Asia-pacific Journal of Convergent Research Interchange
Vol.9, No.7, July 31 (2023), pp.287-297
http://dx.doi.org/10.47116/apjcri.2023.07.23

Navigating the COVID-19 Pandemic: Examining Changes in Global Incidence and Mortality with Emphasis on Vaccine Coverage Base on the Omicron Era

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Abstract: Several studies have examined the clinical efficacy of the COVID-19 vaccine, but there is still a lack of research on the worldwide policy effects of vaccination efforts. Understanding the global impact of vaccination campaigns in managing the spread of COVID-19 is essential. This study explores the influence of worldwide COVID-19 vaccine coverage on the occurrence and death rates before and after the emergence of the Omicron variant. Data from 119 countries on the Our World in Data platform was examined, with daily cases per million people and vaccination rates per 100 people as some of the variables analyzed. In the pre-Omicron era, people vaccinated per hundred had a negative association with daily deaths in the non-lagged model, while the 14 days-lagged models had a significantly positive association. For people fully vaccinated per hundred, both daily cases and daily deaths per million had a negative association. Daily tests per thousand were positively associated with non-lagged and 14 days-lagged models for daily cases and deaths. In the post-Omicron era, people vaccinated per hundred was positively associated with both non-lagged and 14 days-lagged models in daily cases and deaths. In both models, people fully vaccinated per hundred had a negative association with daily cases and deaths. Daily tests per thousand had statistically positive associations with daily cases and deaths, except for the 14 days-lagged models of daily deaths. Vaccination worldwide has been more associated with preventing COVID-19, particularly with reduced mortality. Moreover, in the post-Omicron era, a new dose of vaccine affected incidence and mortality.

Keywords: COVID-19, Vaccination, Omicron, Incidence, Mortality, SARS-CoV-2

1. Introduction

The COVID-19 pandemic is a global health crisis, with hundreds of millions of cases and deaths. The emergence of the Omicron variant, first identified in late 2021, has added a new layer of complexity to the pandemic. The Omicron variant is highly transmissible and has rapidly spread worldwide[1][2], leading to concerns about its impact on health outcomes. COVID-19 are highly effective at preventing COVID-19 infections, reducing the severity of illness, and preventing hospitalization and death. Many studies have consistently shown that the vaccines are effective at preventing COVID-19 infections. For example, the Pfizer-BioNTech vaccine was 95% effective at preventing COVID-19 infection in clinical trials[3], while the Moderna vaccine showed 94.1% effectiveness in the same regard[4].

Vaccination coverage has played a significant role in managing the spread of COVID-19. Immunization initiatives aid in achieving herd immunity by thwarting infection among large segments of the population, reducing the virus transmission rate, and safeguarding vulnerable individuals[5]. Vaccines were distributed after the COVID-19 pandemic, but the emergence of Omicron was a new

Received: March 25, 2023; 1st Review Result: May 10, 2023; 2nd Review Result: June 03, 2023
Accepted: June 30, 2023

challenge of the pandemic, contributing to a new explosion in incidence and mortality[2]. The effectiveness of these vaccines against Omicron strains is clinically effective[6][7]. However, since effectiveness decreases over time, booster shots are known to be necessary[7]. Even though it works in clinical studies, it does not always work at the population level[8].

Since the start of the pandemic, many researchers have been attempting to evaluate the effectiveness of vaccine distribution at a population level. One study from the UK analyzed vaccine effectiveness against the B.1.617.2 (Delta) variant[9], and another study from Canada reported a negative association between vaccination and hospitalization and death[10]. A study in Korea using data up to January 2022 also reported that vaccination is effective in reducing the severity, especially in older adults[11]. Additionally, some studies have reported on the effectiveness of vaccines against COVID-19 through systematic reviews[6-8]. Although these studies suggest that vaccines are effective, some are country-specific or have limitations because they do not provide actual global data. More recently, studies have evaluated vaccine effectiveness using real data from countries worldwide[5][12]. However, these papers also have limitations, such as using data from the early stages of the pandemic or not considering the Omicron variant. The effectiveness of the vaccine in the real world is still insufficient, and its distribution and coverage are uneven[13]. Moreover, there is a dearth of studies regarding the efficacy of vaccines following the emergence of Omicron.

