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Original Research Article

National trends in influenza vaccination coverage rates in South Korea between 2007-2020, including the COVID-19 pandemic: a longitudinal nationwide serial study

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Abstract

Objective: The beneficial relationship of influenza vaccination rate on the COVID-19 pandemic is inconclusive and inconsistent. Thus, we aimed to investigate long-term trend changes in influenza vaccination rate among general population of South Korea before COVID-19 pandemic and during early/mid-pandemic period.

Methods: We analyzed nationwide representative serial study from the Korea National Health and Nutrition Examination Survey (KNHANES). We analyzed data from 2007 to 2020 from KNHANES to calculate the influenza vaccination rates. Influenza vaccination status was obtained from health interviews and questionnaire based on the question of whether the influenza vaccine was vaccinated in the past 12 months.

Results: Among 78,067 participants, the vaccination coverage increased from 2007 to 2020 (27.6% in 2007 to 2008 and 42.2% in 2020). The slope for the vaccination coverage increased between 2007 to 2019 (pre-pandemic, β= 0.310, 95% CI, 0.267 to 0.352), and the slope increased less than expected between 2018 to 2020 (entering the pandemic, β = 0.036, 95% CI, 0.010 to 0.062; β_{diff}= -0.274, 95% CI, -0.323 to -0.224). However, the participants with ≥65 years old and those with medical condition (diabetes, tuberculosis, asthma, angina, myocardial infarction, cancer, chronic kidney disease, hypertension, and hyperlipidemia), the trends of the vaccination coverage increased from 2007 to 2019, whereas the coverage were decreased in 2020 (≥65 years old: 72.9%, 85.5%, and 81.4%; medical condition: 43.3%, 56.3%, and 55.7%, respectively).

Conclusions: In this study using nationwide serial study, the influenza vaccination coverage increased from 2007 to 2020, and the slope increased less than expected in 2020 during the COVID-19 pandemic. On the other hand, the vaccination coverage decreased during the COVID-19 pandemic in the participants with ≥65 years old and those with medical condition. We suggest that influenza vaccination should be encouraged to the elderly and chronic disease patients to prevent twin infection during the COVID-19 pandemic.

Keywords: COVID-19; pandemic; influenza; vaccination.

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1. Introduction

Influenza is an epidemic disease worldwide, which can be self-limiting or lead to death.[1] Worldwide, the disease causes approximately 3–5 million severe cases and about 290,000–650,000 deaths each year.[2] During epidemics, the disease can also result in overload of medical services and capacity, such as usage of clinics and hospitals.[2] The most effective way to prevent influenza infections, which cause many severe cases worldwide, is yearly vaccination.[1]

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In particular, influenza vaccination is recommended, especially in the elderly (>65 years of age), children <5 years of age, pregnant women, and chronically ill individuals who are at high risk for influenza infection.[3, 4] Therefore, many countries around the world are implementing the National Immunization Program (NIP), as a policy to promote vaccination of high-risk groups and improve public health.[3, 4] The NIP for influenza in South Korea was first implemented in 1997 for low-income seniors,[5] and free vaccinations are currently being conducted, mainly for those ≥65 years, children <12 years, and pregnant women. In 2018, as the free vaccination target was expanded to include pregnant women, infants <5 years to children <12 years, the vaccination rate increased significantly.[6] This suggests that the free vaccination policy is an effective strategy for improving coverage.[6]

As of 2015, the vaccination rate of the elderly ≥65 years in Korea was 81.7%,[6] showing a higher vaccination rate than the World Health Organization (WHO)'s target of 75%, as recommended for high-risk groups.[7] However, as the WHO declared a COVID-19 pandemic on March 11, 2020,[8] there are concerns about a 'twin pandemic' and overload of the medical system along with influenza transmission. Because co-infection with COVID-19 and influenza has a greater risk of worsening outcomes,[9] the Korea Disease Control and Prevention Agency (KDCA) in 2020 expanded the number of free vaccination recipients (young individuals <18 years and >62 years) and actively recommended influenza vaccination.[10] However, the beneficial relationship between influenza vaccination rate and the COVID-19 pandemic is inconclusive and inconsistent. Thus, we aimed to investigate long-term trend changes in influenza vaccination rates among the general population of South Korea before and during the early/mid COVID-19 pandemic period. Therefore, to determine how the COVID-19 pandemic affected influenza vaccination rates, we analyzed data from the Korean National Health and Nutrition Examination Survey (KNHANES) conducted by the KDCA.

