Feasibility of COVID-19 control from a pandemic to endemic

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Article

Keywords: Pandemic, Endemic, Transition, Model

Posted Date: February 8th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1283643/v1>

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Abstract

Evaluations of the pandemic to endemic phase are a great concern, especially in Zero-COVID-19 countries. Herein, we developed a mathematical model to simulate future scenarios for the variants of concern (VOCs) in the condition of several immune barriers and controlling measures. The results demonstrated that the Omicron variant would lead to 592.0 (mean $\pm$ standard deviation (SD): 433.9–750.0) million symptomatic, 24.3 (mean $\pm$ SD: 17.4–312.8) million hospital admission, 9.6 (mean $\pm$ SD: 7.0–12.3) million ICU admission, and 5.4 (mean $\pm$ SD: 3.7–7.5) million death cases after simulation with 1,000 days. At the endemic phase, there were nearly 500 death cases per day attributed to reinfection (66% [range: 62–70%]), infection from birth (18% [range: 16–21%]), and infection from migration (16% [range: 14–17%]). Actively treating more than 80% of cases could effectively reduce disease severity and death rates. It is feasible to transmit pandemic to endemic with Omicron variant and other milder VOCs. We recommend that the successful transition strategy is to improve medical resource allocation and enhance the prevention and control capabilities of health agencies.

Introduction

The continuous transmission of SARS-CoV-2 has led to a global pandemic for nearly two years. As of January 7, 2022, 296.50 million confirmed cases and 5.46 million deaths have been reported worldwide.¹ The waves of outbreak have experienced many peaks in countries such as America, Israel, and Germany², despite most of these countries having more than 60% of their populations fully vaccinated³. While these countries have tolerated the existence of the virus, they have faced a problem regarding how to transition from a pandemic to an endemic state. Currently, countries with zero infection, such as China, face an uncertain epidemic scenario and the possibility of a pandemic after reopening their borders. A study indicated that the pandemic will be ended with the high transmission of Omicron.⁴ However, it might be another scenario while Zero-COVID-19 countries re-opening the border. Thus, it is necessary to predict epidemic scenarios and explore how to effectively transition from pandemic to endemic.

The transition is affected by several factors, such as the transmissibility and severity of the virus, government intervention, the population's increased susceptibility, and some meteorological factors. The continuous mutation of SARS-CoV-2, seen by the increased severity of the Delta variant and increased transmissibility of the Omicron variant,⁵ leads to a more challenging transition. Moreover, the Omicron variant has a reinfection risk more than five times that of Delta,⁶ causing the recent sharp rise in reported cases across most countries.² Regarding potential interventions, the World Health Organization published some guidance for the global response to COVID-19, including infection prevention and control, travel advice, risk communication, and community engagement, among other methods.⁷ Furthermore, previous studies have found that the COVID-19 pandemic may exhibit seasonal features^{8–10}. Overall, these factors lead to more challenges in successfully achieving an endemic state. The endemic phase ultimately depends on susceptible individuals arising from birth, immigration, and the waning of immunity in

previously immune individuals.¹¹ However, the influence of these three factors has not been quantified in the endemic phase.

Currently, many dynamic models, such as susceptible-infectious-recovered/removed, susceptible-exposed-infectious-recovered/removed, and susceptible-exposed-symptomatic-asymptomatic-recovered/removed (SEIAR) are used to quantify virus transmission, predict time-trends, and evaluate and optimize interventions.^{12–14} However, most of these models have been adapted to analyze outbreaks but do not consider natural population growth and population migration. Although one study predicted the transition from pandemic to endemic¹¹, scenarios could not be built to reflect real-world situations. Therefore, this study aims to predict pandemic-to-endemic transition scenarios in a country with a large population and find appropriate strategies to effectively complete this transition.

