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Effect of vaccination patterns and vaccination rates on the spread and mortality of the COVID-19 pandemic

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ARTICLE INFO

Keywords:
COVID-19
Vaccination rate
Vaccination pattern
New confirmed case
Mortality

ABSTRACT

Objectives: Acquiring herd immunity through vaccination is the best way to curb the COVID-19 infection. Many countries have attempted to reach the herd immunity threshold as early as possible since the commencement of vaccination at the end of 2020. The purpose of this study is to (1) examine whether the pattern of vaccination rates affects the spread of COVID-19 and the consequent mortality and (2) investigate the level of cumulative vaccination rates that can begin to have an impact on reducing the spread and mortality of the pandemic.

Methods: This study selected 33 countries with higher vaccination rates as its sample set, classifying them into three groups as per vaccination patterns.

Results: The results showed that vaccination patterns have a significant impact on reducing spread and mortality. The full-speed vaccination pattern showed greater improvement in the spread of the COVID-19 pandemic than the other two patterns, while the striving vaccination pattern improved the most in terms of mortality. Secondly, the spread and mortality of the COVID pandemic started to significantly decline when the average cumulative vaccination rate reached 29.06 doses per 100 people and 7.88 doses per 100 people, respectively.

Conclusion: The study highlights the important role of vaccination patterns and the VTMR in reducing the epidemic spread and mortality.

Introduction

Since the outbreak of COVID-19, various response strategies have been adopted in many countries, including mass viral tests, mask wearing, social distancing, and self-quarantine, to mitigate the spread of the disease. Since successful vaccine development by the end of 2020, many countries have started to implement vaccination campaigns. The cumulative vaccination volume has progressed significantly since the global deployment of the COVID-19 vaccine. Fig. 1 shows the total vaccination volume and the average cumulative vaccination rate for each continent. As of 30 September 2021, a total of 6.30 billion doses of COVID-19 vaccines have been administered in the world, including 4.23 billion in Asia, 628 million in North America, 805 million in Europe, 448 million in South America and 150 million in Africa [1]. In Europe, 107.59 doses of vaccine per 100 people were administered, ahead of North America’s 65.94. In contrast, the vaccination rate in Africa was only 10.76 doses per 100 people, much lower than that in other continents.

Following the advent of vaccines that aim to lower basic reproduction of the coronavirus, vaccination rates are believed to be key to reducing mortality. Thus, many studies have focused on vaccination strategy issues associated with the transmission dynamics of COVID-19, by estimating crucial epidemiological parameters, such as reproduction numbers, exponential growth, serial intervals, and the infection fatality rate [2–9]. Alqahtani et al. [9] examined the transmission dynamics of coronavirus to analyze the combined effects of vaccines, vertical transmission, and early hospitalization. By using three models of SEIR (susceptible-exposed-infectious-recovered), Berec et al. [10] compared the difference in mortality between two vaccination rollout regimens for the second vaccine dose: one with the recommended 21 days for the BNT162b2 vaccine (Pfizer/BioNTech) and the second with an additional 3 weeks to 42 days. Furuse [4] conducted a simulation study to explore the impact of vaccination coverage rate on death counts in Japan by assuming that 90% of infections can be prevented after vaccination. The results estimated approximately 50,000 deaths over 150 days in Japan if all restrictions were lifted under high vaccination coverage rates. Mohammadi et al. [6] employed a simulation model to forecast the future dynamics of the COVID-19 epidemic in Ukraine. This study showed that it is more convenient, accurate, and efficient to use linear models to predict morbidity in a short period of time. However, the
Strategies to reduce the negative impact of COVID-19 include response and prevention strategies [12]. The goal of strategies selected by policymakers is to support different policy responses to reduce the risk of the emergence of novel viral pathogens, the spread of pandemics, and the consequent negative impact on society [13]. As prevention strategies are not limited to health systems, climatic and environmental factors associated with the spread and mortality of COVID-19 should be emphasized [14,15]. Coccia [16] constructed indicators to measure the performance of reducing mortality from the COVID-19 pandemic and implementing vaccination campaigns as a prevention strategy to limit the threat of future pandemics, and found that a country with a smaller population and/or better public governance may perform better.

Additionally, some studies have focused on analyzing control strategies, integrated with vaccination policies, based on COVID-19 dynamics. Coccia [17] compared the effect of strong control measures with vaccination policies in Italy, and found that confirmed cases, hospitalizations, and intensive care unit admissions were significantly equal ($p < 0.01$), but not mortality. Benati and Coccia [18] analyzed and validated the positive association between public governance and COVID-19 vaccination. Coccia [13] found that GDP per capita, healthcare spending, and air pollution levels are key factors influencing COVID-19 mortality; therefore, it is recommended that effective and aggressive strategies should be based on strengthening healthcare sector planning and environmental sustainability to reduce the negative impact of future pandemics. Ardito et al. [19] examined the patterns of innovative treatments for COVID-19 and proposed technological exaptation as a potential driving force of innovative treatments for COVID-19.

Several studies suggest that public health systems and emergency surveillance programs may positively impact the spread and mortality of the COVID-19 pandemic [20]. Effective planning should focus on avoiding the collapse of the healthcare system [15,21].

These challenges, including limited vaccine supply, have pushed many countries to develop an effective vaccination program and to optimize waiting lists for reduced wastage of doses to reduce the negative impact. The schedule and strategy to define the priority group for vaccination becomes relatively important for countries with insufficient vaccine supply, because the progression of anti-vaccination movement exists due to the heterogeneity of the population [22]. In fact, different ages and groups may have different demands for vaccination due to different frequencies of interactions [23]; thus, different vaccination strategies were examined by varying the age for routine vaccination and the number of age cohorts vaccinated, population targeted, and number of doses used. Many governments, including the EU, the UK, and the USA, have adopted vaccination strategies, such as prioritizing health-care and aged care workers. For example, EU countries have prioritized elderly people, residents and personnel of long-term care facilities, healthcare workers, social care personnel, and people with certain comorbidities [24]. Several studies suggest a ring vaccination strategy that prioritizes the close contacts of a confirmed case to control the preventive infection disease [25,26].

