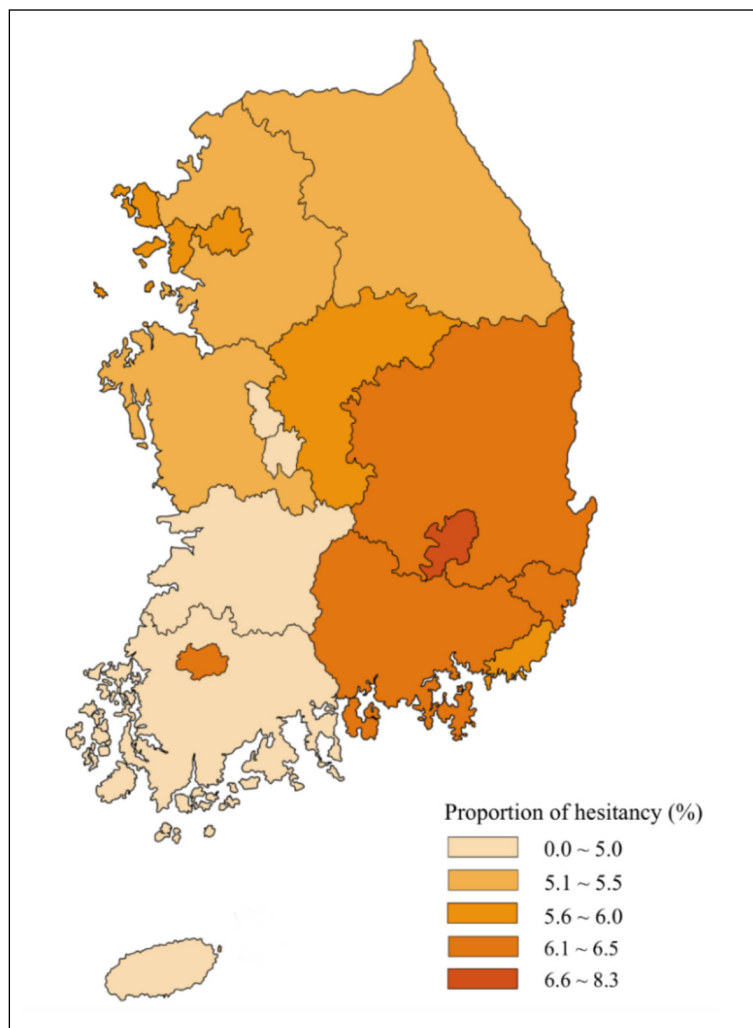
Figure 1. Thematic map showing weighted distribution of the COVID-19 vaccine hesitancy in South Korea.

Table II. Logistic regression model for association between COVID-19 vaccine hesitancy and a variety of risk factors among participants in Community Health Survey (total n=193,495).

		Crude Model	*p*-value	Adjusted Model*	*p*-value
Demographic factors	Age, years				
	Early and middle adulthood (19 to 64)	**2.256 (2.101 to 2.422)**	**<0.001**	**1.509 (1.381 to 1.650)**	**<0.001**
	Late adulthood (≥65)	1.0 (reference)		1.0 (reference)	
	Sex				
	Male	**1.097 (1.044 to 1.152)**	**<0.001**	**1.071 (1.009 to 1.136)**	**0.023**
	Female	1.0 (reference)		1.0 (reference)	
	Area of residence				
	Urban	**1.025 (0.966 to 1.089)**	0.427	0.981 (0.921 to 1.046)	0.566
	Rural	1.0 (reference)		1.0 (reference)	
Medical Condition	Obesity**				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**0.910 (0.859 to 0.956)**	**<0.001**	**0.937 (0.880 to 0.997)**	**0.041**
	Hypertension				
	No	1.0 (reference)		1.0 (ref)	
	Yes	**0.461 (0.429 to 0.496)**	**<0.001**	**0.661 (0.612 to 0.714)**	**<0.001**
	Diabetes mellitus				
	No	1.0 (reference)		1.0 (ref)	
	Yes	**0.566 (0.514 to 0.623)**	**<0.001**	**0.835 (0.753 to 0.925)**	**<0.001**
Socio-economic	Poor medical institution accessibility in neighborhood				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**1.435 (1.350 to 1.529)**	**<0.001**	**1.318 (1.233 to 1.406)**	**<0.001**
	Mistrust of the neighborhood				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**1.809 (1.712 to 1.912)**	**<0.001**	**1.423 (1.343 to 1.508)**	**<0.001**
	University and higher as the highest level of education				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**1.203 (1.136 to 1.275)**	**<0.001**	1.054 (0.989 to 1.125)	0.109
	Recipient of basic livelihood security				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**1.684 (1.502 to 1.887)**	**<0.001**	**1.315 (1.155 to 1.498)**	**<0.001**
	Monthly income of household				
	More than 4 million KRW	1.0 (reference)		1.0 (reference)	
	Under 4 million KRW	**1.222 (1.144 to 1.305)**	**<0.001**	**1.282 (1.191 to 1.380)**	**<0.001**
	Unknown	**1.106 (1.016 to 1.204)**	**0.020**	**1.123 (1.029 to 1.225)**	**0.009**
	Not being involved in economic activity				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**1.538 (1.458 to 1.621)**	**<0.001**	**1.848 (1.738 to 1.965)**	**<0.001**
Psychiatric conditions	Experience of sadness and despair over the past year				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**1.591 (1.463 to 1.729)**	**<0.001**	**1.252 (1.133 to 1.383)**	**<0.001**
	Suicidal thoughts over the past year				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**1.675 (1.540 to 1.822)**	**<0.001**	**1.257 (1.137 to 1.390)**	**<0.001**
Health behavior	Current Smoking status				
	Non smoker	1.0 (reference)		1.0 (reference)	
	Smoker	**1.534 (1.440 to 1.634)**	**<0.001**	**1.216 (1.129 to 1.310)**	**<0.001**
	Insufficient aerobic physical activity***				
	No	1.0 (reference)		1.0 (reference)	
	Yes	1.007 (0.936 to 1.082)	0.861	1.080 (1.001 to 1.165)	0.048