2. Methods

2.1 Study design and population

We analyzed data from the Korea National Health and Nutrition Examination Survey conducted by the KDCA.[11] The KNHANES is a nationwide, annual repeated, general population-based, cross-sectional study to investigate the health and nutritional status of the representative of the Korean general population. This study consisted of a health screening questionnaire and interview, comprehensive nutritional survey, body measurements, influenza vaccination status, individual information (age, sex, and socioeconomic status), and health-related examinations, including serum blood tests and several measurements by well-trained nurses, nutritionists, and medical professionals.[11] Every participant provided written informed consent, and the study protocol was performed in accordance with the Declaration of Helsinki. The study protocol was approved by the KDCA.

We collected data for 14 years between 2007–2020. Among the 108,157 respondents, those who did not answer the following questions were excluded: age, sex, body mass index (BMI; kg/m^2), household income, education level, and influenza vaccination status. Finally, 78,067

individuals (n=10,108 between 2007–2008; n=14,641 between 2009–2010; n=12,294 between 2011–2012; n=10,694 between 2014–2015; n=12,297 between 2016–2017; n=12,427 between 2018–2019; and n=5,606 in 2020) were included in this study (Fig. 1).

2.2. Covariate definitions

A medical condition was defined as a case where at least the following diseases had been diagnosed by a physician: diabetes, tuberculosis, asthma, angina, myocardial infarction, cancer, chronic kidney disease, hypertension, and hyperlipidemia. Household income was classified as lower, lower-middle, higher-middle, and highest according to the quartile.[12, 13] The level of education was considered to be below high school level and above college level. Obesity was calculated based on the following BMI values: <18.5, ≥18.5–23, ≥23–25, and ≥25 kg/m^2.[14] Smoking was indicated as non-smoker, smoker, and ex-smoker, depending on whether or not the individual is currently smoking.[12] Health screening was defined as depending on whether the individual had been examined during the last two years.

2.3. Endpoints

Influenza vaccination status was obtained from health interviews and questionnaires based on the question of whether the influenza vaccine had been administered in the past 12 months.[15]

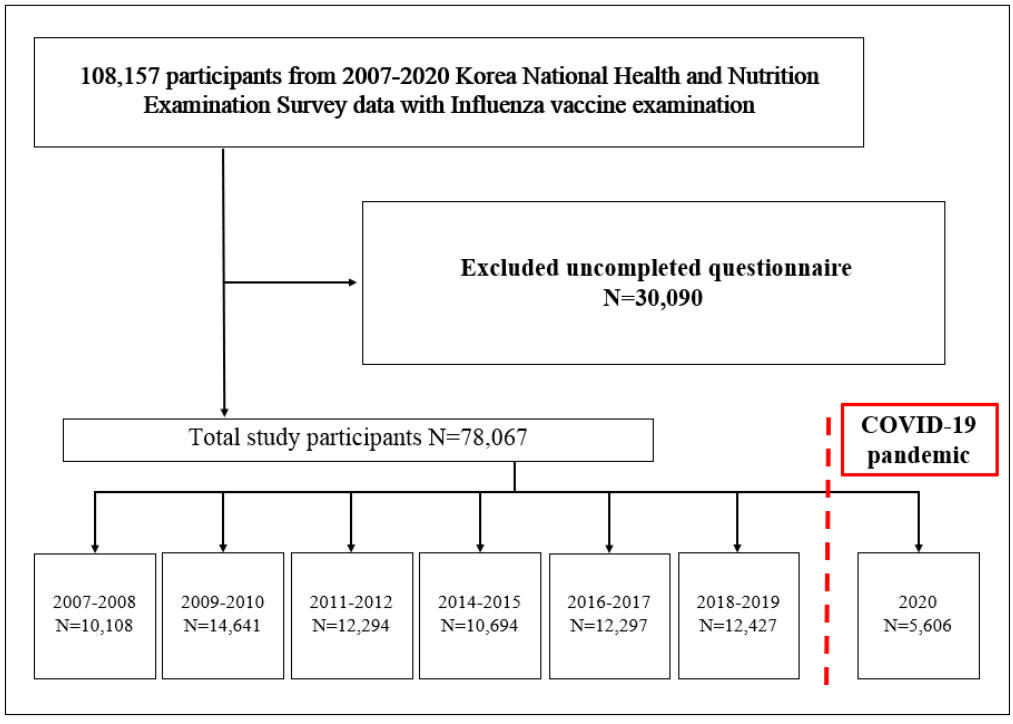

Fig. 1. Flow diagram for the inclusion of study population using the KNHANES between 2007–2020. Abbreviations: BMI, body mass index; KNHANES, Korea National Health and Nutrition Examination Survey.