However, few studies have focused on the relationship between vaccination patterns and effects. Will the vaccination pattern affect the spread and mortality of COVID-19? What vaccination rate can reduce the spread and mortality of the pandemic? This study selected 33 countries with higher cumulative vaccination rates (CVR) to answer these questions. In brief, the purpose of this study is to (1) classify these 33 countries into three different vaccination patterns based on the vaccination rates in each time interval, (2) examine the impact of vaccination patterns on the reduction of epidemic transmission and mortality, and (3) analyze the level CVRs that can start having an impact on reducing the spread and mortality of the pandemic. Considering that the cumulative vaccine uptake in most countries is still very low, far from reaching the herd immunity threshold, effective vaccination strategies may be required in most countries to avoid the pandemic from intensifying. The results of this study could help policymakers design an optimal strategy for COVID-19 vaccination rollout to mitigate the negative effects of pandemic risks.

![Fig. 1. The comparison of vaccine doses administered (VDA) and cumulative vaccination rates (CVRs) by continents.](image-url)
Methods

Sample countries

According to the vaccination rate data provided by Our World in Data [1], as of 20 June 2021, the world’s CVR averaged 34.25 doses per 100 people; it varied from country to country, ranging from less than 1 dose to more than 100 doses, per 100 people. To analyze the impact of vaccination rates and patterns on epidemic transmission and mortality, this study employed two criteria to select sample countries: (1) CVRs of more than 65 doses per 100 people and (2) a population of more than 1,000,000. By 20 June 2021, 36 countries met these two criteria. However, Mongolia, Uruguay, and Bhutan were removed from the sample list because of much later dates of vaccination initiation. The first data of CVRs were available on 25 February, 28 February, and 28 March 2021, for Mongolia, Uruguay, and Bhutan, respectively, while all other countries had already started to vaccinate before 10 January 2021. Eventually, 33 countries were selected as the sample for this study.

Data collection

The data for cumulative confirmed cases and CVRs were provided by Our World [1], and the population data for each country were provided by the World Bank. The descriptive statistics for the CVR on 30 May 2021, the daily number of confirmed cases and deaths at baseline, and on June 14–27, 2021, and the population for the sample countries are shown in Table 1. As of 30 May 2021, the UAE had the highest vaccination rate, reaching 129.53 doses per 100 people, ahead of Israel (122.26 doses per 100 people) and other countries. In contrast, Kuwait ranked the lowest, with a cumulative vaccination rate of 42.62 doses per 100 people. An average of 74 doses per 100 people in 33 countries were vaccinated by 30 May 2021.

Overall, the average number of daily confirmed cases and deaths improved from 12,105 cases and 197 deaths at baseline (13 December 2020–10 January 2021) to 1397 cases and 22 deaths on 14–27 June 2021. At baseline, the USA ranked the highest with 216,071 confirmed cases each day, whereas Singapore only detected 21 infections. On June 14–27, 2021, the number of confirmed cases in all these countries dropped significantly. The UK ranked the highest with 11,919 daily confirmed cases, ahead of the USA (11,667 cases), while Singapore remained at the bottom with 19 daily confirmed cases. During the baseline period, 2779 people died of COVID-19 in the USA; however, the number of deaths in China and Qatar was zero. Cyprus was the least populated country with only 1.21 million people in 2020 among these countries and China was the most populous country, reaching 1439.32 million people.

Measures of variables

The variables for statistical analysis for this paper include:

The spread $S$ of the COVID-19 pandemic is defined as the proportion of confirmed cases to population (PCCP) in each period $t$ in response to level $t$ of CVRs, expressed as

$$S_t = \frac{N_t}{P}$$

where $N_t$ represents the total number of confirmed cases in the period under Level $t$ of CVRs and $P$ is the population.

Mortality $M$ at level $t$ is measured by

$$M_t = \frac{d_t}{P}$$

where $d_t$ represents total deaths in the period, under Level $t$ of CVRs.

Research process

The research process includes following steps:

Step 1. The determination of vaccination patterns

In the first step, we attempt to categorize these 33 countries into different vaccination patterns, based on the vaccination rate in each time interval (TI). The entire analysis period from the initiation of vaccination to 30 May 2021, was separated into 12 TIs. Each TI covered 2 weeks, except for the first one. Considering the variation in vaccination commencement dates, and lower vaccination rates in the earlier days after vaccination, the first TI covered approximately three weeks and ended on 5 January 2021. The CVR for each country was extracted from the data bank of Our World [1], and the vaccination rate for each country in each TI was calculated and obtained. The average vaccination rate for the 33 countries in each TI was used as a separation line to divide the vaccination rate into upper and lower zones. This study categorized vaccination patterns into three types, which were defined as:

(1) Type A (full-speed pattern) included two cases: (1) the vaccination rate in each TI fell into the upper zone, or (2) the vaccination rate fell into the upper zone for several consecutive TIs starting from TI 1, and then dropped into the lower zones, no longer reverting to the upper zones.

(2) Type B (fluctuating pattern) was defined as the vaccination rate in each TI, fluctuating between the upper and lower zones. The intersection of the trend line of a country and the average line of all the countries contains at least two points.

(3) Type III (upstream pattern) included two cases: (1) the vaccination rate in each TI was in the lower zone, and (2) the vaccination rate was in the lower zone for several consecutive TIs starting from TI 1 and then rose into the upper zones, no longer reverting to the lower zones.