(Table continued)

Table II *(continued).* Logistic regression model for association between COVID-19 vaccine hesitancy and a variety of risk factors among participants in Community Health Survey (total n=193,495).

		Crude Model	*p*-value	Adjusted Model*	*p*-value
Health behavior	No influenza vaccination in the last year				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**3.802 (3.571 to 4.032)**	**<0.001**	**2.985 (2.778 to 3.205)**	**<0.001**
	Did not receive national health examination in the last 2 years				
	No	1.0 (reference)		1.0 (reference)	
	Yes	**2.907 (2.742 to 3.067)**	**<0.001**	**1.949 (1.838 to 2.061)**	**<0.001**

Values represent odds ratio (95% confidence interval) for vaccine hesitancy. *The adjusted model was adjusted for all-related covariates. **Obesity status is determined based on body mass index calculated with body height, weight, sex, and age in reference to the 2017 Korean National Growth body mass index-for-age Charts. ***Sufficiency of aerobic physical activity is calculated by metabolic equivalent of task score and considered to meet World Health Organization physical activity guidelines. The bold numbers indicate a significant difference *(p<0.05)*.

Common reasons for vaccine hesitancy were concerns about side effects (41.34%), health problems (24.60%), and the inability to select the type of vaccine (14.13%). These findings suggest that policymakers should target specific vaccine-hesitant groups with typical causal factors to improve vaccine acceptance among the public.

Comparisons with Previous Studies

The majority of previous studies[16-18], such as in Canada (n=15,019)[15], Germany (n=2,029)[16], China (n=29,925)[17], and Japan (n=30,053)[18] reported younger age and lower household income as risk factors for vaccine hesitancy, similar to our main results. However, the association between vaccine hesitancy and sex is inconclusive and inconsistent[17,18]. This inconsistent result between Asian and Western countries might be due to social and cultural differences surrounding gender roles. Furthermore, previous studies[15-18] have provided low-level evidence with a sample size too small to ensure representativeness considering those countries' populations.