2.4. Statistical analysis

We analyzed data between 2007–2020 from the KNHANES to calculate the influenza vaccination rates. The KNHANES did not have a vaccination-related questionnaire in 2013; thus, we excluded the 2013 KNHANES dataset. The main aim of this study was to evaluate whether COVID-19 has affected vaccination through the trend of influenza vaccination rates over the past 14 years. The participants were divided into the following sub-groups based on age and medical condition: age, 14–18, 19–64, and ≥65 years, and those with and without medical conditions.

The COVID-19 pandemic period was defined based on the year 2020 when COVID-19 patients were first reported in Korea.[16] The other periods, 2007–2019, were grouped into two years to stabilize the prevalence trends and was defined as the pre-COVID19 period. Weighted linear regression and logistic regression models were used to analyze influenza vaccination trends to increase the representation of the estimates. A linear regression model was used to obtain weighted β-coefficients with 95% confidence intervals (CIs) for each period, and the estimated β difference indicates the difference between before and during the COVID-19 pandemic. Using the logistic regression model, we calculated the odds ratios (ORs) with 95% CIs of nationwide influenza vaccination coverage in 2020 versus those in 2018–2020.[17, 18] A two-sided P value <0.05 was significant. All analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA).

3. Result

3.1. Participant characteristic

Among the 78,067 participants, the rates of age ≥65 years (33.2% vs. 4.1%), female sex (56.9% vs. 46.9%), overweight (23.4% vs. 21.5%) and obesity (34.0% vs. 31.5%), income third quartile (25.2% vs. 24.9%), highest quartile (26.0% vs. 23.8%), high school graduated or under (65.8% vs. 51.0%), non-alcohol consumers (17.6% vs.11.2%), non-smokers (63.1% vs. 56.7%) and past smokers (21.8% vs. 18.1%), received health screening (65.5% vs. 50.6), and participants with a medical condition (45.1% vs. 22.0%) were higher in the vaccinated group than in the unvaccinated group (Table 1).

Vaccination coverage increased between 2007–2020 (27.6% in 2007–2008 and 42.2% in 2020). In the subgroups of those <65 years old, sex, income, education level, alcohol consumption status, smoking status, received health screening, and participants without a medical condition, the trends of vaccination coverage were consistent with trend in overall coverage. Among those ≥65 years old and participants with medical condition subgroups, the trends of vaccination coverage increased between 2007–2019, whereas the coverage decreased in 2020 (≥65 years old: 72.9%, 85.5%, and 81.4%; medical condition: 43.3%, 56.3%, and 55.7%, respectively; Table 2 and Fig. 2).

The slope for vaccination coverage increased between 2007–2019 (pre-pandemic, β = 0.310, 95% CI, 0.267–0.352), and the slope increased less than expected between 2018–2020 (entering the pandemic, β = 0.036, 95% CI, 0.010–0.062; βdiff = -0.274, 95% CI, -0.323 to -0.224). The

Table 1. General characteristics of influenza vaccination using the KNHANES between 2007–2020

(n=78,067).