Step 2: The performance of vaccination

Typically, individuals need two weeks after a one-dose vaccine, or after the second dose of a two-dose vaccine, for full protection against the COVID-19 virus [27]. The first dose of the vaccine may begin to build up the process of the immune system, and the second dose aims to reinforce this protection and can also yield some immunity [28]. Thus, the 4-week interval from December 13, 2020, to January 10, 2021, was taken as the baseline of PCCP (proportion of confirmed cases to population) and mortality $M$, which represents the normal performance of the epidemic transmission before vaccination. Among the 33 sample countries, the Netherlands was the last country to start vaccination, its first vaccination data being available only on January 10, 2021. To analyze the time for the vaccine to start taking effect, the PCCP and mortality before 10 January 2021, were considered as the baseline. The CVR on January 10, 2021, was selected as the first
level of CVR, and the level was increased every four weeks until May 30, 2021. In this study, six CVR levels were selected to test the effectiveness of vaccination. The date of each CVR level is presented in the Appendix.

In this article, it is assumed that vaccines produced by different technologies have the same effectiveness and that vaccine protection lasts for more than one year. As vaccines require two weeks to produce an antiviral effect, the performance of vaccination was examined two weeks after the date for each level of CVRs. Thus, a two-week period was maintained to evaluate the vaccination effect under each CVR level.

The reduced spread and mortality rates of COVID-19 were calculated for each country. An ANOVA was conducted to test whether $\Delta S$ and $\Delta M$ among countries in each vaccination pattern showed no significant difference.

Step 3. Estimating the effect of vaccination patterns on PCCP reduction and mortality.

An indicator $\Delta S$ is presented to measure the improvement in the spread of COVID-19, expressed as,

$$\Delta S = S_b - S_t$$

(3)

where $S_b$ denotes the PPCP of the baseline, and $S_t$ is the PPCP corresponding to the vaccination rates of Level 6. Another indicator $\Delta M$ is employed to measure the improvement in mobility caused by COVID-19, defined as

$$\Delta M = M_b - M_t$$

(4)

where $M_b$ denotes the mobility of the baseline, and $M_t$ denotes the mobility corresponding to the vaccination rates of Level 6.

Step 4. Estimating the minimum vaccination rate to reduce the transmission and mortality of COVID-19

The PCCP and mortality at baseline, and at each level of cumulative vaccination rate for each country, were calculated based on Eqs. (1) and (2). A pairwise comparison was made, using a t-test to estimate the difference in PCCP and mortality between baseline and each vaccination level, as follows:

$$H_0 : \mu_b - \mu_t = 0 \quad t = 1, 2, \ldots, 6$$

$$H_t : \mu_b - \mu_t \neq 0$$

where the subscript $b$ denotes the baseline, $t$ represents various levels of CVR, and $\mu$ is the mean value of the PCCP and mortality. The significance levels of 0.01, 0.05 and 0.10 are selected to conclude $H_0$. After the t-test on each vaccination rate level, the minimum requirement of CVRs was determined.

Results

The categorization of countries into different vaccination patterns was conducted according to the description in Step 1, introduced in the research methods. In TI, the average vaccination rates of all sample countries are shown in Fig. 2. The average vaccination rate continued to increase, starting from 1.20 doses per 100 people in Period 1 to 11.78 in Period 12, except for Period 5. The trend in average vaccination rates implies that vaccine supply was limited in earlier periods but increased over time. The vaccination rate for each TI in each country was compared with the average vaccination trend line. According to Step 1, vaccination patterns were classified into three types. The average vaccination rate in each TI for Type A countries increased very quickly from 6.08 dose per 100 people in TI 1 (before 3 January 2021) to a peak of 12.58 doses per 100 people in TI 3 between 18 and 31 January 2021, and then declined. However, the vaccination rate in each TI of Type C countries continued to increase, whereas that of Type B countries fluctuated.

Vaccination patterns

These 33 countries were classified into three vaccination patterns according to Step 1, and the results are listed in Table 2. Among these three patterns, the average CVR of Type A on 30 May 2021 was 102.03

Table 2

| Vaccination patterns | Countries classified | CVRs Aver. | St. dev. | Max. | Min. |
|----------------------|----------------------|------------|----------|------|------|
| Type A (Full Speed Pattern) | Israel, the UK, and the USA | 102.03 | 14.62 | 122.26 | 88.19 |
| Type B (Fluctuating Pattern) | Bahrain, Chile, Cyprus, Denmark, Estonia, France, Greece, Serbia, Singapore, Spain, Sweden, Swiss, UAE | 69.18 | 23.86 | 100.31 | 42.62 |
| Type C (Striving Pattern) | Austria, Belgium, Canada, China, Czech, Finland, Germany, Hungary, Ireland, Italy, Lithuania, Netherlands, Norway, Poland, Portugal, Qatar, Slovenia | 58.33 | 12.09 | 90.67 | 44.41 |

![Fig. 2. The vaccination rate in each period for different vaccination modes.](image)
doses per 100 people, much higher than that of Type B (69.18 doses per 100 people) and Type C (58.33 doses per 100 people). An ANOVA analysis was conducted to test whether the three vaccination patterns differed in cumulative rates on 30 May 2021. The results listed in Table 3 indicate a significant variation in CVRs among the three groups.

The vaccination pattern implemented in Type A countries, including Israel, the UK, and the USA, is called the full-speed pattern, as the vaccination rate in these countries in earlier TIs was much higher than that in other groups. For example, Israel’s CVR reached 55 doses per 100 people within a short period of time after the start of vaccination on January 30, 2021. Israel started vaccination earlier than other countries and led the world in terms of vaccination rates until 21 May 2021. The vaccination rate in the UK for each TI remained higher than the average for all countries. The vaccination rate in the USA, in each TI, was maintained beyond the average line till TI 10 (4/26–5/9 2021).

