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

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Highlights

1. This paper examines the effect of vaccination patterns on the spread and mortality of the COVID-19 pandemic.

2. Vaccination patterns are found to play significant roles in mitigating negative impacts of the pandemic and the full speed vaccination pattern had much more improvement in the spread and mortality of the pandemic.

3. This paper suggests that vaccination rates are not the only determinant of pandemic improvement and need to be combined with non-pharmaceutical interventions to form effective vaccination policies.

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

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.

Keywords: COVID-19; vaccination rate; vaccination pattern; new confirmed case; mortality

1. 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. Figure 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.

Insert Figure 1 about here

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

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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 linear regression model loses the

precision to predict over longer time ranges. Karabay et al. [7] examined the impact of vaccination strategies on viral

propagation by using a particle-based SEIR epidemic simulator based on the experience of the province of Lecco, Italy, and

found that the sterilizing-age-based vaccination leads to lower deaths, and older people are suggested to be prioritized for the

first vaccination to reduce the overall mortality rate. Voigt et al. [8] focused on the effect of vaccination strategies on the

spread of the epidemic and the ability of each strategy to achieve herd immunity based on a typical SEIR model. They found

that age-based strategies had much less impact on the spread of the epidemic and generally made it difficult to achieve herd

immunity. Drolet et al. [11] developed a mathematical model to examine the optimal use of human papillomavirus (HPV)

vaccines in low- and middle-income countries, using India, Vietnam, Uganda, and Nigeria as sample countries.

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 healthcare 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.

2.   Methods

2.1 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.

2.2 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.

Insert Table 1 about here

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 1,397 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, 2,779 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 1,439.32 million people.

2.3 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

$$S_t = \frac{N_t}{P} \qquad (1)$$

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

$$M_t = \frac{d_t}{P} \qquad (2)$$

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

2.4 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

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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 ΔS and ΔM 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 ΔS is presented to measure the improvement in the spread of COVID-19, expressed as,

$$\Delta S = S_b - S_6 \qquad (3)$$

where S_b denotes the PPCP of the baseline, and S_6 is the PCCP corresponding to the vaccination rates of Level 6. Another

indicator ΔM is employed to measure the improvement in mobility caused by COVID-19, defined as

$$\Delta M = M_b - M_6 \qquad (4)$$

where M_b denotes the mobility of the baseline, and M_6 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 Eq. (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:

$$H_0 : \mu_b - \mu_t = 0 \qquad\qquad t = 1, 2, \dots 6$$

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

where the subscript b denotes the baseline, t represents various levels of CVR, and μ 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.

3. 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

Figure 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 18-31 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.

Insert Figure 2 about here

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 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.

Insert Table 2 about here

Insert Table 3 about here

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.

Insert Table 4 about here

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 each day. The reduction in mortality in the striving pattern of Type C

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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.

Insert Table 5 about here

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 25.48 cases per 100,000 people at Level 4 of CVRs (4/18–5/2 2021). After Level 4, the PCCP

was reduced further to 15.28 cases per 100,000 people in Level 5 (5/17–5/30 2021), and 6.95 cases per 100,000 people in

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%.

Insert Table 6 about here

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.

Insert Table 7 about here

4. 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 indicated in Table 3. The results in

Table 4 suggest that the full-speed vaccination pattern (type A) may rapidly improve the spread of infection and reduce

mortality. However, implementation of the full-speed vaccination pattern requires a sufficient supply of vaccines. These three

countries had administered a total of 370.43 million doses of vaccines including 294.93 million doses for the USA, 64.92

million doses for the UK and 10.58 million doses for Israel, accounting for 19.39% of the world's 1.91 billion doses [1].

Owing to the uncertainty of the vaccine supply, Type B countries were forced to fluctuate vaccination. The vaccination rate

in each TI in Type B countries was relatively unstable compared with that in the other two types. The limited supply of

vaccines could be the major cause of the slow progress of vaccination for earlier TIs in Type C countries.

The uneven 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

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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 1625.18 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 [38,39,40,41]. Paul [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

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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.

Shen et al.[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%-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 Novax 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 80-90%. 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 MacIntyre 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 P.1), 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.

5. 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

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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.

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Appendix: The date for each level of CVRs (cumulative vaccination rates) and corresponding dates for PCCP (proportion of

confirmed cases to population) and mortality

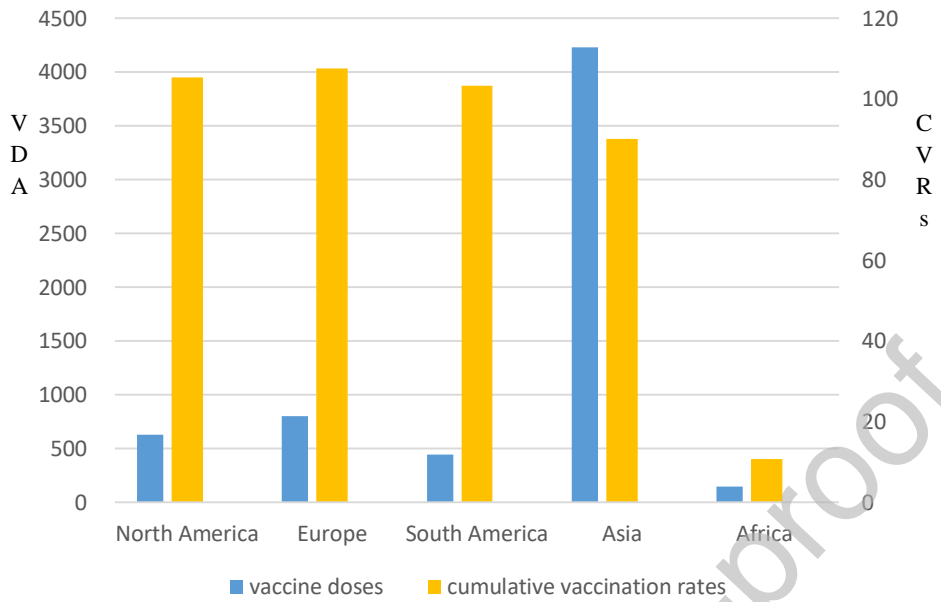| Level of CVRs	Date for CVRs	Periods for PCCP and mortality
Baseline	Before vaccination	2020/12/3-2021/1/10
Level 1	2021/1/10	2021/1/25-2/7
Level 2	2021/2/7	2021/2/22-3/7
Level 3	2021/3/7	2021/3/22-4/4
Level 4	2021/4/4	2021/4/19-5/2
Level 5	2021/5/2	2021/5/17-5/30
Level 6	2021/5/30	2021/6/14-6/27