Characteristic	Unvaccinated group	Vaccinated group
Number, n (%)	46,804 (59.95)	31,263 (40.05)
Overall, weighted % (95% CI)	66.4 (65.9–66.9)	33.6 (33.1–34.1)
Age, years, weighted % (95% CI)		
14–18	8.6 (8.3–9.0)	4.9 (4.5–5.2)
19–64	87.3 (86.9–87.6)	61.9 (61.1–62.8)
≥ 65	4.1 (3.9–4.3)	33.2 (32.3–34.0)
Sex, weighted % (95% CI)		
Male	53.1 (52.6–53.5)	43.1 (42.5–43.7)
Female	46.9 (46.5–47.4)	56.9 (56.3–57.5)
Obesity, weighted % (95% CI)		
<18.5	6.0 (5.8–6.3)	4.6 (4.3–4.9)
18.5–23.0	41.0 (40.4–41.5)	38.0 (37.3–38.7)
23.0–25.0	21.5 (21.1–21.9)	23.4 (22.8–24.0)
≥25.0	31.5 (31.0–32.0)	34.0 (33.3–34.7)
Income, weighted % (95% CI)		
Lowest quartile	25.9 (25.1–26.6)	24.2 (23.4–25.0)
Second quartile	25.4 (24.7–26.0)	24.7 (23.9–25.4)
Third quartile	24.9 (24.3–25.6)	25.2 (24.5–25.9)
Highest quartile	23.8 (23.0–24.6)	26.0 (25.1–26.9)
Education, weighted % (95% CI)		
High school or lower	51.0 (50.2–51.8)	65.8 (64.9–66.8)
College or higher	49.0 (48.2–49.8)	34.2 (33.2–35.1)
Alcohol consumption, weighted % (95% CI)		
No	11.2 (10.9–11.6)	17.6 (17.0–18.1)
Yes	88.8 (88.4–89.1)	82.4 (81.9–83.0)
Smoking, weighted % (95% CI)		
Non-smoker	56.7 (56.2–57.3)	63.1 (62.5–63.8)
Smoker	25.1 (24.6–25.7)	15.1 (14.5–15.6)
Ex-smoker	18.1 (17.7–18.5)	21.8 (21.3–22.3)
Nationwide health screening within 2 years, weighted % (95% CI)		
Yes	50.6 (50.0–51.2)	65.5 (64.8–66.2)
No	49.4 (48.8–50.0)	34.5 (33.8–35.2)
Medical condition, weighted % (95% CI)		
With medical condition	22.0 (21.5–22.5)	45.1 (44.3–45.9)
Without medical condition	78.0 (77.5–78.5)	54.9 (54.1–55.7)

Abbreviations: BMI, body mass index; CI, confidence interval; KNHANES, Korea National Health and Nutrition xamination Survey.

Medical conditions include one or more of the following conditions: diabetes, tuberculosis, asthma, angina, myocardial infarction, cancer, chronic kidney disease, hypertension, and hyperlipidemia.