As we enter the fourth year since the emergence of COVID-19, our lives are gradually returning to normal. It is crucial to comprehend the global ramifications of vaccination efforts in controlling the spread of COVID-19. The emergence of new infectious diseases and pandemics has highlighted the significance of global collaboration and collective actions. Therefore, evaluating vaccine policies for COVID-19 becomes necessary to prepare for future crises and challenges. Effective distribution policies for COVID-19 vaccines during the pandemic are imperative. Furthermore, while vaccines have proven effective in clinical trials against the Omicron strain, their effectiveness in the real world must be clarified, and more research is needed on this topic. Therefore, this study aims to examine the impact of vaccine coverage on incidence and mortality rates during the pre and post-Omicron periods. To clarify, the hypothesis of this study is that COVID-19 response activities, such as country-specific vaccine coverage, fully vaccinated coverage, and daily tests, are related to daily deaths per million and daily cases per million.

2. Summary of Related Studies

There are numerous studies related to COVID-19; however, at the global level, it is still insufficient to determine whether the government's vaccine policy has affected reducing the incidence or mortality of COVID-19. The limitations of previous studies are summarized as follows. Firstly, as a randomized controlled trial (RCT) study, assessing vaccine policies in terms of population groups or national governments is not feasible. Secondly, due to the restricted data scope limited to a specific region or country, its validity cannot be confirmed on a global scale. Lastly, it fails to encompass the early stages of the pandemic or the period following the emergence of the Omicron variants. Therefore, this study holds significance in evaluating the effectiveness of vaccine policies on a global scale. It targets the entire duration of the pandemic, starting from its onset until the World Health Organization (WHO) lifted the state of emergency related to COVID-19 [Table 1].

[Table 1] Summary of Related Studies

Limitations	Subject
Due to its nature as an RCT study, it is not feasible to assess the effectiveness of vaccine policies implemented by national governments or authorities.	[3, 4, 6, 7, 14]

Non-global level, specific region, or country research	[15][16]
Not actual global data	[6-8]
Assessing only part of the pandemic, not the entire period	[5-9, 12]

3. Methods

3.1 Research Design and Settings

This study utilizes panel data to evaluate the efficacy of vaccine policies implemented in response to the emergence of COVID-19. The data utilized in this study was obtained from Our World in Data, which is a comprehensive database providing global data across various domains. The reliability of the COVID-19 statistics available in this database has also been verified[17]. The data utilized in this study spans from January 3, 2020, when COVID-19 was first reported, to March 29, 2023, the most current data available at the time of data extraction. While data is available for 218 countries, this study specifically focuses on analyzing 119 countries where analyzing key variables as longitudinal data is feasible. Meanwhile, Omicron was first discovered in samples collected before November 23, 2021. The first case of Omicron was confirmed in the United States on November 1, 2021, and confirmed cases were reported in 38 countries around the world on December 3. Therefore, a distinction was made between the period before and after discovering the Omicron variant in the United States based on the specific date[18].

3.2 Selection of Variables

The dataset provided by Our World in Data offers a multitude of variables that can be analyzed. Nevertheless, adding more variables to the analysis would reduce the number of countries that can be included in the study. These parameters can be downloaded from the website's 'Coronavirus Pandemic (COVID-19)' topic. To optimize the number of target countries, only two dependent variables were chosen: daily cases per million and daily cases per million. Moreover, as an independent variable, people vaccine per hundred, people fully vaccine per hundred, daily people vaccine per hundred and daily tests per thousand. People vaccine per hundred receive one or more doses, and people fully vaccinated per hundred have received two or more doses.

3.3 Statistics

For each variable in the dataset, a descriptive analysis was conducted. In order to facilitate comprehension of the data before and after the emergence of the Omicron variant, box plots were utilized to represent the data visually. Additionally, a correlation matrix was used to investigate the relationships between the various variables. Since this study is a longitudinal investigation utilizing panel data, a fixed-effects analysis was carried out at the national level, which is a commonly employed technique in longitudinal studies. The body generally takes a few weeks to produce antibodies after being vaccinated against COVID-19. According to the Centers for Disease Control and Prevention (CDC) of the United States, the body typically takes about two weeks after completing the vaccine series to build full protection against the virus[19]. As a result, a 14-day lagged model was also utilized in further analyses. Except for descriptive analysis, all analyses were converted to natural logarithmic values.

