phrp
OSONG PUBLIC HEALTH AND RESEARCH PERSPECTIVES

pISSN 2210-9099 eISSN 2233-6052
https://doi.org/10.24171/j.phrp.2023.0096
Osong Public Health Res Perspect 2023;14(3):164-172

Original Article

Estimating the number of severe COVID-19 cases and COVID-19-related deaths averted by a nationwide vaccination campaign in Republic of Korea

Ji Hae Hwang, Ju Hee Lee, Eun Jung Jang, Ryu Kyung Kim, Kil Hun Lee, Seon Kyeong Park, Sang Eun Lee, Chungman Chae, Sangwon Lee, Young Joon Park

Division of Epidemiological Investigation Analysis, Korea Disease Control and Prevention Agency, Cheongju, Republic of Korea

ABSTRACT

Objectives: The Korea Disease Control and Prevention Agency promotes vaccination by regularly providing information on its benefits for reducing the severity of coronavirus disease 2019 (COVID-19). This study aimed to analyze the number of averted severe COVID-19 cases and COVID-19-related deaths by age group and quantify the impact of Republic of Korea's nationwide vaccination campaign.

Methods: We analyzed an integrated database from the beginning of the vaccination campaign on February 26, 2021 to October 15, 2022. We estimated the cumulative number of severe cases and COVID-19-related deaths over time by comparing observed and estimated cases among unvaccinated and vaccinated groups using statistical modeling. We compared daily age-adjusted rates of severe cases and deaths in the unvaccinated group to those in the vaccinated group and calculated the susceptible population and proportion of vaccinated people by age.

Results: There were 23,793 severe cases and 25,441 deaths related to COVID-19. We estimated that 119,579 (95% confidence interval [CI], 118,901–120,257) severe COVID-19 cases and 137,636 (95% CI, 136,909–138,363) COVID-19-related deaths would have occurred if vaccination had not been performed. Therefore, 95,786 (95% CI, 94,659–96,913) severe cases and 112,195 (95% CI, 110,870–113,520) deaths were prevented as a result of the vaccination campaign.

Conclusion: We found that, if the nationwide COVID-19 vaccination campaign had not been implemented, the number of severe cases and deaths would have been at least 4 times higher. These findings suggest that Republic of Korea's nationwide vaccination campaign reduced the number of severe cases and COVID-19 deaths.

Keywords: COVID-19; Patient acuity; Republic of Korea; SARS-CoV-2; Vaccination campaign

Received: April 14, 2023
Revised: April 18, 2023
Accepted: April 23, 2023

Corresponding author:
Young Joon Park
Division of Epidemiological Investigation Analysis, Korea Disease Control and Prevention Agency, 187 Osongsaengmyeong 2-ro, Osong-eup, Heungdeok-gu, Cheongju 28159, Republic of Korea
E-mail: pahmun@korea.kr

Introduction

Coronavirus disease 2019 (COVID-19) first emerged in China in 2019 and was declared a

pandemic by the World Health Organization (WHO). As of April 12, 2023, a total of 762,791,152 COVID-19 cases and 6,897,025 COVID-19-related deaths had been reported globally according to the WHO [1]. Following the rollout of COVID-19 vaccinations, infections and deaths were reduced in many countries and regions [2–4]. The WHO reported that COVID-19 vaccinations prevented 14.4 million COVID-19-related deaths in 186 countries in 2021 [5].

In Republic of Korea, a national vaccination campaign began in February 2021, promoting 2 viral vector-based vaccines (ChAdOx1 nCoV-19 and Ad26.COV2.S) and 2 mRNA-based vaccines (BNT162b2 and mRNA-1273). The vaccination campaigns were gradually expanded to the entire population older than 6 months of age. As of April 17, 2023, 44,393,483 people (86.7% of the total population) had received 2 doses of the COVID-19 vaccine [6].

The Korea Disease Control and Prevention Agency (KDCA) has advocated for the importance and necessity of vaccination by regularly providing information on the benefits of vaccination for reducing the severity of COVID-19 and COVID-19-related mortality, but the number of severe cases and deaths averted by vaccination has not been sufficiently analyzed [7,8]. As the number of cases continued to increase due to the spread of the Omicron variant, bivalent vaccines were administered beginning in October 2022, and their necessity and importance are being actively promoted to increase vaccination rates.

In Republic of Korea, all confirmed COVID-19 cases, severe COVID-19 cases, and COVID-19-related deaths were reported to the government through the COVID-19 National Surveillance System, and all COVID-19 vaccinations were registered in the National Immunization Registry. Therefore, by linking these 2 databases, we aimed to analyze the public impact of the nationwide vaccination campaign by estimating the number of averted severe COVID-19 cases and COVID-19-related deaths during the mass vaccination campaign in Republic of Korea. Our findings will increase public awareness of vaccination and improve vaccine coverage.

HIGHLIGHTS

- As a result of estimating the number of severe cases and deaths after implementation of the coronavirus disease vaccination, we found that 95,786 severe cases and 112,195 deaths were prevented between February 26, 2021, and October 15, 2022.
- Therefore, the implications of the study highlight that Republic of Korea's nationwide vaccination campaign reduced the number of severe cases and deaths due to COVID-19.

Materials and Methods

Study Population and Design

In this study, we aimed to estimate the number of severe COVID-19 cases and COVID-19-related deaths averted by Republic of Korea's nationwide vaccination campaign. We analyzed data from February 26, 2021 to October 15, 2022, on people aged 12 years and older. This study excluded those aged 4 to 11 years old due to differences in characteristics between the vaccinated and unvaccinated groups. In this age group, the severity of the disease is low, and vaccination was recommended specifically for high-risk groups. Therefore, the study excluded this age group from the analysis.