Plausible Mechanism

Those who were young and healthy worried more about the side effects of the vaccine than
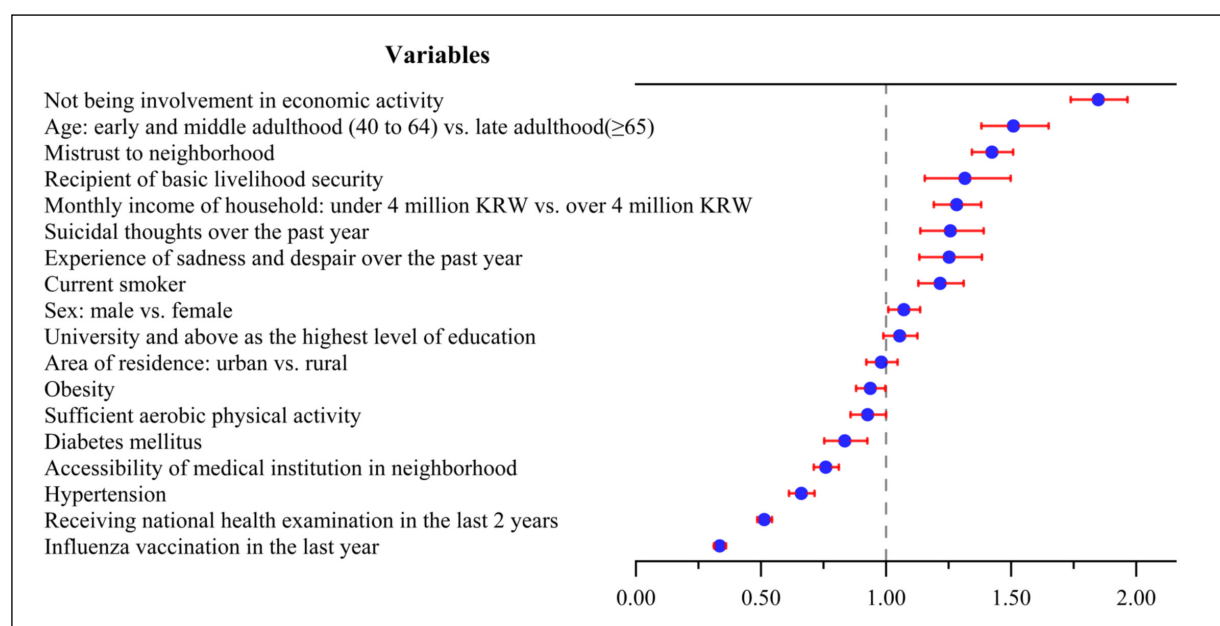
Figure 2. Logistic regression model for association between COVID-19 vaccine hesitancy and a variety of risk factors among participants in Community Health Survey (total n=193,495).
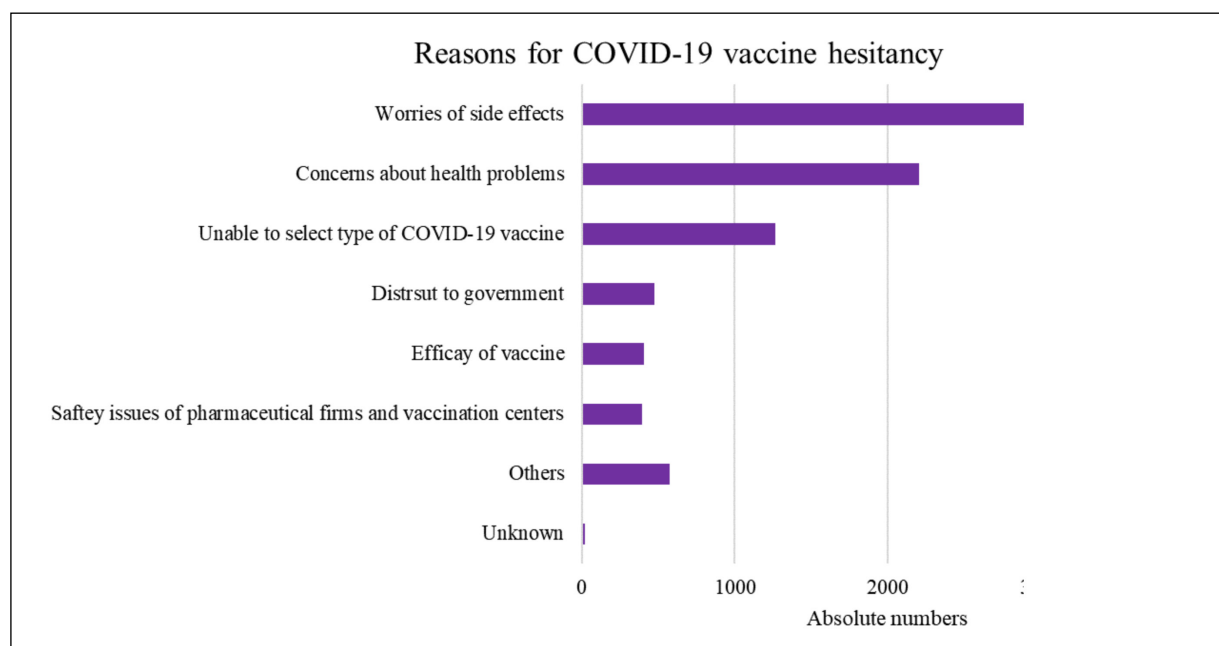
Figure 3. The reasons for hesitancy in COVID-19 vaccines among the study participants with COVID-19 vaccines in South Korea (n=8,966).

the risk of being infected with COVID-19. This tendency can be attributed to the belief that COVID-19 vaccine side effects occur across age groups more or less equivalently, while getting infected brings serious symptoms, especially for the elderly[9]. Moreover, the health belief model suggests that an individual's perceptions of the risks and advantages of preventing a particular problem influence their actions and behavior. This model effectively explains the behavior of individuals[9].