Table 2. Trend of influenza vaccination rate using the KNHANES between 2007–2020

	Trends in influenza vaccinated						
	Pre-COVID-19 pandemic era						COVID-19 pandemic
	2007–2008	2009–2010	2011–2012	2014–2015	2016–2017	2018–2019	2020
Number, n (%)	3,598 (11.51)	4,959 (15.86)	4,998 (15.99)	4,324 (13.83)	5,247 (16.78)	5,507 (17.62)	2,630 (8.41)
Weighted % (95% CI)							
Overall	27.6 (26.2–29.0)	27.7 (26.5–28.8)	32.5 (31.1–33.9)	33.0 (31.7–34.3)	35.9 (34.7–37.0)	38.7 (37.4–40.1)	42.2 (40.0–44.3)
Age, years							
14–18	13.5 (10.0–16.9)	17.8 (14.6–21.1)	25.4 (21.7–29.2)	22.1 (18.7–25.6)	18.9 (15.7–22.1)	27.2 (23.1–31.3)	43.0 (34.7–51.3)
19–64	22.5 (21.2–23.8)	21.2 (20.1–22.2)	25.7 (24.3–27.0)	25.3 (24.0–26.7)	28.2 (27.1–29.4)	30.2 (28.8–31.6)	34.7 (32.5–36.9)
≥65	72.9 (70.2–75.5)	75.7 (73.4–77.9)	78.7 (76.6–80.7)	81.0 (79.1–82.9)	83.4 (81.8–85.0)	85.5 (83.8–87.1)	81.4 (78.8–84.0)
Sex							
Male	24.0 (22.4–25.7)	24.2 (22.9–25.6)	28.4 (26.7–30.1)	27.5 (26.0–29.1)	30.8 (29.4–32.3)	33.6 (32.0–35.2)	37.6 (35.0–40.3)
Female	31.1 (29.4–32.8)	31.1 (29.7–32.5)	36.5 (34.9–38.1)	38.3 (36.6–39.9)	40.8 (39.3–42.3)	43.8 (42.2–45.4)	46.8 (44.2–49.5)
Income							
Lowest quartile	24.8 (22.4–27.2)	25.4 (23.3–27.5)	32.1 (29.8–34.4)	32.3 (29.8–34.8)	34.6 (32.3–36.9)	38.1 (35.6–40.6)	38.9 (35.5–42.4)
Second quartile	27.5 (25.2–29.9)	28.1 (26.1–30.2)	32.4 (29.9–34.9)	31.4 (29.0–33.8)	35.0 (32.8–37.1)	37.0 (34.6–39.4)	42.2 (38.4–45.9)
Third quartile	27.6 (25.2–29.9)	27.3 (25.3–29.2)	32.9 (30.5–35.2)	32.8 (30.5–35.1)	35.7 (33.6–37.9)	38.6 (36.3–41.0)	45.0 (41.4–48.6)
Highest quartile	30.2 (27.6–32.8)	30.1 (28.1–32.1)	32.7 (30.4–35.0)	35.5 (33.2–37.8)	38.1 (35.7–40.5)	41.1 (38.8–43.5)	42.4 (38.6–46.1)
Education							
High school or lower	32.3 (30.4–34.1)	32.4 (30.8–34.0)	38.0 (36.3–39.7)	39.2 (37.5–40.8)	43.9 (42.3–45.4)	46.7 (45.0–48.4)	50.8 (47.9–53.6)
College or higher	19.6 (17.8–21.4)	20.1 (18.6–21.6)	24.0 (22.3–25.7)	25.5 (23.8–27.2)	27.3 (25.8–28.7)	30.6 (28.9–32.3)	34.3 (31.8–36.7)
Alcohol consumption							
No	35.9 (33.1–38.7)	40.4 (37.7–43.2)	43.5 (40.3–46.8)	43.0 (40.2–45.7)	46.9 (44.0–49.9)	49.7 (46.6–52.9)	55.8 (50.0–61.6)
Yes	26.1 (24.7–27.6)	25.5 (24.3–26.6)	30.7 (29.3–32.1)	31.4 (30.0–32.7)	34.2 (33.0–35.5)	37.3 (35.9–38.7)	40.4 (38.3–42.5)
Smoking							
Non-smoker	28.7 (27.1–30.3)	29.6 (28.2–31.0)	34.9 (33.2–36.6)	35.5 (33.9–37.1)	38.3 (36.8–39.7)	41.6 (40.0–43.3)	45.5 (42.8–48.2)
Smoker	20.9 (18.7–23.1)	19.2 (17.4–20.9)	23.7 (21.6–25.8)	22.0 (19.8–24.2)	24.8 (22.8–26.8)	26.0 (23.9–28.1)	30.9 (27.0–34.7)
Ex-smoker	33.0 (30.4–35.6)	33.2 (31.1–35.4)	36.3 (33.7–38.9)	36.7 (34.3–39.1)	39.8 (37.6–41.9)	42.2 (40.0–44.5)	42.6 (39.0–46.2)

Table 2. Continued

	Trends in influenza vaccinated						
	Pre-COVID-19 pandemic era						COVID-19 pandemic
	2007–2008	2009–2010	2011–2012	2014–2015	2016–2017	2018–2019	2020
Nationwide health screening within 2 years							
Yes	34.8 (33.0–36.7)	34.3 (32.6–35.9)	38.5 (36.8–40.3)	38.1 (36.5–39.7)	40.9 (39.4–42.4)	42.9 (41.4–44.5)	46.8 (44.3–49.2)
No	21.6 (20.1–23.2)	21.5 (20.2–22.8)	26.4 (24.7–28.1)	26.6 (25.0–28.3)	27.7 (26.1–29.3)	31.1 (29.2–32.9)	33.7 (30.8–36.5)
Medical condition							
With medical condition	43.3 (40.8–45.8)	44.2 (42.2–46.2)	49.9 (47.7–52.1)	50.7 (48.7–52.7)	53.6 (51.7–55.5)	56.3 (54.3–58.2)	55.7 (52.8–58.7)
Without medical condition	22.1 (20.6–23.6)	21.5 (20.3–22.7)	26.0 (24.6–27.5)	25.6 (24.2–26.9)	27.4 (26.1–28.6)	30.1 (28.6–31.6)	35.0 (32.6–37.4)

Abbreviations: CI, confidence interval; KNHANES, Korea National Health and Nutrition Examination Survey.
Medical conditions include one or more of the following conditions: diabetes, tuberculosis, asthma, angina, myocardial infarction, cancer, chronic kidney disease, hypertension, and hyperlipidemia.