Results

Pandemic scenario

The COVID-19 pandemic scenario found that two peaks would occur during the transition from pandemic to endemic according to the transmission pattern of the Delta variant, with 80–90% of the population expected to be covered by the vaccine. The second peak would be formed owing to the loss of vaccine effectiveness. In the next three years, there are expected to be a cumulative 690.2 (mean $\pm$ standard deviation (SD): 418.5–755.1) million asymptomatic individuals, 586.8 (537.4–843.0) million symptomatic cases, 24.8 (mean $\pm$ SD: 17.0–324.3) million hospital admissions, 9.6 (mean $\pm$ SD: 6.7–12.2) million ICU admissions, and 5.3 (mean $\pm$ SD: 3.6–7.1) million deaths (Fig. 2). Among the above processes, reinfection would result in a much higher proportion of cases than natural changes in population variation and population mobility, regardless of infection, hospital admission, ICU admission, and death.

The second epidemic peak disappeared due to poor vaccine effectiveness against the Omicron variant, which differed from the transmission model of the Delta variant. The first peak was slightly higher than the Delta variant, but the final size would essentially be the same. There are expected to be a cumulative of 713.9 (mean $\pm$ SD: 433.9–862.3) million asymptomatic cases, 592.0 (mean $\pm$ SD: 433.9–750.0) million symptomatic cases, 24.3 (mean $\pm$ SD: 17.4–312.8) million hospital admissions, 9.6 (mean $\pm$ SD: 7.0–12.3) million ICU admissions, and 5.4 (mean $\pm$ SD: 3.7–7.5) million deaths (Fig. 3).

However, coronaviruses may still mutate further to either reduce or enhance disease severity and death. The former may reduce the total number of patients admitted to the ICU to 4.7 (mean $\pm$ SD: 3.1–6.2) million, and those dying to 2.6 (mean $\pm$ SD: 1.7–3.6) million (Fig. 4A). The latter may increase the total number of ICU admissions and deaths to 14.2 (mean $\pm$ SD: 10.1–18.3) and 8.0 (mean $\pm$ SD: 5.3–10.8) million, respectively (Fig. 4B).

Endemic scenario

The pandemic would eventually transition to the endemic phase after one or two peaks of the outbreak. In the above phase, seasonal waves with one or two peaks per year were caused by reinfection (approximately 66% [range: 62–70%]), natural changes in the population (18% [range: 16–21%]), and population migration (16% [range: 14–17%]). In addition, the Delta variant would lead to a daily average of 47.8 (range: 31.4–64.2) thousand asymptomatic individuals, 48.5 (mean $\pm$ SD: 26.3–70.7) thousand symptomatic cases, 2,241 (mean $\pm$ SD: 1,201–3,281) hospital admissions, 779 (mean $\pm$ SD: 505–1,053) ICU admissions, and 480 (mean $\pm$ SD: 267–693) deaths (Fig. 5 & Extended Data Fig. 1). The Omicron variant would produce a daily average of 64.2 (mean $\pm$ SD: 41.6–86.9) thousand asymptomatic individuals, 62.6 (mean $\pm$ SD: 47.3–78.0) thousand symptomatic cases, 2,872 (mean $\pm$ SD: 2,000–3,744) hospital admissions, 1,019 (mean $\pm$ SD: 766–1,272) ICU admissions, and 635 (mean $\pm$ SD: 432–838) deaths (Fig. 6 and Extended Data Fig. 2).

Simulation of intervention

Comprehensive strategies would be beneficial to improve the control of future epidemics, especially to deal with the two peaks of the pandemic, as vaccine effectiveness continues to decay. According to the simulation over 1,000 days, pharmacological interventions do not have a large impact on the final size of the pandemic; the immune barrier and antiviral treatment are unlikely to control the infection alone. However, NPIs have a strong effect in reducing infection, with the following most to least effective: wearing a mask, case isolation, and reducing the degree of contact (Fig. 7).