The vaccination trend implemented by Type B, including 13 countries, is called a fluctuating pattern, as their vaccination rates fluctuate between the upper and lower zones. Contrary to Type A, the vaccination rate in all Type C countries was lower than the average of all countries in earlier TIs. These countries tried to catch up with other leading countries in the rate of vaccination in latter TIs, so their vaccination patterns are called striving patterns. These countries strove to catch up with other types, and thus, their vaccination patterns were called striving patterns.

- Impact of vaccination patterns on reduced PCCP and mortality

The reduction in PCCP and mortality between the baseline and Level 6 CVRs for each group of vaccination patterns is listed in Table 4. The PCCP was reduced by 54.42, 13.43 and 33.30 cases per 100,000 people each day for these three vaccination patterns, respectively. Full-speed patterns (Type A countries) made greater progress in terms of the spread of COVID-19, reducing PCCP by 54.42 cases per 100,000 people each day. In contrast, the reduction of the COVID-19 spread in Type B countries was the least among the three patterns, with PCCP only reducing by 13.43 cases per 100,000 people each day.

Similar to a reduction in the spread of COVID-19, mortality rate also declined for these three patterns, with a reduction of 6.4, 2.06 and 9.85 deaths per million people each day. The reduction in mortality in the striving pattern of Type C countries reached 9.85 deaths per million people per day, ahead of Type A (6.40 deaths per million people per day) and Type B (2.06 deaths per million people per day).

ANOVA was performed to test whether the three patterns showed the same improvement in the transmission and mortality of the COVID-19 pandemic. The results are listed in Table 5, indicating that the reduction in both PCCP and mortality was significantly different among the three groups. The results demonstrate that different vaccination patterns may affect the consequences of COVID-19 transmission and mortality.

Minimum vaccination rates to make the vaccine effective. The PCCP and mortality at each CVR level were calculated according to Step 3, and the pairwise comparison of the PCCP and mortality between the baseline and each CVR level was conducted according to Step 4. Table 6 indicates that the vaccination was significantly effective in reducing the PCCP from Level 4 of CVRs on 4 April 2021, and the PCCP reduction was maintained at Level 6 of CVRs on 30 May 2021. The average PCCP was reduced from 34.34 cases per 100,000 people at baseline to 25.49 cases per 100,000 people at Level 6 (6/14–6/27). The pairwise comparison of PCCP between the baseline and Level 1, Level 2, and Level 3 found no evidence showing a significant reduction in PCCP; as the P-value of the t-statistics was higher than 10%.

In contrast, Table 7 indicates that the mortality rate at L1 of CVRs was 5.97 deaths per million people, and no significant reduction in mortality was found, compared to the baseline. However, the average mortality rate dropped significantly from 6.00 deaths per million people at baseline to 3.69 deaths per million people at Level 2 of CVRs; thereafter the reduction in mortality was maintained till Level 6. Based on the change in mortality rate at each level compared to the baseline, this study suggests that the 7.88 doses per 100 people of CVRs is the minimum vaccination rate to reduce mortality.

Discussion

Table 2 indicates that the average CVR in Type A countries (full-speed vaccination patterns), including Israel, the UK, and the USA, was much higher than that in the other two types, through the ANOVA test.

Table 4

| Type | Full Speed | Fluctuating | Striving |
|------|------------|-------------|----------|
| PCCP | 54.42      | 13.43       | 33.30    |
| Mortality | 6.40 | 2.06 | 7.25 |

Table 5

Effects of vaccination patterns on improving PCCP and mortality.

Table 6

| Source | Variance | No. of obs. | t statistics | p-value |
|--------|----------|-------------|--------------|---------|
| Baseline | 34.34 | 622.37 | 33 | 1.5430 | 0.1327 |
| L1 | 28.43 | 525.62 | 33 | 1.4311 | 0.1621 |
| L2 | 27.79 | 601.25 | 33 | 1.6939 | 0.0972 |
| L3 | 34.49 | 797.83 | 33 | 1.8181 | 0.0784*** |
| L4 | 15.28 | 813.04 | 33 | 2.8930 | 0.0080*** |
| L5 | 6.95 | 86.99 | 33 | 5.5746 | 0.0000*** |

Table 7

Result of pairwise comparison for PCCP between the baseline and each level of vaccination rates.