According to Republic of Korea's COVID-19 Response Guidelines, confirmed COVID-19 cases refer to when an individual tests positive for COVID-19 using polymerase chain reaction, rapid antigen testing, or an emergency screening (emergency use-approved products). All confirmed infections, severe cases, and deaths are reported to the government through the COVID-19 National Surveillance System.

In Republic of Korea, vaccinations were first targeted to healthcare workers and high-risk groups, such as residents of long-term care facilities, beginning on February 26, 2021. In August of the same year, large-scale vaccination campaigns were conducted to distribute vaccines to all people over 18 years of age (Table S1).

Data Source

In Republic of Korea, confirmed COVID-19 cases are reported through the COVID-19 National Surveillance System, and COVID-19 vaccination records are reported and managed through the National Immunization Registry. In this analysis, we linked these 2 large databases to organize a database of 54,471,326 COVID-19 vaccination records and 23,008,640 confirmed cases. A total of 46,864,039 eligible people were analyzed (Figure 1).

Case Definition

We estimated the number of averted severe COVID-19 cases and COVID-19-related deaths. According to the COVID-19 Response Guidelines in Korea, we defined severe COVID-19 cases as COVID-19-confirmed cases for which the patient received treatment using high-flow oxygen therapy, mechanical ventilation, continuous renal replacement therapy, or extracorporeal membrane oxygenation within 28 days of a positive COVID-19 test. COVID-19-related deaths were

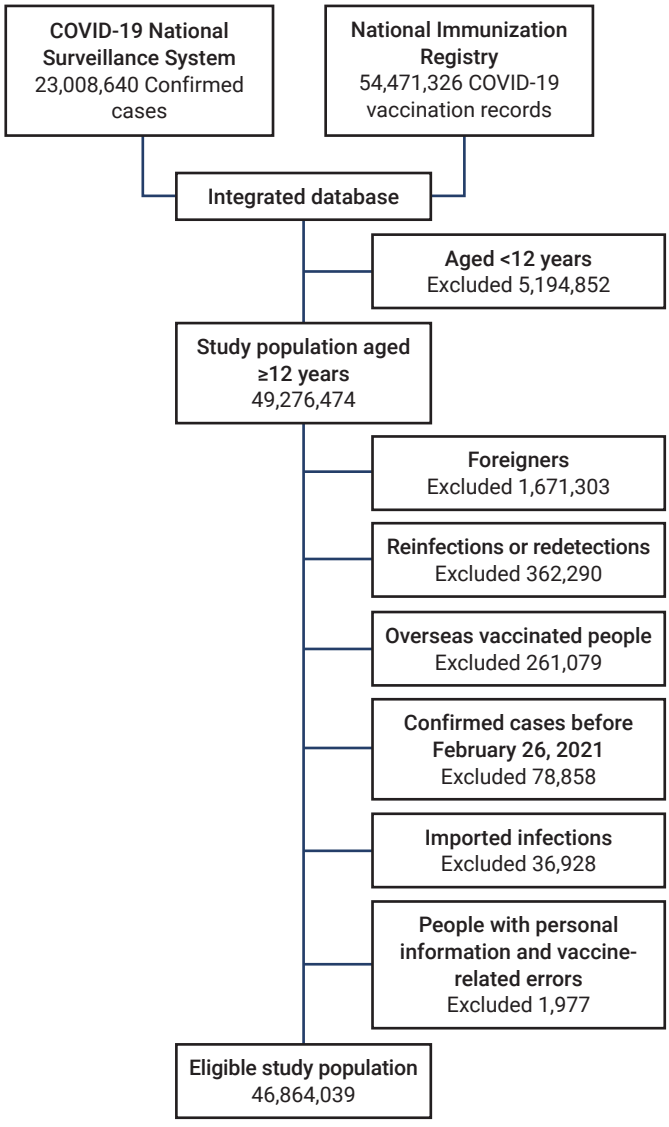

Figure 1. Flow chart of the study population.

defined as deaths within 28 days of a positive COVID-19 test.

Vaccination status was defined in this study as follows: (1) the unvaccinated group comprised those who were completely unvaccinated and those for whom only 0 to 13 days had passed after receiving the second dose of a COVID-19 vaccine; (2) the vaccinated group comprised those for whom 14 days had passed since receiving the second dose of a COVID-19 vaccine. Those who received 1 dose of the Janssen vaccine were classified into the vaccinated group.

Dominant Variants

According to the dates during which certain severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants were most dominant, the dominant variant was classified based on the period when >50% of cases were caused by a specific variant. The periods when certain variants were dominant in this study were pre-Delta (February 26, 2021 to July 24, 2021), Delta (July 25, 2021 to January 15, 2022), Omicron (January 16, 2022 to September 3, 2022), and Omicron sub-variants, which included BA.1 (January 16, 2022 to March 19, 2022), BA.2 (March 20, 2022 to July 23, 2022), and BA.5 (July 24, 2022 to October 15, 2022).

Data Analysis

We estimated differences in age group and sex by vaccination status. We then estimated the number of averted severe cases and deaths for all individuals who were vaccinated through the national vaccination campaign. The classification of vaccination subgroups and the analysis, which were similar to those described in other studies, were undertaken to estimate the projected burden of averted COVID-19 cases [9–14].