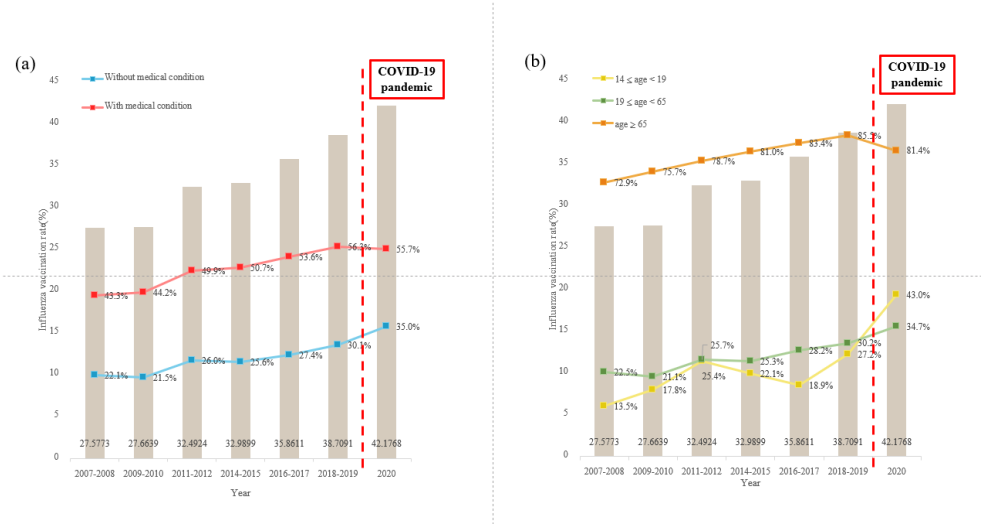

Fig. 2. Trends of influenza vaccination coverage rate (a) total and by age groups, and (b) medical condition, 2007–2020. The bar graph means the overall coverage rate for each period.

changes in vaccination coverage from other subgroups except those ≥65 years old and the participants with medical condition subgroups were consistent with the overall findings.

Among those ≥65 years old and the participants with medical condition subgroups, there was an increased slope at the pre-pandemic period, and a decreased slope after entering the pandemic (β_{diff} = -0.532, 95% CI, -0.636 to -0.427 among those aged ≥65 years old; β_{diff} = -0.320, 95% CI, -0.391 to -0.250 among the participants with medical condition).

The adjusted ORs (95% CI) for influenza vaccination was 1.175 (1.051–1.312) in 2020 compared with 2018–2019. The findings of those <65 years old, sex, second and third quartiles of income, and participants without a medical condition sub-group were consistent with the

overall findings. In the subgroup aged ≥65 years, the adjusted OR (95% CI) for influenza vaccination was 0.753 (0.603–0.942) in 2020 compared with 2018–2019 (Table 3).

4. Discussion

4.1 Key results

In this study, using national survey data, we investigated trends in influenza vaccination coverage rates. Influenza vaccination coverage increased between 2007–2020, and the slope increased to less than expected in 2020 during the COVID-19 pandemic. In contrast, vaccination coverage decreased during the COVID-19 pandemic in participants aged ≥65 years and in those with medical conditions.

Table 3. Estimated β-coefficients of odds ratios with 95% CIs by KNHANES from 2007 to 2020

	Trends in influenza vaccination			Odds ratios for influenza vaccination (95% CI)	
	Pre-pandemic trend, β (95% CI) 2007 to 2019	Pandemic trend, β (95% CI) 2018 to 2020	Trend difference, β_{diff} (95% CI)	Crude	Adjusted*
Overall	**0.310 (0.267–0.352)**	**0.036 (0.010–0.062)**	**-0.274 (-0.323 to -0.224)**	**1.155 (1.039–1.284)**	**1.175 (1.051–1.312)**
Age, years					
14–18	**0.337 (0.186–0.488)**	**0.175 (0.079–0.271)**	-0.162 (-0.341 to 0.017)	**2.026 (1.363–3.010)**	**2.084 (1.400–3.102)**
19–64	**0.263 (0.215–0.310)**	**0.051 (0.022–0.081)**	**-0.211 (-0.267 to -0.156)**	**1.228 (1.090–1.383)**	**1.217 (1.077–1.375)**
≥65	**0.457 (0.368–0.547)**	**-0.074 (-0.128 to -0.020)**	**-0.532 (-0.636 to -0.427)**	**0.743 (0.598–0.923)**	**0.753 (0.603–0.942)**
Sex					
Male	**0.279 (0.224–0.334)**	**0.044 (0.010–0.078)**	**-0.235 (-0.300 to -0.171)**	**1.192 (1.040–1.366)**	**1.209 (1.050–1.392)**
Female	**0.339 (0.291–0.387)**	0.031 (-0.001 to 0.063)	**-0.308 (-0.366 to -0.251)**	1.132 (0.998–1.285)	**1.144 (1.001–1.308)**
Income					
Lowest quartile	**0.360 (0.284–0.436)**	0.008 (-0.036 to 0.053)	**-0.352 (-0.440 to -0.264)**	1.035 (0.864 to 1.239)	1.017 (0.838–1.235)
Second quartile	**0.258 (0.184–0.331)**	**0.054 (0.008–0.100)**	**-0.204 (-0.291 to -0.117)**	**1.241 (1.032–1.492)**	**1.289 (1.062–1.565)**
Third quartile	**0.313 (0.240–0.387)**	**0.065 (0.021–0.110)**	**-0.248 (-0.333 to -0.162)**	**1.300 (1.089–1.552)**	**1.331 (1.097–1.615)**
Highest quartile	**0.308 (0.231–0.384)**	0.013 (-0.033 to 0.058)	**-0.295 (-0.384 to -0.206)**	1.052 (0.876–1.262)	1.067 (0.874–1.302)
Medical condition					
With medical condition	**0.315 (0.254–0.376)**	-0.005 (-0.041 to 0.031)	**-0.320 (-0.391 to -0.250)**	0.980 (0.848–1.132)	1.044 (0.906–1.202)