The fixed-effects formula is:

Daily deaths per million & Daily cases per million, $(Y_{it}) = \alpha i + \beta_1 \cdot ln$ *People vaccine per hundred* $_{it} + \beta_2 \cdot ln$ *people fully vaccine per hundred* $_{it} + \beta_3 \cdot ln$ *Daily people vaccine per hundred* $_{it} + \beta_4 \cdot ln$ *Daily tests per thousand* $_{it} + E_{it}$

It includes n entity-specific intercepts, denoted by αi (where i ranges from 1 to n), which are unknown constants for each entity. The model also includes coefficients, β1 to βn, for independent variables. Yit which represents the dependent variables where i refers to the entity and t refers to time. The term "it" represents the time interval effect, and the term Eit represents the error term.

3.4 Ethical approval

The research was performed following the principles outlined in the Declaration of Helsinki. None of the authors of this article conducted any studies involving human participants or animals. Therefore, ethical approval was not required.

4. Results

4.1 Descriptive Statistics of key variables

In terms of daily cases per million, the post-Omicron era had a higher rate of 288.91 compared to the pre-Omicron era of 83.80. Additionally, daily deaths per million were higher during the pre-Omicron period at 1.27 compared to the post-Omicron at 0.74. The percentage of people vaccinated per hundred was 31.82 during the pre-Omicron, which increased to 67.92 in the post-Omicron. Similarly, the percentage of people fully vaccinated per hundred was 25.41 in the pre-Omicron, which increased to 62.52 in the post-Omicron. In terms of daily vaccinations per hundred, the pre-Omicron had a rate of 0.17 compared to the post-Omicron at 0.03. Additionally, the number of daily tests per thousand increased from 2.70 in the pre-Omicron to 5.60 in the post-Omicron [Table 2].

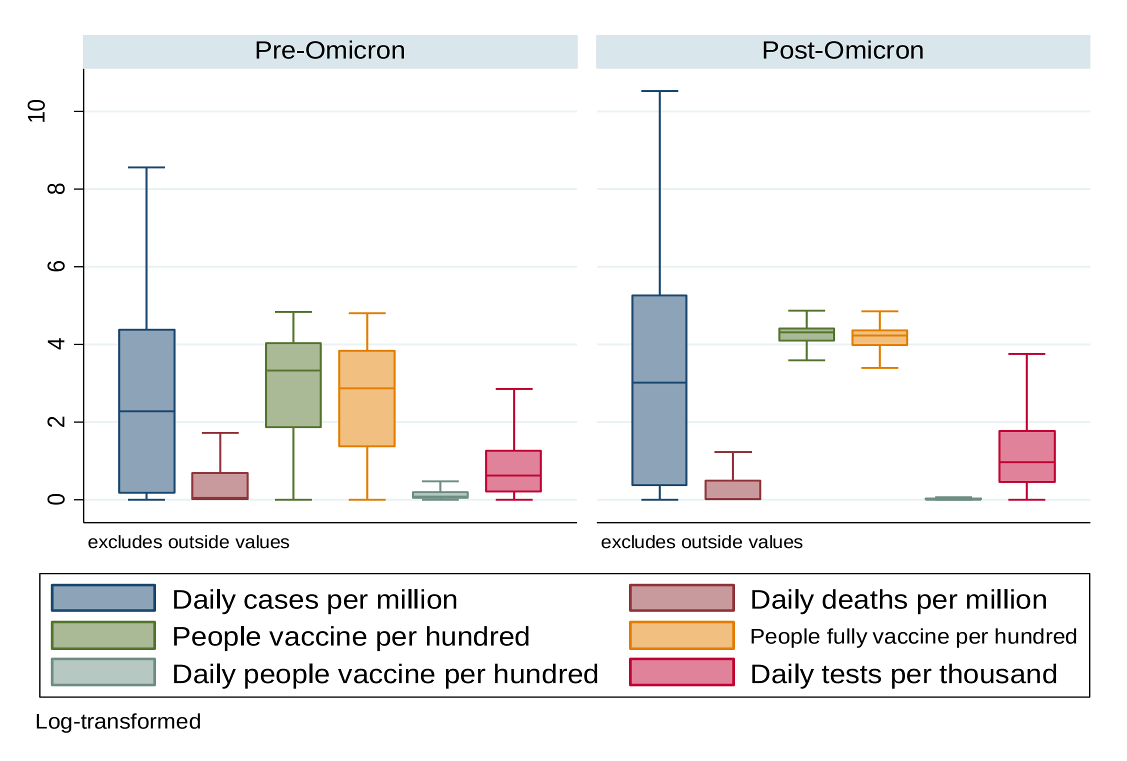
[Table 2] Descriptive Analysis of Each Variables (Unit: Mean and Standard Deviation)