First, we calculated the daily age-adjusted incidence rates (age ranges [y]: 12–17, 18–29, 30–39, 40–49, 50–59, 60–74, and ≥75) of severe cases and deaths for the unvaccinated group and the vaccinated group. The person-days for the unvaccinated group were calculated for each day by deducting the person-days contributed by those who had received vaccination from the overall demographic approximations for each age group. The person-days for the vaccinated group were determined for each day by multiplying the proportion of individuals who were vaccinated by the demographic approximations for each age group. Individuals with previously confirmed SARS-CoV2 infection were excluded from the susceptible population and the totals for severe cases and deaths. Differences in these rates between the unvaccinated group and the vaccinated group were then calculated for each day and each age group during the study period. The above procedure was repeated for every day during the study period and for severe cases and deaths. The results were then added together to determine the overall projected burden of COVID-19 from averted cases.

The total burden, number of severe COVID-19 cases, and number of COVID-19-related deaths were analyzed using the following formula:

$$\sum_{age\ stratum=1}^{8} \sum_{February\ 26,\ 2021}^{October\ 15,\ 2022} N \times V_{X \geq 2dose} \left(COVID_{unvaccinated\ \&\ 1\ dose} - COVID_{\geq 2dose} \right)$$

N was the daily total susceptible population in each age stratum, with those with a history of COVID-19 diagnosis excluded for each day. $V_{x \geq 2dose}$ was the cumulative daily vaccination coverage of people within each age group who

https://doi.org/10.24171/j.phrp.2023.0096

had received at least 2 doses of vaccines. $COVID_{Unvaccinated\ \&\ 1dose}$ was the daily rate of severe cases and deaths in the unvaccinated group. $COVID_{2dose}$ was the daily rate of severe cases and deaths in the vaccinated group. The population of each age group was determined, and the age-adjusted incidence rate of severe COVID-19 cases and COVID-19-related deaths was calculated according to vaccination status. This was calculated as the ratio of the number of severe cases and deaths and the total observation period (person-day) per 1,000,000 people per day. Therefore, according to the aforementioned formula, the number of severe COVID-19 cases and COVID-19-related deaths averted during the study period was estimated through statistical modeling using the number of susceptible people (N), vaccination coverage ($V_{x \geq 2dose}$), and the difference in the incidence rates of severe cases and death ($COVID_{Unvaccinated\ \&\ 1dose}$-$COVID_{2dose}$. All analyses were performed using SAS ver. 9.4 (SAS Institute) and Excel 2016.

Ethics Statement

This study was conducted in accordance with the Infectious Disease Prevention and Control Act (no. 12444 and no. 13392) and was approved by the Institutional Bioethics Committee of the KDCA and the requirement for informed consent was waived (No: 2021-12-03-PE-A).

Results

From February 26, 2021 to October 15, 2022, 43,601,286 (86.5%) of the total population (50,403,942 people aged ≥4 years) were vaccinated through the national vaccination campaign. Of those, 43,157,609 (85.6%) were vaccinated through the national vaccination campaign, and 32,387,611 (64.3%) completed the third and fourth vaccine doses. Republic of Korea recorded its highest number of COVID-19 cases around the BA.1 period (January to March 2022) (Figure 2).

During the same period, of the total study population, 43,096,261 people (92.0%) were vaccinated through the national vaccination campaign. While the difference in vaccination coverage by sex was not statistically significant, the vaccination rate of men was 92.3%, which was 0.6% higher than that of women. The vaccination rate for the third and fourth vaccine doses among women was 69.4%, which was 0.5% higher than the percentage for males (68.8%). Vaccination coverage tended to increase in older age groups. For example, individuals aged 60 to 74 years showed the highest vaccination coverage, with a 95.1% rate of complete vaccination, and the rate of booster vaccinations (third and fourth doses) was also the highest among this age group at 89.3% (Table 1).

Table 2 shows the median daily differences (interquartile range [IQR]) in the rate of severe COVID-19 cases and COVID-19-related deaths per 1,000,000 population in each age group between those who had not been vaccinated and those who were vaccinated through the national vaccination campaign. During the study period, the median daily differences in rate between the unvaccinated group and the vaccinated group were 0.99 severe cases per 1,000,000 population (IQR, 0.30–4.47) and 0.68 deaths per 1,000,000 population (IQR, 0.06–3.73). Although the dominant variant and age group differences were diverse as Republic of Korea recorded the highest number of cases around the BA.1