Table 3. Continued

	Trends in influenza vaccination			Odds ratios for influenza vaccination (95% CI)	
	Pre-pandemic trend, β (95% CI) 2007 to 2019	Pandemic trend, β (95% CI) 2018 to 2020	Trend difference, β_{diff} (95% CI)	Crude	Adjusted*
Without medical condition	**0.253 (0.201–0.304)**	**0.056 (0.024–0.088)**	**-0.197 (-0.257 to -0.136)**	**1.250 (1.100–1.420)**	**1.258 (1.103–1.435)**

Abbreviations: CI, confidence interval; KNHANES, Korea National Health and Nutrition Examination Survey
Medical conditions include one or more of the following conditions: diabetes, tuberculosis, asthma, angina, myocardial infarction, cancer, chronic kidney disease, hypertension, and hyperlipidemia.
*The model was adjusted for age (14–18, 19–64, and ≥65 years), sex, obesity (<18.5, 18.5–23.0, 23.0–25.0, and ≥25.0 kg/m^2), income (lower, lower-middle, higher-middle, and highest quartile), education level, alcohol consumption, smoking status, nationwide health screening within 2 years, and medical condition.
Numbers in bold indicate a significant difference ($P < 0.05$).

4.2 Comparison of previous studies

A previous study that used data from the KNHANES analyzed trends in influenza vaccination coverage in Korea (N=61,036) between 2005–2014; the study found that the overall influenza vaccination coverage rate increased (38.0% in 2005 and 44.1% in 2014).[19] Additionally, previous studies using KNHANES data reported trends in influenza vaccination coverage by participant groups between 2010–2019 (N = 80,861).[19] Between 2017–2019, the vaccination coverage for those ≤12 years old and pregnant women increased (66.2% to 83.1% for the ≤12 years old participants and 44.1% to 68.5% for pregnant women).[19] The highest influenza vaccination coverage was for participants ≥65 years old (85.8% in 2019), and the lowest was for participants with chronic diseases (41.9% in 2019). As of 2019, after financial support for children aged ≤12 years and pregnant women was expanded,[6] and influenza vaccination coverage increased significantly in both groups. Therefore, we suggest that free vaccination policy is one of the most effective strategies to increase vaccination coverage and propose expanding NIP in patients with chronic diseases having low influenza vaccination coverage. In the United States, between 2011–2020, the influenza vaccination coverage among adults with a history of cardiovascular disease (CVD) increased from 38.6% in 2011 to 44.3% in 2020 (N=476,227). Influenza vaccination in adults with CVD has improved slightly over the past decade; however, the trend has fallen well behind the national targets goal.[20] In the case of Shanghai, China, using data from the Shanghai Immunization Information System, the influenza vaccination coverage between 2016–2020 increased from 10.8% in 2016 and 2017 to 50.8% in 2020 and 2021, respectively (N=2,522,076).[21] In a meta-analysis of the association between influenza vaccination and SARS-CoV-2 infection (N=55,996,841), the authors suggested that influenza vaccination may contribute to reducing the risk of COVID-19 infection and severe cases.[22] Influenza vaccination coverage increased in South Korea, the United States, and China, which is similar to our findings. A previous study showed an increasing trend until 2019, and we found that entering the COVID-19 pandemic in 2020, influenza vaccination coverage decreased in those aged ≥65 years old and among those with medical condition subgroups.