| Source | Variance | No. of obs. | t statistics | p-value |
|--------|----------|-------------|--------------|---------|
| Baseline | 6.00 | 29.50 | 33 | 0.0343 | 0.9729 |
| L1 | 5.97 | 30.48 | 33 | 0.0327 | 0.0048 |
| L2 | 4.03 | 27.06 | 33 | 2.1506 | 0.0392 |
| L3 | 3.98 | 27.06 | 33 | 2.6097 | 0.0137 |
| L4 | 1.78 | 3.80 | 33 | 4.6656 | 0.0001 |
| L5 | 0.87 | 1.83 | 33 | 5.2741 | 0.0000 |
of mistrust of vaccine benefit and concerns about future unforeseen side manufacturing and delivery systems, vaccination policies, and health the COVID-19 pandemic [31,32]. However, various studies find that the required to support the appropriate distribution of vaccines, especially pandemic and increased mortality, a decision-making approach is The vaccination rate in each TI in Type B countries was relatively un convenience and limitations, confidence in safety and efficacy, benefits rates could reach a natural level of 70% but could be increased to 90% mate the maximum vaccination rate of a society, found that vaccination could play a key role in preventing the spread of infection and reducing the mortality of COVID-19. The even vaccination rates among the three patterns demonstrated in Tables 2 and 3 can be considered a microcosm of the uneven distribution of COVID-19 vaccines worldwide. In the real world, there has been disparity in the distribution of vaccines between rich and poor countries since the successful development of vaccines in the end of 2020. As of 30 May 2021, high-income and upper-middle-income countries received 1625.13 million doses, lower-middle-income countries, 279.3 million doses, and low-income countries, only 5.88 million doses [1]. Reliefweb [29] emphasized that more than 80% of vaccine doses administered have been delivered to high- or upper middle-income countries, while only 0.2% have been sent to their low-income counterparts. The low CVR in low-income countries may result in the global re-emergence of COVID-19 for this vaccine-preventable disease [30]. Overall, the uneven distribution of vaccines may have a devastating impact on global public health and cannot completely stop the spread of the COVID-19 pandemic. To achieve an efficient preventive measure against the spread of the COVID-19 pandemic and increased mortality, a decision-making approach is required to support the appropriate distribution of vaccines, especially as vaccine supply remains limited. Vaccination plans play a vital role in reducing the negative effects of the COVID-19 pandemic [31,32]. However, various studies find that the rollout of vaccination campaigns may generate high resistance to vaccines [15,17,33]. A possible explanation for the variation in vaccination patterns among these countries may be attributed to different cultures, institutions, and political systems. People in many developed countries are more concerned about privacy and human rights issues, and thus protest against mandatory vaccinations and other restrictions [34]. The implementation of an effective policy to reinforce the rollout of vaccines requires strong support from public governance [35]. Forman et al. [36] examined policy challenges for successful vaccination campaigns and highlighted the key role of sustaining R&D incentives, conducting clinical trials, public governance, post-market surveillance, manufacturing and delivery systems, vaccination policies, and healthcare system adaptation. Furuse [4] argued that low vaccination coverage scenarios require the regular implementation of stringent measures, as do high vaccination coverage scenarios occasionally. However, empirical research by Coccia [37], which attempted to estimate the maximum vaccination rate of a society, found that vaccination rates could reach a natural level of 70% but could be increased to 90% with strict mandates. Several studies argue that factors affecting vaccination acceptance may be complex and country-specific, including the risk of side effects, convenience and limitations, confidence in safety and efficacy, benefits of vaccination, and so on [38-41]. Paul et al. [42] estimated that four domains of negative attitudes affect the willingness to receive a COVID-19 vaccine, including mistrust of vaccine benefit, worries about unforeseen effects, concerns about commercial profiteering, and preference for natural immunity, and found that intermediate to high levels of mistrust of vaccine benefit and concerns about future unforeseen side effects were the most important determinants of both uncertainty and unwillingness to vaccinate against COVID-19. The widespread acceptance of vaccines seems to be a challenge, as vaccination behavior may be affected by individuals’ attitudes and perceived risks, and exerts a great impact on the implementation of vaccination strategies [43]. To increase the vaccination rate, Loomba et al. [44] examined the impact of misinformation about COVID-19 vaccines on vaccination acceptance and found that scientific-sounding misinformation was closely related to a decline in vaccination intention. Even with complete information on the susceptibility and severity of COVID-19, a large proportion of people in some countries refuse to be vaccinated [45]. A new poll from Monmouth University reported at the beginning of March 2021, that one of four Americans is still unwilling to be vaccinated [46]. The survey presented by Ruiz and Bell [47] found that 14.8% of respondents reported unwillingness to receive a vaccine for COVID-19, and another 23% were unsure. Kawata and Nakabayashi [48] conducted a randomized conjoint analysis survey on the willingness to receive vaccination, by recruiting a non-probability sample of 15,000 Japanese adults and found that a mandatory vaccination policy may increase the choice probability by less than 1% for all vaccine types. If the herd immunity threshold is not reached through vaccination or infection, the pandemic cannot be eradicated, and public health cannot be ensured. Consequently, normal life cannot be restored without global vaccination herd immunity [49]. The CVR of the striving vaccination pattern (Type C) shown in Table 2 was lower than that of the fluctuating vaccination pattern (Type B); however, the spread and mortality of the striving vaccination pattern in Table 4 showed better improvement. The possible reason why the vaccination performance of the fluctuating vaccination pattern lags behind the striving vaccination pattern may be the unstable vaccination rate implemented by the fluctuating vaccination pattern. This result implies that with minimum vaccine supply, the vaccination pattern could play a key role in preventing the spread of infection and reducing the mortality of COVID-19. Tables 6 and 7 show that vaccination started to reduce, (a) the spread of the pandemic at Level 4 of CVRs, and (b) the mortality at Level 2 of CVRs. As the CVR at Level 4 and Level 2 was 29.06 doses per 100 people and 7.88 doses per 100 people, respectively, this paper suggests that the CVR of 7.88–29.06 doses per 100 people is the vaccination threshold of minimum requirements (VTMR) to curb the COVID-19 pandemic. Coccia [13], developed a dynamic mathematical model to predict the COVID-19 transmission and evaluated its effectiveness. The study of Shen et al. [50], showed that an 80% effective vaccine only requires a 48–78% vaccination coverage rate, and a 100% effective vaccine requires a 35–58% vaccination coverage rate to suppress the spread of the pandemic without using a brand. Macintyre et al. [51] suggested that 66% vaccination coverage with a 90% effective vaccine may prevent transmission of the COVID pandemic through a mathematical model simulation. Chen [52] suggested that a cumulative vaccination rate of 1.46–50.91 doses per 100 people can mitigate the spread of COVID-19 based on the empirical data of eight countries selected. Integrating the studies of Shen et al. [50] and Macintyre et al. [51], the herd immunity threshold ranges from 48 to 78% (equivalent to approx. 96–156 doses per 100 people) with an 80–90% effective vaccine. The suggested VTMR 7.88–29.06 doses per 100 people in this study was in the middle of the VTMR achieved by individual countries suggested by Chen [52] and lower than the herd immunity threshold suggested by Shen et al. [50] and Macintyre et al. [51]. This value of VTMR may provide countries with low vaccination rates with reliable and valuable information for planning appropriate vaccination strategies. Several studies suggest that vaccination to obtain herd immunity is the best way to slow the spread of the pandemic or even eliminate the epidemic [49] as it may significantly reduce the spread of the COVID-19 pandemic [53,54]. When the herd immunity threshold is reached, the transmission of the epidemic in society may decline. Eventually, unvaccinated individuals can be protected by herd immunity, and the epidemic will be eradicated [55]. However, Askitas et al. [56] estimated the dynamic impact of non-pharmaceutical interventions (NPIs) on the spread of COVID-19 and demonstrated that the spread was significantly
reduced. The case study presented by Tran et al. [57] suggests that vaccination coverage higher than 28% and NPIs (e.g., social distancing, mask wearing) may result in low or near-zero transmission levels in Rhode Island and Massachusetts by Q4 2021, by the second quarter of 2021. Walker et al. [58] focused on health policies in low-income countries and suggested that NPIs are still needed to avoid medical overcapacity. Pharmacological intervention remains a global priority if an equitable oxygen supply is ensured. Therefore, various NPIs should be combined with vaccination campaigns to control the spread of the pandemic.