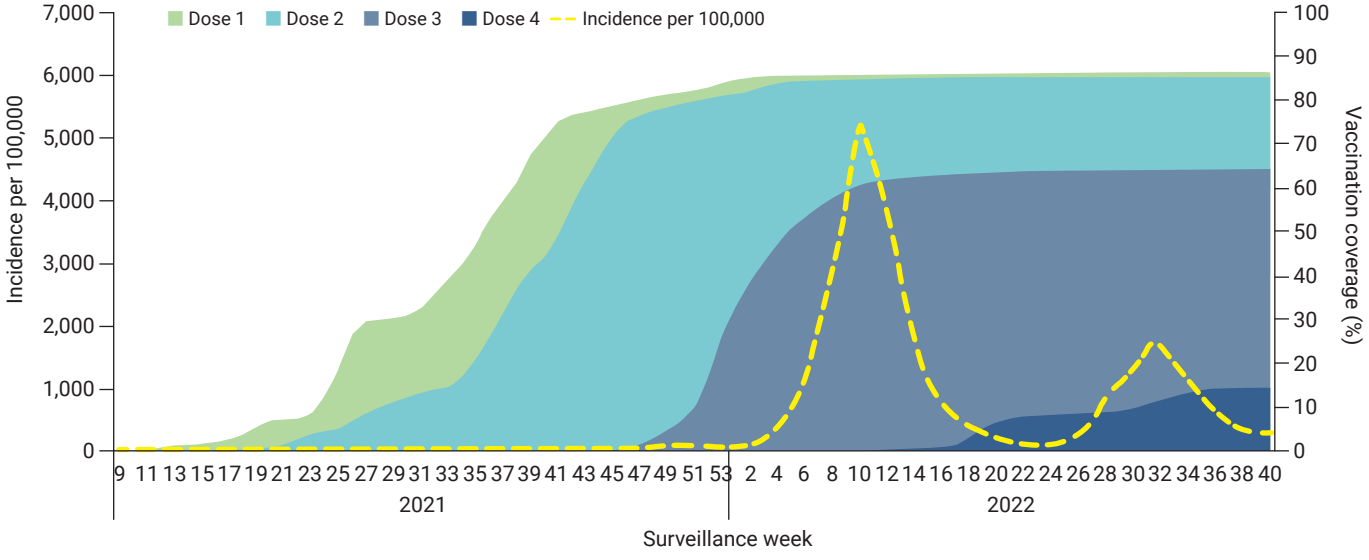

Figure 2. Weekly trends in the age-adjusted incidence of COVID-19 and vaccination coverage.

Table 1. Number and percentage of people in Republic of Korea by sex, age (≥12 years), and vaccination status (February 26, 2021 to October 15, 2022)

Characteristic	Vaccination status[a]					
	Total	Unvaccinated group		Vaccinated group		
		Unvaccinated	1st dose	2nd dose	3rd dose	4th dose
Total	46,864,039	3,348,786 (7.1)	418,992 (0.9)	10,705,357 (22.8)	25,108,518 (53.6)	7,282,386 (15.5)
Sex						
Male	23,328,521	1,607,487 (6.9)	200,210 (0.9)	5,460,570 (23.4)	12,525,019 (53.7)	3,535,235 (15.2)
Female	23,535,518	1,741,299 (7.4)	218,782 (0.9)	5,244,787 (22.3)	12,583,499 (53.5)	3,747,151 (15.9)
Age group (y)						
12–17	2,764,194	479,613 (17.4)	68,481 (2.5)	1,738,158 (62.9)	477,634 (17.3)	308 (0.0)
18–29	7,645,787	463,745 (6.1)	72,571 (0.9)	2,698,109 (35.3)	4,388,855 (57.4)	22,507 (0.3)
30–39	6,762,180	690,817 (10.2)	86,144 (1.3)	2,248,924 (33.3)	3,704,601 (54.8)	31,694 (0.5)
40–49	8,164,150	610,468 (7.5)	62,293 (0.8)	2,082,978 (25.5)	5,243,537 (64.2)	164,874 (2.0)
50–59	8,586,091	428,320 (5.0)	44,100 (0.5)	1,191,229 (13.9)	5,557,534 (64.7)	1,364,908 (15.9)
60–74	9,196,464	405,549 (4.4)	46,046 (0.5)	535,463 (5.8)	4,612,996 (50.2)	3,596,410 (39.1)
≥75	3,745,173	270,274 (7.2)	39,357 (1.1)	210,496 (5.6)	1,123,361 (30.0)	2,101,685 (56.1)

Data are presented as *n* (%).
[a]Vaccination status: doses 1–4, at least 14 days after receipt of doses 1–4; unvaccinated: unvaccinated or <14 days after receipt of dose 1.

periods owing to the fifth wave of COVID-19 infection, the largest differences in the median daily rates of severe cases (6.77 cases per 1,000,000 population [IQR, 2.50–15.03]) and deaths (10.29 deaths per 1,000,000 population [IQR, 2.55–27.06]) were observed between the unvaccinated group and the vaccinated group. Regarding age, the largest median daily differences in rate were observed among those aged ≥75 years for severe cases at 10.28 cases per 1,000,000 population (IQR, 1.37–28.61) and deaths at 9.99 deaths per 1,000,000 population (IQR, 0.89–38.66) (Table 2).

Between February 26, 2021, and October 15, 2022, there were 23,793 severe COVID-19 cases and 25,441 deaths related to COVID-19. A total of 95,786 severe cases (95% confidence interval [CI], 94,659–96,913) and 112,195 deaths (95% CI, 110,870–113,520) were prevented (Figure 3; Table 3). The associations of the prevented number of severe cases and deaths through the COVID-19 vaccination campaign by age group are shown in Figure S1.

Other than children and adolescents who were not the initial targets of the COVID-19 vaccination campaign, over 90% of the population aged 18 years and older received the COVID-19 vaccine. Although people aged 60 years and older accounted for only 27.6% of the 46,864,039 people included in the study aged 12 years and older, the number of averted severe cases was 43,732 (95% CI, 43,499–43,965) for those aged 60 to 74 years and 36,271 (95% CI, 35,908–36,634) for those aged 75 years or older, comprising 83.5% of the total averted severe cases. In total, 34,549 (95% CI, 34,368–34,730) people aged 60 to 74 years and 69,812 (95% CI, 69,336–70,288) people aged 75 years or older accounted for 93.0% of the 112,195 (95% CI, 110,870–113,520) averted deaths (Table 3).