To analyze the effect of socio-economic activity on vaccine hesitancy, Lazarus et al[9] focused on 'why' more socio-economically active people were more likely to get vaccinated. They suspected that the possibility of loss of financial stability and socio-economic status made these people want an uninterrupted normal lifestyle by getting vaccinated. Therefore, employees of major companies, and thus probably of high or moderate income, were more likely to be vaccinated by the time they were interviewed[19].

Policy Implications

Our study highlights the need to adopt new strategies for ensuring adequate vaccination compliance by motivating people to come forward and voluntarily get vaccinated. First, we should encourage healthy people with a low risk of severe symptoms and death due to COVID-19 infection to get vaccinated[20]. Even though they

are relatively safe when infected, they can still infect other people who might be susceptible and vulnerable to infectious disease[21]. Second, we should encourage people who are negligent in adhering to public health issues to agree to get vaccinated voluntarily. To educate them about public health problems, we should use influential social media as a promotional tool by continuously providing objective information and professionals' opinions on the safety and efficacy of COVID-19 vaccine[22,23].

Limitation and Strengths

Several limitations of this study should be noted when interpreting the results. First, given that the survey was based on a questionnaire, our study was subject to self-response and non-response biases. However, we found that this survey was reliable, with high kappa values (0.44 to 0.93), as reported in another study[24]. Also, the response rate was over 90% for all questions included in this survey[25]. Secondly, the risk factors of vaccine hesitancy identified in this study may be biased due to the government measures taken during the period that the survey was conducted. Just before the survey was conducted, from August to October 2021[26], the South Korean government first provided vaccines to the elderly due to insufficient supplies. This would have affected our analysis of risk

factors, especially age. Therefore, additional analysis would be required that is based on 2022 survey data[25]. Third, our results may be influenced by SARS-CoV-2 major strain (i.e., original strain, Delta, and Omicron) and the phase of the COVID-19 pandemic[27]. The appearance of new variants has brought about a change in the perception of pandemic situations and vaccinations. Vaccine hesitancy rates vary by country depending on the fluctuating epidemic waves[28]. Considering that this survey was conducted before the emergence of omicron variants, our study has limitations in reproducibility[29]. Thus, the transition of public perception of COVID-19 should be further studied. Despite these limitations[26], our study is the first nationwide investigation to comprehensively identify key causal factors for vaccination hesitancy in South Korea. We could ensure reliability and representativeness based on the large number (n=193,495) of participants and the methodology of sampling and analysis in our study, while previous studies had been conducted on specific occupation[30] or with smaller sample sizes[31]. This study provides critical public health information for raising vaccine acceptance, particularly meaningful messages for policymakers[32-35]. Therefore, COVID-19 vaccination strategies should target young adults and individuals who do not engage in economic activities. Overall, our study suggests an efficient way to achieve herd immunity by encouraging vaccination among the general public nationwide, even in the event of another pandemic.

Conclusions

This is the first large-scale study (n=193,495) to investigate the national prevalence of COVID-19 vaccine hesitancy and demographic, medical, socioeconomic, psychiatric, and health behavior factors among persons with vaccine hesitancy in South Korea. Finally, we need to communicate with the public, especially hesitant people, by providing trustworthy medical information about the risks and safety of vaccines to encourage them to get vaccinated.

Ethics Approval
The CHS 2021 data were anonymous, and the study protocol was approved by the Korea Disease Control and Prevention Agency (KDCA) and Kyung Hee University (KHUH 2022-06-042).

Informed Consent
Every participant provided written informed consent, and the study protocol was performed in accordance with the Declaration of Helsinki.

Availability of Data and Materials
Data are available on reasonable request. Study protocol, statistical code: available from DKY (e-mail: yonkkang@gmail.com). Data set: available from the Korea Disease Control and Prevention Agency (KDCA) through a data use agreement.

Conflicts of Interest
The authors declare no conflicts of interest.

Authors' Contributions
Dr DKY had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final version before submission. Study concept and design: JS and DKY; Acquisition, analysis, or interpretation of data: JS and DKY; Drafting of the manuscript: JS and DKY; Critical revision of the manuscript for important intellectual content: Jiyoon Song, Jaeyu Park, Jinseok Lee, Young Joo Lee, Wonyoung Cho, Chanyang Min, Min Seo Kim, Masoud Rahmati, Yong Sung Choi, Dong Keon Yon, Seung Geun Yeo; Statistical analysis: JS and DKY; Study supervision: Yong Sung Choi, Dong Keon Yon, Seung Geun Yeo. DKY supervised the study and is guarantor for this study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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