	Pre-Omicron era	Post-Omicron era
Daily cases per million	83.80(195.04)	288.91(967.8)
Daily deaths per million	1.27(3.36)	0.74(2.32)
People vaccine per hundred	31.82(26.98)	67.92(20.62)
People fully vaccine per hundred	25.41(24.93)	62.52(21.27)
Daily people vaccine per hundred	0.17(0.17)	0.03(0.07)
Daily tests per thousand	2.70(6.98)	5.60(14.43)

Using box plots a comparison between the pre-and post-Omicron eras was conducted for each element. The results revealed an overall increase in daily cases per million, people vaccinated per hundred, people fully vaccinated per hundred, and daily tests per thousand in the post-Omicron era. Furthermore, the range of people vaccinated per hundred and people fully vaccinated per hundred was greatly reduced in the post-Omicron era. Figure 1 also shows the change in daily deaths per million and daily tests per thousand on the graph [Fig 1].

4.2 Correlation among key variables

A correlation matrix was utilized to analyze the relationship between variables. Prior to the analysis, all variables were transformed to their natural logarithm. The results indicated that all variables were statistically significant at the $p < 0.001$ level with each other. A correlation matrix was utilized, with the color scheme indicating positive correlations represented in purple and negative correlations in pink. The analysis confirmed that the trends of the variables varied based on the pre-and post-Omicron eras [Fig 2].



[Fig. 1] Box plot comparison of variables between pre- and post-Omicron eras. All variables included in the models were log-transformed.

Pre-Omicron

	Daily cases per million	Daily deaths per million	People vaccine per hundred	People fully vaccine per Hundred	People vaccine smooth per hundred	Daily tests per thousand
Daily cases per million						
Daily deaths per million	0.735					
People vaccine per hundred	0.243	-0.053				
People fully vaccine per Hundred	0.172	-0.126	0.948			
People vaccine smooth per hundred	0.199	0.144	0.327	0.107		
Daily tests per thousand	0.564	0.286	0.364	0.304	0.207	

Post-Omicron

	Daily cases per million	Daily deaths per million	People vaccine per hundred	People fully vaccine per hundred	People vaccine smooth per hundred	Daily tests per thousand
Daily cases per million						
Daily deaths per million	0.630					
People vaccine per hundred	0.436	0.186				
People fully vaccine per hundred	0.455	0.187	0.987			
People vaccine smooth per hundred	-0.096	-0.022	-0.155	-0.207		
Daily tests per thousand	0.642	0.366	0.294	0.358	-0.111	

[Fig. 2] Correlation Matrix Analysis of Variables: All variables were found to be significant at the $p < 0.001$

level. Positive correlations are shown in purple and negative correlations are shown in pink. Variables transformed to natural log before analysis.

4.3 Fixed effect model

In the pre-Omicron era, people vaccinated per hundred had a negative association in the non-lagged model (Coef.=-0.081, p<0.01). However, the 14 days-lagged model had a significantly positive association with daily deaths. For people fully vaccinated per hundred, both daily cases and daily deaths per million were negatively associated and statistically significant. Daily people vaccinated per hundred had an overall significant positive association with daily cases and daily deaths per million but was not significant in the 14 days-lagged models of daily deaths. Finally, daily tests per thousand were positively associated with both non-lagged and 14 days-lagged models for daily cases and deaths [Table 3].

[Table 3] Fixed-effect model of pre-Omicron era COVID-19 incidence, mortality rates, vaccination coverage, and testing rates: people vaccine per hundred, people fully vaccine per hundred, daily people vaccine per hundred, and daily tests per thousand. All variables included in the models were log-transformed.