Discussion

In Republic of Korea, a vaccination campaign began with the BNT162b2 vaccine (Pfizer-BioNTech) for healthcare workers and the ChAdOx1 nCoV-19 vaccine (AstraZeneca) for high-risk people (aged ≥65 years), such as residents in long-term care facilities, on February 26, 2021. In June of the same year, vaccinations with the Ad26.COV2.S vaccine (Janssen) and mRNA-1273 vaccine (Moderna) were initiated. Vaccination campaigns then began to distribute vaccines to healthy people (Table S1). Vaccination coverage gradually expanded to the entire population of Republic of Korea, and as of October 15, 2022, 43,096,261 people have been vaccinated through the national vaccination campaign, representing high vaccination coverage (92.0%) among the total population.

COVID-19 vaccination prevents the spread of the SARS-CoV-2 virus; however, it is now aimed at minimizing the disease burden not only at the individual level but also at the national level by preventing severe COVID-19 outcomes. Since it is impossible to directly measure and observe the impact of the COVID-19 vaccination campaign without actual data, though, a mathematical model is needed to quantify the impact of vaccination.

Since the initial outbreak of COVID-19 in 2019, SARS-CoV-2 variants such as the Alpha, Beta, and Delta variants have continued to appear, and the Omicron variant, classified as the fifth variant of concern, has been reported in more than 200 countries worldwide [15]. New SARS-CoV-2 variants can increasingly evade the immune system, which reduces the effectiveness of vaccines in preventing infections [16,17]; however, the effectiveness of vaccination in preventing severe COVID-19 cases and death has been

https://doi.org/10.24171/j.phrp.2023.0096

Table 2. Daily differences in the rate of COVID-19 outcomes between unvaccinated and fully vaccinated groups by the dominant variant and age group (February 26, 2021 to October 15, 2022)

Outcome	Age group (y)	Total	Pre-Delta	Delta	BA.1	BA.2	BA.5
		Feb. 26, 2021–Oct. 15, 2022	Feb. 26, 2021–Jul. 24, 2021	Jul. 25, 2021–Jan. 15, 2022	Jan. 16, 2022–Mar. 19, 2022	Mar. 20, 2022–Jul. 23, 2022	Jul. 24, 2022–Oct. 15, 2022
Severe cases[a]	Total	0.99 (0.30–4.47)	0.24 (0.15–0.32)	0.85 (0.44–3.80)	6.77 (2.50–15.03)	1.88 (0.72–5.86)	3.86 (1.92–5.50)
	12–17	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	18–29	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.26)	0.00 (0.00–1.75)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	30–39	0.00 (0.00–0.64)	0.00 (0.00–0.15)	0.53 (0.20–0.83)	1.11 (0.00–2.28)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	40–49	0.19 (0.00–1.34)	0.12 (0.00–0.25)	0.70 (0.39–1.45)	1.40 (0.00–3.94)	0.00 (0.00–1.47)	0.00 (−0.21 to 1.95)
	50–59	0.66 (0.00–3.76)	0.12 (0.12–0.36)	1.53 (0.62–5.32)	5.17 (1.80–8.00)	0.00 (−0.12 to 4.36)	0.78 (−0.37 to 4.73)
	60–74	2.71 (0.55–13.26)	0.45 (0.33–0.66)	6.21 (1.37–19.05)	20.77 (7.52–42.79)	4.76 (0.00–15.18)	7.20 (2.01–13.10)
	≥75	10.28 (1.37–28.61)	0.80 (0.47–1.42)	12.21 (5.25–25.12)	46.52 (21.16–90.57)	13.64 (3.50–38.38)	25.14 (14.00–35.08)
Deaths[b]	Total	0.68 (0.06–3.73)	0.04 (0.02–0.06)	0.28 (0.07–2.55)	10.29 (2.55–27.06)	1.99 (0.66–8.72)	3.28 (1.90–5.21)
	12–17	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	18–29	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	30–39	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–1.10)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	40–49	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.07)	0.00 (0.00–1.40)	0.00 (0.00–1.61)	0.00 (0.00–0.00)
	50–59	0.00 (0.00–1.56)	0.00 (0.00–0.00)	0.00 (0.00–1.21)	3.09 (0.00–7.63)	0.00 (0.00–2.55)	0.00 (−0.19 to 2.33)
	60–74	1.16 (0.00–7.90)	0.00 (0.00–0.11)	1.80 (0.23–8.97)	15.68 (5.59–53.34)	2.75 (0.00–9.74)	4.65 (1.88–7.98)
	≥75	9.99 (0.89–38.66)	0.38 (0.00–0.84)	10.73 (3.61–34.10)	101.22 (28.26–228.46)	18.86 (3.88–79.22)	27.32 (13.29–48.47)

Data are presented as median differences in daily incidence rates (interquartile range) per 1,000,000 population.
[a]Severe disease: infected person treated with high-flow oxygen therapy, mechanical ventilation, extracorporeal membrane oxygenation, or continuous renal replacement therapy within 28 days of laboratory confirmation of COVID-19. [b]Death: infected person who died within 28 days of laboratory confirmation of COVID-19.

identified in previous studies [18]. During the Omicron (BA.1)-dominant period in Republic of Korea, the median daily differences in rates between vaccinated and unvaccinated people were the largest at 6.77 severe cases per 1,000,000 population and 10.29 deaths per 1,000,000 population. It was confirmed that, even if an epidemic caused by the variant resulted in a sharp increase in the number of infected people, vaccination was still effective in preventing severe cases and death. A positive impact from COVID-19 vaccination in reducing the incidence of severe cases and death, similar to that found in Republic of Korea, has been reported in other countries, especially in Israel and Japan [9,10–12,19].