However, the goal of an effective transition should be to reduce the number of severe and fatal cases. It would also not have a significant impact on the final size of hospital and ICU admissions and death, regardless of the ultimate vaccine effectiveness between Omicron and Delta variants. However, universal medication use, with 60% antiviral efficacy, would help to reduce hospital admission rates. It could also help to reduce daily hospital admissions to below 50 cases (Fig. 8), ICU admissions to below 20 cases (Fig. 9), and death to 10 cases (Fig. 10). It was found that the comprehensive effectiveness of NPIs and medication was higher than that between NPIs and vaccines. However, we still recommend medication as an intervention because NPIs cannot restore immunity from recovery after infection.

Sensitivity analysis

We found that neither the vaccinated proportion of the immigrant population nor the proportion of infected individuals affected the final scale of the pandemic but did slightly advance the peak of the outbreak (Extended Data Fig. 3). Furthermore, the model is very sensitive to the parameters of medication and mask use, suggesting that more data should be collected on these parameters (Fig. 9).

Discussion

Most countries with open strategies will eventually transition from a pandemic to an endemic phase. Successful transition requires herd immunity after enduring at least one epidemic peak. Mutation of the

virus, leading to loss of vaccine effectiveness, would have a serious impact on the public in the endemic phase. Active treatment and NPIs should be further applied to reduce disease severity and death, especially at the peak of the pandemic.

Model effectiveness

The VEFIAR model is suitable for modelling the infection process of SARS-CoV-2 because it considers both the infectivity of pre-symptomatic individuals and reinfection. Most parameters of the model are estimated from first-hand data analysis combined with population changes, which could lead to more reliable evidence to support long-term simulation. People who are infected with SARS-CoV-2 are reported to be most contagious within the 1 to 2 days before symptom onset,¹⁵ which is consistent with our results. The time from illness onset to hospitalization is reported to range from 1 to 8 days.^{16,17} We adapted the infectious period in the model to 4 to 6 days. However, the infectious period may be further extended during the pandemic phase. Furthermore, the infection probability from a single contact simulated by different R_0 and contact degrees could be further used in simulation by other types of models, such as the agent-based model.

Predicting epidemics

One study indicated that at least two outbreak peaks would occur during the transition from pandemic to endemic,¹¹ which is similar to our prediction under conditions of low vaccine effectiveness. According to our prediction, the transition will undergo at least two outbreak peaks based on a good vaccine effect, while under a low vaccine effect, only one peak occurs. The second peak was mainly caused by a decline in vaccine effectiveness. Low vaccine effectiveness would account for a large outbreak if some countries with interrupted COVID-19 transmission reopened their borders, especially in East Asia and Pacific regions such as China.^{11,18} In terms of the Omicron variant, the second peak could not be formed or was very low due to immune escape.

We predicted that the peak numbers of hospital admissions, ICU admissions, and fatalities were nearly 5 million, 2 million, and 1 million, respectively. There are more than 800 million medical beds and 600 million hospital beds in China, which can tightly cope with the demands of the pandemic.¹⁹ Additionally, the number of ICU beds was reported to be 3.7 per 100,000 population in 2017 in China.²⁰ Although the number of ICU beds has been increasing in recent years, it is still not enough to cope with the peak of the pandemic (nearly 2 million ICU admissions). The shortage of medical resources may lead to more deaths during the pandemic phase. About 1 million deaths due to illness at peak or 1,000 average deaths per day could not be adequately managed by all countries, including China. Coronavirus mutations could result in a large number of severe and fatal cases. Therefore, it is necessary to implement more interventions against mutations of the coronavirus (such as the Delta and Omicron variants) to reduce severity and death, and to promote the feasibility of controlling the COVID-19 pandemic to the point of an endemic phase after reopening. Furthermore, this study found that controlling imported infections would not affect the final pandemic size but would accelerate the peak of the outbreak from a long-term perspective.

Regardless of intervention, an outbreak will still occur even if all migrated people have vaccine certificates.