Shen et al. [50] indicated that the impact of vaccination on the transmission of COVID-19 may be attributable to the vaccine effectiveness and vaccination coverage rates, and the WHO [59] suggested that the eradication of the pandemic depends on several factors, including the effectiveness of the vaccines, vaccination coverage rates, effective delivery of vaccines, and emerging new variants. To examine the temporal evolution of vaccine efficacy and effectiveness against COVID-19, McDoland et al. [60] conducted a systematic review and meta-analysis of vaccine efficacy and effectiveness. The results showed that the vaccine’s efficacy against SARS-CoV-2 infection with COVID-19 decreased over time, but protection against severe COVID-19 remained high. Currently, the efficacy of most vaccines used worldwide ranges from 70 to 95%. For example, the Pfizer-BioNTech BNT162b2 mRNA vaccine has 95% efficacy against symptomatic infection of COVID-19 [61]. Moderna uses the same technology as Pfizer-BioNTech and has a similar efficacy of 94.1% in preventing symptomatic disease, with no evidence of previous COVID-19 infection. Johnson & Johnson and Oxford-AstraZeneca use the same technology and have 72% and 74.6% efficacy, respectively, while Novavax is 90% effective against lab-confirmed, symptomatic infections [62]. In most countries, these vaccines are purchased and used in different proportions worldwide, and the average efficacy of the vaccines used may be between 80 and 90%. Thus, the COVID-19 pandemic starts to mitigate when vaccination rate reaches 7.88–29.06 dose per 100 people suggested by this paper, and can be eradicated only if the vaccination coverage rate reaches 96–156 doses per 100 people according to Shen et al. [50] and Maclntyre et al. [51].

As COVID-19 vaccines need to be stored at extremely low temperatures, timely and cost-effective distribution of COVID-19 through a reliable cold chain logistics network is required to ensure and maintain vaccine quality. The effective delivery system of vaccines is also a challenge for low- and low-middle-income countries, as most people in many low-income or low-middle-income countries still live in rural areas. For example, the degree of urbanization in Africa was only 43% in 2020, which is much lower than the world level of 56.15% [63]. Thus, the development of a vaccine delivery system that includes effective vaccine transport, storage, and continuous cold-chain monitoring, as well as vaccination infrastructure, such as qualified vaccination personnel and vaccination clinics, is needed to support the required vaccination capacity. Shen et al. [50] developed a route optimization simulation model to improve the logistics performance of vaccine distribution, and showed that the service level, cost-effectiveness, environmental performance, and equity of a cold chain vaccine logistics system can be significantly affected by fleet size, fleet composition, vehicle type, and route optimization.

Furthermore, the emergence of new variants may be a challenge for these vaccines. Not only is the transmissibility of most new variants, including the Alpha (lineage B.1.1.7), Beta (lineage B.1.351), Gamma (lineage B.1.1.288) and Delta (lineage B.1.617) variants, found to be substantially higher than that of pre-existing SARS-CoV-2 variants, but they may also reduce the protective power of vaccines. Moderna suggested that a third dose of vaccine may boost the protection power to resist the attack of Beta and other variants [64]. A study published in the Annals of Internal Medicine also suggested that a third dose of vaccines may help people with weakened immune systems to reinforce protection against the COVID-19 virus [65]. Considering the discovery of an increasing number of new variants and the expanding demand for the third vaccination dose, the global demand for vaccines may quickly exceed the current production capacity and worsen the uneven distribution of vaccine supply. Without new investments in the production of effective vaccines, it is expected that their supply in low-income countries will still be insufficient. Therefore, the lack of vaccine protection in low- and middle-income countries, accompanied by an uneven distribution of vaccines, will create a gap in global epidemic prevention.

Conclusions

This paper highlights the important role of vaccination patterns and the VTMR in reducing epidemic spread and mortality. The critical role of vaccination patterns found in this study implies that vaccination is not the only way to mitigate the negative impact of the COVID-19 pandemic when CVRs are below the herd immunity threshold. Non-pharmaceutical interventions (NPIs) such as lockdowns, mask wearing, viral testing, and social distancing are still required.

The second contribution of this study is the identification of the value of VTMR based on these 33 sample countries. Owing to the substantial inequalities in the distribution of vaccines across the world, the suggested value of VTMR can be employed in low- and low-middle-income countries to plan vaccination strategies, including the optimal use of limited vaccine supplies, the prioritization of the target group for vaccination, and the vaccination schedule to eliminate or reduce the attack of the pandemic. The findings from this study are also valuable for the countries, which, despite high vaccination rates, are below the herd immunity threshold, to evaluate their vaccination programs.