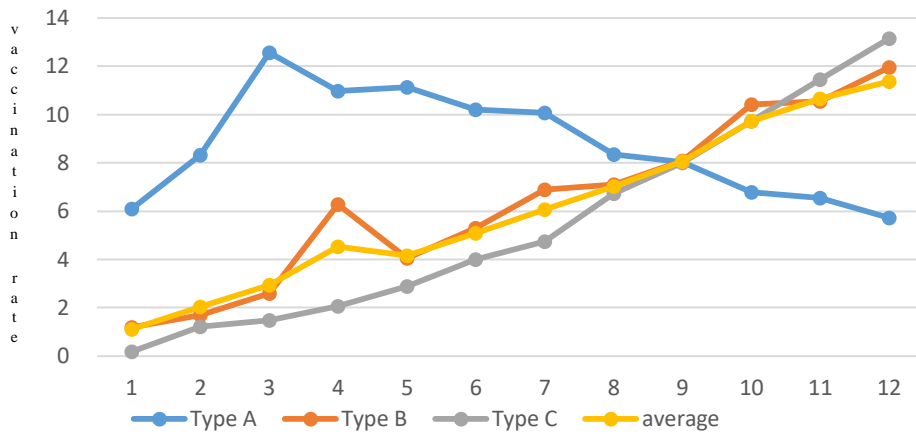Figure 1. The comparison of vaccine doses administered (VDA) and cumulative vaccination rates (CVRs) by continents

Figure 2. The vaccination rate in each period for different vaccination modes

Table 1. The basic descriptive statistics

	Average	St. dev.	Max.	Min.
CVRs on 2021/05/30 (doses per 100 people)	66.57	22.04	129.53	42.62
Daily new cases in the baseline	12,105	37,598	216,071	21
Daily new deaths in the base line	197	496	2,779	0
Daily new cases on 14-27 June 2021 in response to vaccination date on 2021/05/30	1,397	2,895	11,919	19
Daily new deaths on 14-27 in response to vaccination date on 2021/05/30	22	52	287	0
Population (million)	68.56	260.20	1,439.32	1.21

Table 2. The categorization of vaccination patterns and the CVR (doses per 100 people) on 30 May 2021

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

Table 3. The result of ANOVA on the difference of CVRs among the three patterns

Source	SS	d.f.	MS	F	P-value
Between	5014.90	2	2507.45	7.1470	0.002895
Within	10525.17	30	350.83		
Total	15540.07	32			

Table 4. The impact of vaccination patterns on the reduced PCCP and mortality

	Type A (Full Speed pattern)	Type B (Fluctuating pattern)	Type C (Striving pattern)
Number of countries	3	13	17
Average PCCP	54.42	13.43	33.30
Average mortality	6.40	2.06	7.25

Table 5. Effects of vaccination patterns on improving PCCP and mortality

	source	SS	d.f.	MS	F	P-value
PCCP	between	5316.33	2	2658.17	3.95	0.0300
	within	20181.43	30	672.71		
	total	25497.76	32			
mortality	between	204.24	2	102.12	3.86	0.0323
	within	794.40	30	26.48		
	total	998.64	32			

Table 6. Result of pairwise comparison for PCCP between the baseline and each level of

vaccination rates

	Average	Variance	no. of ob.	t statistics	p-value
baseline	34.34	622.37	33		
L1	28.43	525.62	33	1.5430	0.1327
L2	27.79	601.25	33	1.4311	0.1621
L3	34.49	797.83	33	1.6939	0.9792
L4	25.48	404.98	33	1.8181	0.0784*
L5	15.28	813.04	33	2.8303	0.0080***
L6	6.95	86.99	33	5.5746	0.0000***

Table 7. Result of pairwise comparison for mortality between the baseline and each level of

CVRs

	Average	Variance	no. of ob.	t statistics	p-value
Baseline	6.00	29.50	33		
L1	5.97	30.48	33	0.0343	0.9729
L2	3.69	11.82	33	3.0272	0.0048
L3	4.03	27.06	33	2.1506	0.0392
L4	3.98	27.60	33	2.6097	0.0137
L5	1.78	3.80	33	4.6656	0.0001
L6	0.87	1.83	33	5.2741	0.0000

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Author contribution

Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing, others, who have contributed in other ways should be listed as contributors.

Yi-Tui Chen designed the study, collected the data, analyzed the data and wrote the paper

Signature (a scanned signature is acceptable, but each author must sign)

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