Pre-Omicron	Daily cases per million (Coef & t value)		Daily deaths per million (Coef & t value)	
	Non-lagged	14 days-lagged	Non-lagged	14 days-lagged
People vaccine per hundred	-0.081(-2.67)**	0.831(2.77)**	0.078(4.45)***	0.143(8.20)***
People fully vaccine per hundred	-0.954(-3.86)***	-0.077(-3.08)**	-0.258(-18.02)***	-0.205(-14.24)***
Daily people vaccine per hundred	0.702(10.85)***	0.290(4.45)***	0.404((10.77)***	0.006(17.89)
Daily tests per thousand	1.454(65.44)***	1.045(47.74)***	0.503(39.08)***	0.963(45.52)***
Constants	3.068(78.74)***	1.389(38.00)***	0.733(32.51)	-3.022(-33.95)***
R square	.237	0.254	0.227	0.281
Number of countries	119	113	119	113
Observations	16269	16017	16265	16014

* p<0.05, ** p<0.01, *** p<0.0001

In the post-Omicron era, people vaccinated per hundred was positively associated with both non-lagged and 14 days-lagged models in daily cases and deaths. In contrast, people fully vaccinated per hundred had a statistically significant negative association between non-lagged and 14 days-lagged models for daily cases and deaths. Daily people vaccinated per hundred was positively associated with daily cases and daily deaths per million (Coef.=1.610, p<0.0001; Coef.=0.990, p<0.0001, respectively), but was negatively associated (Coef.=-1.013, p<0.0001; Coef.=-0.671, p<0.0001, respectively) in the 14 days-lagged models between daily cases and daily deaths. Lastly, daily tests per thousand had statistically positive associations with daily cases and deaths in all other models except for the 14 days-lagged model of daily deaths [Table 4].

[Table 4] Fixed-effect model of post-Omicron era COVID-19 incidence, mortality rates, vaccination coverage, and testing rates: people vaccine per hundred, people fully vaccine per hundred, daily people vaccine per hundred, and daily tests per thousand. All variables included in the models were log-transformed

Post-Omicron era	Daily cases per million		Daily deaths per million	
	Non-lagged	14 days-lagged	Non-lagged	14 days-lagged
People vaccine per hundred	0.680(11.34)***	13.92(14.41)***	1.768(5.95)***	3.005(7.87)***
People fully vaccine per hundred	-3.527(-7.00)***	-6.76(-9.41)***	-1.051(-4.77)***	-1.854(-6.54)***
Daily people vaccine per hundred	1.610(4.94)***	-1.013(-2.48)*	0.990(6.94)***	-0.671(-4.15)***
Daily tests per thousand	1.373(61.51)***	0.652(20.41)***	0.357(36.55)***	0.180(1.42)
Constants	-14.356(-10.51)***	0.612(13.57)***	-2.704(-4.53)***	0.383(21.50)***
R square	0.358	0.254	0.183	0.105
Number of countries	115	113	115	106
Observations	8012	16017	8011	7236

* p<0.05, ** p<0.01, *** p<0.0001

5. Discussion

The COVID-19 pandemic has significantly impacted the world, with the emergence of the Omicron variant leading to changes in the daily cases and deaths per million, as well as vaccination and testing rates. This study analyzed the trends of these variables in the pre-and post-Omicron eras to provide a comprehensive understanding of the changes that occurred. These results showed a significant increase in daily cases per million in the post-Omicron era compared to the pre-Omicron era. In the post-omicron era, the incidence increased more than three times compared to before. In general, when the number of confirmed cases explodes, it causes an increase in the number of deaths because medical care and hospital beds may not be properly treated due to saturation[20][21].

Omicron is known to be much more contagious than the previous delta virus and has a relatively low fatality rate[22]. Accordingly, in this study, it was confirmed that the death rate per million people rather decreased in the post-Omicron era. People vaccine per hundred and people fully vaccine per hundred increased. Because these variables are cumulative, the number of people who have completed vaccination increases over time. On the other hand, it can be confirmed that the distribution range in post-Omicron is significantly reduced compared to the pre-Omicron, which shows that the inequality of vaccination was severe before Omicron, but improved in post-Omicron. In the early stages of the pandemic, issues about vaccine inequality between developed and developing countries were raised[23]. In addition, there were cases in which vaccines could not be sufficiently vaccinated, even in developed countries, due to initial supply shortages. Since then, vaccines have been supplied to underdeveloped countries through the COVAX program by the World Health Organization, UNICEF, and Gavi[24]. Even excess vaccines have been discontinued in some developed countries[25]. In 2021, WHO implemented a vaccine distribution policy to achieve 70% global vaccination coverage by mid-2022[26]. This objective had been accomplished by the time the WHO declared COVID-19 was no longer a global health emergency in May 2023[27]. The result means that inoculation rates in post-omicrons worldwide have leveled upward compared to before.