As the herd immunity threshold has not been reached in most countries, this research can be extended to focus on the integration of NPIs and vaccination to form an overall COVID-19 prevention strategy in the future. The combination of preventive health policies and effective vaccination campaigns through good public governance may help increase vaccination rates. In addition, new variants continue to emerge, affecting the transmissibility of the virus and the effectiveness of vaccines. This emerging variant poses a potential threat to the healthcare system because it can attack the immune system and reduce vaccine efficacy. This study can be extended to analyze the impact of vaccine types used by countries, on vaccination campaigns.

These contributions seem interesting and provide insights for policymakers; however, some limitations remain. First, because the criteria for selecting sample countries are concentrated in leading vaccinated countries, the sample is likely to be dominated by wealthy countries, which typically have higher vaccination rates. Second, the sample size was only 33 countries, which is relatively small, so the results obtained in this study may lose their representativeness for global epidemic prevention. Third, factors other than vaccination patterns that may affect the spread and mortality of the COVID-19 pandemic require further study, and the sample may be expanded to include low-income countries. Considering the role of vaccination patterns in responding to the threat of a pandemic, the results presented here may help health policies in planning vaccination campaigns. The findings of this study could be applied to low- or low-middle-income countries without loss of generalization because the protection power of vaccines may be constant across species and countries.

Funding

This study was funded in part by Ministry of Science and Technology (MOST) in Taiwan under grant number MOST 109-2410-H-227-003 to Yi-Tui Chen.

Ethical approval

Not required.
Appendix: The date for each level of CVRs (cumulative vaccination rates) and corresponding dates for PCCP (proportion of confirmed cases to population) and mortality

| Level of CVRs | Date for CVRs | Periods for PCCP and mortality |
|----------------|----------------|-----------------------------|
| Baseline | Before vaccination | 2020/12/3–2021/1/10 |
| Level 1 | 2021/1/10 | 2021/1/25–2/7 |
| Level 2 | 2021/2/7 | 2021/2/22–3/7 |
| Level 3 | 2021/3/7 | 2021/3/22–4/2 |
| Level 4 | 2021/4/4 | 2021/4/19–5/2 |
| Level 5 | 2021/5/2 | 2021/5/17–5/30 |
| Level 6 | 2021/5/30 | 2021/6/4–6/27 |

References

[1] Our World in Data. Coronavirus (COVID-19) Vaccinations. [Internet]. 2021 [cited 2021 Jun 21]. Available from: https://ourworldindata.org/covid-vaccinations.

[2] Nishiura H, Linton NM, Akhmetzhanov AR. Serial interval of novel coronavirus (COVID-19) infections. Int J Infect Dis 2020;93:284–6. Apr.

[3] Du Z, Xu X, Wu Y, Wang L, Cowling BJ, Meyers LA. Serial interval of COVID-19 among publicly reported confirmed cases. Emerg Infect Dis 2020;26(6):1341. Jun.

[4] Furuse Y. Simulation of future COVID-19 epidemic by vaccination coverage scenarios in Japan. J Glob Health 2021;11:05025. Nov.

[5] Markovic R, Sterk M, Marx M, Perc M, Gonak M. Sociodemographic and health factors drive the epidemic progression and should guide vaccination strategies for best COVID-19 containment. Results Phys 2021;26:104433. Jul.

[6] Mohammad A, Meniallov I, Bazelevych K, Yakovlev S, Chumachenko D. Comparative study of linear regression and SIR models of COVID-19 propagation in Ukraine before vaccination. Radioelectron Comput Syst 2021;5:5–18. Mar.

[7] Karabay A, Kuzduesov A, Osanpava S, Lewis M, Varol HA. A vaccination simulator for COVID-19: effective and sterilizing immunization cases. IEEE J Biomed Health Inform 2021;25(12):4317–27. Sept.

[8] Voigt A, Omholt S, Almaas E. Comparing the impact of vaccination strategies on the spread of COVID-19, including a novel household-targeted vaccination strategy. PLoS One 2022;17(2):e0263155. Feb.

[9] Alqahtani RT, Musa SS, Yusuf A. Unravelling the dynamics of the COVID-19 pandemic with the effect of vaccination, vertical transmission and hospitalization. Results Phys 2022;9:105715. Aug.

[10] Berco I, Levinsky R, Weiner J, Smid M, Nerus R, Videnovci P, et al. Importance of vaccine action and availability and epidemic severity for delaying the second vaccine dose. Sci Rep 2022;12(17):6736. May.

[11] Drolet M, Laprise JF, Martin D, Jit M, Brouwer D, Girgis G, et al. Optimal human papillomavirus vaccination strategies to prevent cervical cancer in low-income and middle-income countries in the context of limited resources: a mathematical modelling analysis. Lancet Infect Dis 2021;SI473-3099(20):30860–4. Jul.

[12] Bundy J, Pfizer MD, Short CE, Coombs WT. Crises and crisis management: integration, interpretation, and research development. J Manag 2016;43(6):1661–92. Dec.

[13] Coccia M. High health expenditures and low exposure of population to air pollution as critical factors that can reduce fatality rate in COVID-19 pandemic crisis: a global analysis. Environ Res 2021;199:11339. Aug.

[14] Coccia M. Pandemic prevention: lessons from COVID-19. Encyclopedia 2021;1(2):433–44. May.

[15] Coccia M. Optimal levels of vaccination to reduce COVID-19 infected individuals and deaths: a global analysis. Environ Res 2022;204:122514. Mar.

[16] Coccia M. Preparedness of countries to face COVID-19 pandemic crisis: strategic positioning and underlying structural factors to support strategies of prevention of pandemic threats. Environ Res 2022;205:111078. Jan.

[17] Coccia M. COVID-19 pandemic over 2020 (with lockdowns) and 2021 (with vaccinations): similar effects for seasonality and environmental factors. Environ Res 2022;208(15):112711. May.