4.3 Plausible mechanism

According to our study findings, influenza vaccination coverage decreased in elderly and chronic disease patients after entering the COVID-19 pandemic. The COVID-19 pandemic has caused an estimated 290,000 to 650,000 deaths.[2] During the COVID-19 pandemic, outdoor activities were low due to anxiety regarding SARS-CoV-2 infection,[23] hence, social distancing and work from home have increased.[24] In particular, in the case of the elderly and chronic disease patients, outdoor activities might be further reduced because of the anxiety of the high risk of SARS-CoV-2 infection. Death due to influenza infection mostly occurs in individuals ≥65 years old and chronic disease patients.[25] Nevertheless, in the case of the elderly, vaccination is hesitant due to uncertainty about vaccines, underestimation of vulnerability, and concerns about safety.[26, 27] For the above reasons, the coverage of influenza vaccination seems to have decreased in the elderly and in participants with medical conditions.

4.4 Policy implication

A decrease in influenza vaccination coverage is associated with the COVID-19 pandemic, and there is a need to recommend influenza vaccination during the COVID-19 pandemic. In particular, elderly patients and those with chronic diseases are vulnerable to viral infections. A previous study reported that the risk of SARS-CoV-2 infection was reduced from 22% to 24% when vaccinated against influenza in participants ≥66 years old.[28] Compared to unvaccinated patients, COVID-19 patients vaccinated against influenza may reduce the clinical outcomes of COVID-19.[29] However, policies for patients with chronic diseases in the high-risk group are insufficient. Co-infection with influenza and COVID-19 is fatal; thus, co-infection must be prevented for the situation of a 'twin pandemic.[30] [31] In order to prevent the 'twin pandemic' and medical system overload along with the spread of influenza, the KDCA should expand the number of free vaccination recipients and actively recommend influenza vaccination.[32]

4.5 Strengths and limitations

Our study has several limitations. The use of KNHANES data was limited to Korea and does not represent the world. The year 2013 was excluded from the study because the survey related to influenza vaccination did not provide data for 2013. The KNHANES data are survey data, and the size of the data is limited; however, the representativeness of the estimate is increased, as much as possible by using the weights provided by the KNHANES. The data were uploaded only up to December 2020; therefore, the findings are not full representative of the actual situation of the COVID-19 pandemic, but the early stage of the COVID-19 pandemic will help prevent and prepare for the COVID-19 pandemic. Despite these limitations, this is the first study to investigate long-term trends in influenza vaccination in South Korea.

5. Conclusion

We found that influenza vaccination coverage increased between 2007–2020. In contrast, in 2020, entering the COVID-19 pandemic, the slope decreased compared to 2007–2019 in the

participants aged ≥65 years old and those with medical condition subgroups. We suggest that influenza vaccination should be encouraged in the elderly and patients with chronic disease to prevent co-infection infections during the COVID-19 pandemic.

Capsule Summary

In this study using nationwide serial study, the influenza vaccination coverage increased from 2007 to 2020, and the slope increased less than expected in 2020 during the COVID-19 pandemic.

Ethics Statements

The study protocol was approved by the Korea Disease Control and Prevention Agency (KDCA).

Patient and Public Involvement

No patients were directly involved in designing the research question or conducting the research. No patients were asked to interpret or write up the results. However, we plan on disseminating the results of this study to any of the study participants or wider relevant communities on request.

Data Availability Statement

Data are available on reasonable request. Study protocol, statistical code: available from DKY (email: yonkkang@gmail.com). Data set: available from the Korean Centers for Disease Control and Prevention Agency (KCDA) through a data use agreement

Transparency Statement

The leading authors (Dr. MR) are an honest, accurate, and transparent account of the study being reported.

Author Contribution

Dr MR and 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*: all authors; *Acquisition, analysis*, *or interpretation of data*: all authors; *Drafting of the manuscript*: all authors; Critical revision of the manuscript for important intellectual content: all authors; *Statistical analysis*: Hyeowon Park, Hyeon Jin Kim, and Dong Keon Yon; *Study supervision*: all authors. MR and 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. HJK and HP were equally contributed.

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Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest..

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