In a study conducted in Israel, the differences in the daily median incidence by vaccination status were 2.0 severe cases per 100,000 population and 0.5 deaths per 100,000 population, which were much higher than those in this study, which showed estimated differences of 0.99 severe cases per 1,000,000 population and 0.68 deaths per 1,000,000 population. By investigating the ratios of observed instances of severe cases and deaths to prevent further such cases in both countries, the differences could be ascribed to lower incidences rather than to a declining positive impact on immunity and differences in incidence between vaccinated and unvaccinated groups [9]. In Japan, the differences in the daily median incidence by vaccination status were lower than ours. In this study, there were 9.99 deaths per 1,000,000 population among those aged 75 years or older. There were 1.54 cases per 1,000,000 population in Japan among men aged 65 years or older, while the rate was only 1 case per 1,000,000 among women [10].

We estimated that 119,579 (95% CI, 118,901–120,257) COVID-19-related severe cases and 137,636 (95% CI, 136,909–138,363) COVID-19-related deaths would have occurred if vaccination had not been performed for the 597 days from February 26, 2021 to October 15, 2022. We also found that vaccination prevented 95,786 (95% CI, 94,659–96,913) severe cases and 112,195 (95% CI, 110,870–113,520) deaths due to COVID-19, representing reductions in risk of 80.1% (95,786/119,579) and 81.5% (112,195/137,636), respectively. This also indicates that if the nationwide COVID-19 vaccination campaign had not been implemented in Republic of Korea, the number of severe cases and deaths during the same period would have been at least 4 times higher.

When compared to other studies, our study estimated that vaccination averted more COVID-19-related deaths than severe COVID-19 cases, but most other studies estimated that more severe cases or hospitalizations were prevented than deaths [9–11]. This discrepancy is likely due to the limitations of the data sources. First, as the number of confirmed COVID-19 infections increased rapidly, it

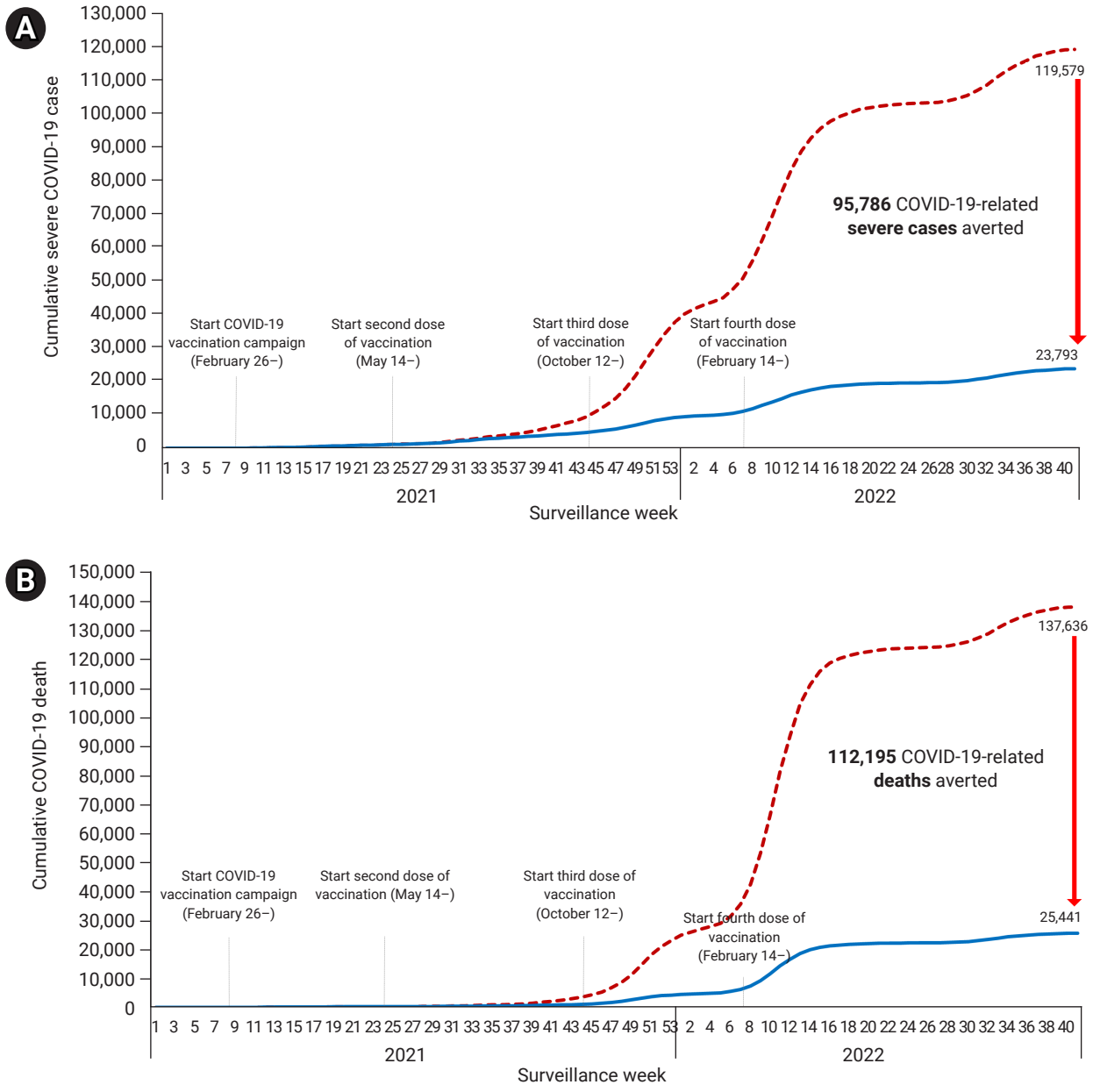

Figure 3. Weekly trends in the age-adjusted incidence of severe COVID-19 cases and COVID-19-related deaths by vaccination status. (A) COVID-19-related severe cases. (B) COVID-19-related deaths.

is assumed that there was a difference in the number of deaths in the early stages after infection without passing through the severe stage. Second, the surveillance system for severe cases collects clinical information reported by medical institutions and public health centers; therefore, after the number of confirmed COVID-19 cases increased sharply, underestimation is possible since clinical information about those infected with severe cases was not reported promptly.