[18] Benati I, Coccia M. Global analysis of timely COVID-19 vaccinations: improving governance to reinforce response policies for pandemic crises. Int J Health Gov Plan Res 2022. https://doi.org/10.1186/s12857-021-00972 [cited 2022 July]. Available from.

[19] Aritio L, Coccia M, Petruzzielli AM. Technological exaptation and crisis management: evidence from COVID-19 outbreaks. R&D Monag 2021;51:381–92. Feb.

[20] iyanda AE, Adeleke R, Lu Y, Oyewumi T, Adareagbe A, Lasode M, et al. A retrospective cross-national examination of COVID-19 outbreak in 175 countries: a multiscale geographically weighted regression analysis (January 11–June 28, 2020). J Infect Public Health 2020;13(10):1438–45. Oct.

[21] Yoshikawa T. Implementing vaccination policies based upon scientific evidence in Japan. Vaccine 2021;39(38):5447–50. Sept.

[22] Sand-Roy CM, Wagner CE, Baker RE, Morris SE, Farrar J, Graham AL, et al. Immune life history, vaccination, and the dynamics of SARS-CoV-2 over the next 5 years. Science 2020;370(6518):811–8. Nov.

[23] Britton T, Ball P, Trapman P. A mathematical model reveals the influence of population heterogeneity on herd immunity to SARS-CoV-2. Science 2020;369(6505):846–9. Aug.

[24] European Centre for Disease Prevention and Control. Overview of the implementation of COVID-19 vaccination strategies and deployment plans in the EU/EEA. [Internet]. 2021 [cited 2021 Jun 20]. Available from: https://www.ecdc.europa.eu/en/publications-data/overview-implementation-covid-19-vaccination-strategies-and-deployment-plans.

[25] Strassburg MA. The global eradication of smallpox. Am J Infect Control 1982;10(2):53–9. May.

[26] Kucharski AJ, Eggo RM, Watson CH, Camacho A, Funk S, Edmunds WJ. Effectiveness of ring vaccination as control strategy for Ebola virus disease. Emerg Infect Dis 2016;22(12):1943–7. Sept.

[27] Centers for Disease Control and Prevention. Frequently asked questions. [Internet]. 2021 [cited 2021 May 06]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/keythingstoknow.html.

[28] Healthline. Why do you need two doses for some COVID vaccines? [Internet]. 2021 [cited 2021 May 04]. Available from: https://www.healthline.com/health/why-two-doses-of-covid-vaccine.

[29] Reliefweb. Unequal vaccine distribution self-defeating. World Health Organization chief tells economic and social council’s special ministerial meeting. [Internet]. 2021 [cited 2021 May 04]. Available from: https://reliefweb.int/report/world/unequal-vaccine-distribution-self-defeating-world-health-organization-chief-tells.

[30] Siani A. Measles outbreaks in Italy: a paradigm of the reemergence of vaccine-preventable diseases in developed countries. Prev Med 2021;132:99–104. Apr.

[31] Frederiksen LSF, Zhang Y, Foged C, Thakur A. The long road toward COVID-19 herd immunity: vaccine platform technologies and mass immunization strategies. Front Immunol 2020;11:1817. Jul.

[32] Harrison EA, Wu JW. Vaccine confidence in the time of COVID-19. Eur J Epidemiol 2020;35(4):325–30. Apr.

[33] Verger P, Peretti-Watel P. Understanding the determinants of acceptance of COVID-19 vaccines: a challenge in a fast-moving situation. Lancet Public Health 2021;6(4):e195–6. Feb.

[34] Anttiouko A. Successful government responses to the pandemic: contextualizing national and urban responses to the COVID-19 outbreak in east and west. Int J Plan Res 2021;10(2):1–17. Jun.

[35] Glattman-Freedman A, Cohen ML, Nichols KA, Porges RF, Saludes IR, Steffens K, et al. Factors affecting the introduction of new vaccines to poor countries: a comparative study of the Haemophilus influenzae type b and hepatitis B vaccines. PLoS One 2010;5(11):e13809. Nov.

[36] Forman R, Shah S, Jeurissen P, Jit M, Mossialos E. COVID-19 vaccine challenges: what have we learned so far and what remains to be done? Health Policy 2020;125(3):355–67. (New York)Nov.

[37] Coccia M. Improving preparedness for next pandemics: max level of COVID-19 vaccinations without social impositions to design effective health policy and avoid flawed democracies. Environ Res 2022;213:115566. Oct.
Lane S, MacDonald NE, Marti M, DuMosch L. Vaccine hesitancy around the globe: analysis of three years of WHO/UNICEF joint reporting form data-2015–2017. Vaccine 2018;36(26):3861–7. Jun.

Larson HJ. The state of vaccine confidence. Lancet 2018;392(10161):2244–6. Nov.

Loomba S, de Figueiredo A, Piatek SJ, de Graaf K, Larson HJ. Measuring the impact and efficacy of the COVID-19 vaccine misinformation on vaccination intent in the UK and USA. Nat Hum Behav 2021;5(3):337–48.

Ruiz JB, Bell RA. Predictors of intention to vaccinate against COVID-19: results of a nationwide survey. Vaccine 2021;39(7):1080–6. Feb.

Shen M, Jian Zu, Fairley CK, Pagán JA, An L, Du Z, et al. Projected COVID-19 epidemic in the United States in the context of the effectiveness of a potential vaccine and implications for social distancing and face mask use. Vaccine 2021;39(16):2295–302. Apr.

MacIntyre CR, Costantino V, Trent M. Modelling of COVID-19 vaccination strategies and herd immunity, in scenarios of limited and full vaccine supply in NSW, Australia. Vaccine 2021;40(17):2506–13. Apr.S0264-410X(21)00501-6.

Chen YT. The effect of vaccination rates on the infection rate of COVID-19 under the vaccination rate below the herd immunity threshold. Int J Environ Res Public Health 2021;18(4):7491. Jul.