In the fixed effect model, the association between vaccine and incidence and mortality differed according to pre- and post-Omicron eras. Overall, the number of vaccine doses administered per hundred people was positively associated with COVID-19 incidence and mortality. However, full vaccination contributed to reductions in both incidence and mortality rates. It is important to note that even though individuals have been vaccinated against COVID-19, breakthrough cases can still occur[28]. However, since the vaccine's effectiveness reduces hospitalization and severity[29], it suggests that it had a more significant effect on reducing mortality in the real world. It is also known that fully vaccinated protects more safely from COVID-19 than single-dose vaccination[30]. In this study, being fully vaccinated showed a negative association with incidence and mortality in general. In this study, people vaccine per hundred, simply the proportion of people vaccinated, had higher coefficients for positive associations with incidence rates post-Omicron than pre-Omicron. The reason behind this observation cannot be disclosed in the current model. However, one possible inference is that persistence of antibodies decreases over time, even after vaccination[31]. For this reason, the protective effect against the COVID-19 virus may have been lower post-Omicron if additional vaccination was not performed. In addition, since Omicron's propagation power is stronger, there may be an interaction effect between the two variables. Daily vaccination can provide another perspective on the effectiveness of COVID-19 prevention. In this study, the daily people vaccine per hundred showed different trends according to the pre-and post-Omicron period. We should note that vaccination showed a negative association with COVID-19 in the 14 days-lagged model of the post-omicron era. This is because it should be considered that the characteristics of people receiving vaccines in pre- and post-omicron eras may differ. In other words, many new vaccinations in pre-Omicron are likely to be the first vaccination. In contrast, post-Omicron, the daily vaccination is more likely to be a full or booster shot. Even previously developed COVID-19 vaccines protect against SARS-CoV-2 infection against the Omicron strain[32]. Therefore, since immunity to the virus that causes COVID-19 typically develops in the body 14 days after vaccination[19], from a global perspective, regardless of the type of vaccine, the lagged model 14 days after vaccination of a new vaccine turns into a negative association. What happened is likely due to the effectiveness of the vaccine.

This study has several limitations. First, each country may have different characteristics. For example, different countries have different government controls and people's reactions to COVID-19. To understand this more precisely, doing a subgroup analysis according to income group or Global Burden of Disease regions may be helpful. Second, this study did not reflect the characteristics that could be different in pre- and post-Omicron. Due to the prolonged COVID-19, there is a possibility that even confirmed patients may not be counted in the statistics. Third, three or more booster shots have a higher preventive effect, but this study did not include boosters[32]. Fourth, this model did not consider other variables that could affect the other than the vaccine. I tried including as many variables and countries as possible in the analysis. However, since the number of countries to be analyzed decreases as variables are input, it may not be sufficient for analysis from a global perspective. For example, if government control policies are included in the analysis model, the number of subjects is significantly reduced. The present study has a notable advantage in comparing vaccine effectiveness in the real world between the pre-and post-Omicron periods, based on global data. In reality, overcoming all of these limitations can be challenging. However, in future studies, it would be valuable to consider subgroup analysis based on the emergence of significant variants. Nonetheless, this study possesses strengths despite its limitations. Notably, this study focused on a larger scale by targeting 119 countries and covering almost the entire pandemic period, unlike prior studies that concentrated on one country or the early phase of the pandemic. Moreover, one of the distinctive features of this study is that it highlights the possible variations in vaccine effectiveness according to the time of administration, i.e., before or after the emergence of the Omicron variant.

6. Conclusions

This study assessed the correlation between global-level vaccine policies during the pandemic and the incidence and mortality rates of COVID-19. Vaccination rates per hundred increased in the post-Omicron era, indicating a reduction in vaccination inequality globally. The fixed effect model revealed that full vaccination was negatively associated with incidence and mortality, highlighting the importance of complete vaccination. People's vaccine per hundred was positively associated with incidence and mortality, particularly in the post-Omicron era. Daily people vaccine per hundred also showed a negative association with COVID-19 incidence in the 14-day lagged model of the post-Omicron era. Overall, this study suggests that vaccination plays a crucial role in preventing COVID-19 and reducing its severity and mortality. In particular, it shows that only full vaccines can be effective in the post-Omicron era. This study confirms that global vaccine supply policies and efforts effectively combat COVID-19. As a result, it underscores the importance of ensuring adequate vaccine supply worldwide in future global infectious disease crises, such as pandemics. It also highlights the need for equitable distribution of vaccines from surplus countries to those lacking cooperation to achieve comprehensive vaccination coverage.

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