SARS-CoV-2 can cause infection regardless of age, but symptoms that worsen with age can increase the risk of a severe case and death, especially among the elderly [20,21]. In this study, 80.3% of all severe cases and 94.0% of deaths during the analysis period occurred in infected people older than 60 years of age. The study population aged 60 years and older accounted for only 27.6% of the total population but 83.5% of the total number of averted severe cases and 93.0% of the total averted deaths. Therefore, we believe that the strategy of the Korean COVID-19 vaccination campaign, which prioritized vaccination for high-risk populations such as those aged 60 years or older, had an impact on preventing serious infection and death. Similar findings were reported in Israel and Japan, where the vaccination

https://doi.org/10.24171/j.phrp.2023.0096

Table 3. Cumulative expected and observed COVID-19 outcomes averted by the vaccination campaign (February 26, 2021 to October 15, 2022)

Age group (y)	Population size	Vaccination coverage (≥2 doses, %)	Severe COVID-19 cases[a]			COVID-19-related deaths[b]		
			Expected no. of severe cases (unvaccinated group)	Observed severe cases	Averted severe cases	Expected no. of deaths (unvaccinated group)	Observed deaths	Averted deaths
Total	46,864,039	92.0	119,579 (118,901–120,257)	23,793	95,786 (94,659–96,913)	137,636 (136,909–138,363)	25,441	112,195 (110,870–113,520)
12–17	2,764,194	80.2	193 (166–220)	63	130 (121–139)	34 (23–45)	11	23 (19–27)
18–29	7,645,787	93.0	1,137 (1,071–1,203)	282	855 (822–888)	411 (371–451)	64	347 (331–363)
30–39	6,762,180	88.5	2,015 (1,927–2,103)	662	1,353 (1,303–1,403)	466 (424–508)	115	351 (330–372)
40–49	8,164,150	91.8	4,340 (4,211–4,469)	1,217	3,123 (3,052–3,194)	1,750 (1,668–1,832)	343	1,407 (1,370–1,444)
50–59	8,586,091	94.5	12,775 (12,553–12,997)	2,453	10,322 (10,204–10,440)	6,697 (6,537–6,857)	991	5,706 (5,635–5,777)
60–74	9,196,464	95.1	52,132 (51,684–52,580)	8,400	43,732 (43,499–43,965)	39,849 (39,458–40,240)	5,300	34,549 (34,368–34,730)
≥75	3,745,173	91.7	46,987 (46,562–47,412)	10,716	36,271 (35,908–36,634)	88,429 (87,846–89,012)	18,617	69,812 (69,336–70,288)

Data are presented as no. of cases (95% confidence interval).
[a]Severe disease: infected person treated with high-flow oxygen therapy, mechanical ventilation, extracorporeal membrane oxygenation, or continuous renal replacement therapy within 28 days of laboratory confirmation of COVID-19. [b]Death: infected person who died within 28 days of laboratory confirmation of COVID-19.

of the elderly was prioritized, as in Republic of Korea [9,17]. In Israel, those aged 65 years and older accounted for only 17% of the total population but 74% of severe cases and 91% of deaths; hence, this age group is an important target population for preventing severe disease and death [9].

There are some limitations to our study. First, there is a possibility of unmeasured differences from nonpharmaceutical interventions, including wearing face masks, practicing handwashing hygiene, avoiding large gatherings, and maintaining physical distance as well as from the characteristics of different variants in each period. These factors may have influenced the results of the study. Second, when analyzing the impact of COVID-19 vaccination, differences in the risk of infection between the vaccinated and unvaccinated groups may not be solely attributable to the vaccine but also to differences in health status. This increased the possibility of overestimating the impact of the vaccination. Unfortunately, due to data limitations, we were unable to include some factors in our analysis, including information on socioeconomic status and health status, such as underlying diseases, which could be potential confounders. Data related to these factors were limited and could not be added as additional factors. Thus, we conducted a stratified analysis based on age and date to control for key confounding variables to mitigate this issue. Therefore, in future studies, more detailed data with a wider range of items such as underlying diseases or comorbidities should be used.

Despite these limitations, this study's results provide a comprehensive evaluation of the COVID-19 vaccination campaign, showing the substantial impact of vaccinations on the entire population for over 500 days in preventing more than 90,000 severe cases and deaths. It is important to establish a response strategy to minimize the negative impact of COVID-19 on high-risk infected people and their daily lives, especially to reduce the number of severe cases and deaths. Through this analysis, we found that Republic of Korea's nationwide vaccination campaign reduced the number of severe cases and deaths due to COVID-19; therefore, vaccination was critical for preventing severe cases and deaths, especially among the elderly population, who have a high disease burden.

Supplementary Material

Table S1. Timeline of vaccination start date, Republic of Korea, February 2021–October 2022; **Figure S1.** Weekly trend in the incidence of (A) severe disease and (B) death by age group (years) and vaccination status. Supplementary data is available at https://doi.org/10.24171/j.phrp.2023.0096.

Notes

Ethics Approval

This study was conducted in accordance with the Infectious Disease Prevention and Control Act (no. 12444 and no. 13392) and was approved by the Institutional Bioethics Committee of the KDCA (No: 2021-12-03-PE-A).

Conflicts of Interest

The authors have no conflicts of interest to declare.

Funding

None.

Availability of Data

The datasets are not publicly available but are available from the corresponding author upon reasonable request.

Authors' Contributions

Conceptualization: JHH, SEL, SL, YJP; Data curation: JHH, JHL, SKP, RKK; Formal analysis: JHH, JHL, SKP, EJJ; Investigation: JHH, JHL; Methodology: JHH, JHL, SKP, KHL, CC; Software: JHH, RKK; Validation: EJJ, RKK; Visualization: JHH, JHL; Writing–original draft: JHH, SEL, SL, YJP; Writing–review & editing: all authors. All authors read and approved the final manuscript.

Acknowledgements

We thank the COVID-19 Vaccination Task Force and Division of National Immunization, Korea Disease Control and Prevention, and all relevant ministries (including the Ministry of Interior and Safety and those at the *si/do* and *si/gun/gu* levels), medical staff at health centers, and medical facilities for their efforts to respond to the COVID-19 outbreak. This study was part of the Korea COVID-19 Vaccine Effectiveness (K-COVE) Initiative.

References

1. World Health Organization (WHO). WHO Coronavirus (COVID-19) dashboard [Internet]. WHO; 2023 [cited 2023 Apr 18]. Available from: https://covid19.who.int/.
2. Hall VJ, Foulkes S, Saei A, et al. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. Lancet 2021;397:1725–35.
3. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA COVID-19 vaccine in a nationwide mass vaccination setting. N Engl J Med 2021;384:1412–23.
4. Harder T, Koch J, Vygen-Bonnet S, et al. Efficacy and effectiveness of COVID-19 vaccines against SARS-CoV-2 infection: interim results of a living systematic review, 1 January to 14 May 2021. Euro Surveill 2021;26:2100563.
5. Watson OJ, Barnsley G, Toor J, et al. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infect Dis 2022;22:1293–302.
6. Korea Disease Control and Prevention Agency (KDCA). KDCA Coronavirus (COVID-19) dashboard [Internet]. KDCA; 2023 [cited 2023 Apr 18]. Available from: https://ncov.kdca.go.kr/. Korean.
7. Shim E. Projecting the impact of SARS-CoV-2 variants and the vaccination program on the fourth wave of the COVID-19 pandemic in South Korea. Int J Environ Res Public Health 2021;18:7578.
8. Ryu B, Shin E, Kim NY, et al. Severity of COVID-19 associated with SARS-CoV-2 variants circulating in the Republic of Korea. Public Health Wkly Rep 2022;15:2873–83.
9. Haas EJ, McLaughlin JM, Khan F, et al. Infections, hospitalisations, and deaths averted via a nationwide vaccination campaign using the Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine in Israel: a retrospective surveillance study. Lancet Infect Dis 2022;22:357–66.
10. Kayano T, Sasanami M, Kobayashi T, et al. Number of averted COVID-19 cases and deaths attributable to reduced risk in vaccinated individuals in Japan. Lancet Reg Health West Pac 2022;28:100571.
11. Sacco C, Mateo-Urdiales A, Petrone D, et al. Estimating averted COVID-19 cases, hospitalisations, intensive care unit admissions and deaths by COVID-19 vaccination, Italy, January-September 2021. Euro Surveill 2021;26:2101001.
12. Vilches TN, Sah P, Moghadas SM, et al. COVID-19 hospitalizations and deaths averted under an accelerated vaccination program in northeastern and southern regions of the USA. Lancet Reg Health Am 2022;6:100147.
13. Yi S, Choe YJ, Lim DS, et al. Impact of national COVID-19 vaccination Campaign, South Korea. Vaccine 2022;40:3670–5.
14. Santos CV, Noronha TG, Werneck GL, et al. Estimated COVID-19 severe cases and deaths averted in the first year of the vaccination campaign in Brazil: a retrospective observational study. Lancet Reg Health Am 2023;17:100418.
15. GISAID. Tracking of hCoV-19 variants [Internet]. GISAID; 2022 [cited 2022 Nov 10]. Available from: https://gisaid.org/hcov19-variants/.
16. Ssentongo P, Ssentongo AE, Voleti N, et al. SARS-CoV-2 vaccine effectiveness against infection, symptomatic and severe COVID-19: a systematic review and meta-analysis. BMC Infect Dis 2022;22:439.
17. Cele S, Jackson L, Khoury DS, et al. Omicron extensively but incompletely escapes Pfizer BNT162b2 neutralization. Nature 2022;602:654–6.
18. Matrajt L, Eaton J, Leung T, et al. Vaccine optimization for COVID-19: who to vaccinate first? Sci Adv 2021;7:eabf1374.
19. Schneider EC, Shah A, Sah P, et al. Galvani AP. The U.S. COVID-19 vaccination program at one year: how many deaths and hospitalizations were averted? Commonwealth Fund; 2021 [cited 2023 Apr 18]. Available from: https://www.doi.org/10.26099/3542-5n54.
20. Liu Y, Mao B, Liang S, et al. Association between age and clinical characteristics and outcomes of COVID-19. Eur Respir J 2020;55:2001112.
21. Bonanad C, García-Blas S, Tarazona-Santabalbina F, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. J Am Med Dir Assoc 2020;21:915–8.

https://doi.org/10.24171/j.phrp.2023.0096