In the endemic phase, this study found that the disease burden of COVID-19 could be mainly attributed to reinfection (66% [range: 62–70%]), infection from birth (18% [range: 16–21%]), and infection from migration (16% [range: 14–17%]). However, considering that immigrants may be infected, the possibility of this group becoming susceptible is very low. Therefore, we should focus on reducing newborn infection and reinfection to prevent outbreaks in the endemic phase. In addition, the endemic phase would exhibit seasonal outbreak waves with one or two peaks per year, and a greater number of cases would be caused by the Omicron variant than by Delta. Further studies should explore seasonal characteristics after the pandemic phase.

Pandemic interventions

A successful transition must be based on the immunity of most people after recovery from infection. It is important to control severe and fatal cases to an acceptable level using interventions, including vaccines and medicine, during the transition. Compared with controlling infection, vaccines have been reported to reduce severity and death.²¹ As of December 28, 2021, 85.64% of the population has been fully vaccinated in China.³ Severity and death decreased significantly under high vaccine coverage, but could not cut off viral transmission.²² Several studies have reported that some medicines, such as Paxlovid and Molnupiravir, also have significant effects on reducing disease severity and fatality.^{23,24} Therefore, we suggest that it is necessary to popularize antiviral treatment while continuously strengthening vaccination, which should first be used to control poor disease outcomes.

During the pandemic period, NPIs should be implemented alongside pharmacological interventions, especially in the first and second peaks. NPIs play an important role in delaying the epidemic,^{25,26} but do not affect the final size. To reduce severe and fatal cases during the pandemic, this study proposed the continuous application of NPIs, especially mask-wearing and isolation at a national level. Concerning the effects of medication and masks, our models assumed that medication had a 60% effect for reducing deaths and masks had an 85% effect for controlling infections. This may tend to overestimate the effects of the two interventions. Our results of the sensitivity analysis revealed that these two parameters would introduce uncertainties. Thus, we should collect more first-hand data for real-world analysis in the future. Furthermore, other studies could identify the optimal intervention strategies regarding new variants of SARS-CoV-2 in real-time to strengthen parameters and improve public health benefits.

Limitation

In this study, we just simulated infections and deaths caused by SARs-CoV-2 in the pandemic but did not estimate the more severe disease burden due to lack of medical resources during this period. However, the interventions advocated in this study could effectively reduce severity and death, which may relieve disease burden and medical resource scarcities. Furthermore, a previous study recommends that health managers should focus on high-risk people after re-opening¹⁸. Further studies should quantify the

infectious risk by different groups of age and occupation. Finally, we need to collect most parameters of transmission and death of Omicron to reflect the situation of the real world.

Conclusion

If only protected by vaccination, one or two peaks of the outbreak might appear on the transition from pandemic to endemic after re-opening in a country with zero infection. In the pandemic phase, we should firstly popularize antivirals and vaccines while adapting appropriate NPIs for reducing severe and death cases. In the endemic phase, newborn infection and re-infection should be regarded as a priority.

Declarations

Data availability statement

Data of Hospital and ICU admission, and death cases were collected from Our World in Data (<https://ourworldindata.org/>). Data of Guangzhou City was collected from a published paper (<http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2021.148>). Data of Hunan Province could be obtained by contact: 87616498@qq.com (Kai-wei Luo, China).

Insert code availability statement

The model was performed using Anylogic SD simulation tool, version *Anylogic 8.5.2 Personal* (<https://cloud.anylogic.com/assets/embed/?modelId=1eef307e-795e-4446-b651-5a199b1325ad>).

COMPETING INTEREST DECLARATION

The authors declare no competing interests.

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Methods

Study design

Some countries with zero infection, such as China, might be affected by several factors after reopening (Table 1). First, the transmission rate of the virus (i.e., from new variants such as Omicron), the population's degree of contact, and susceptibility could be associated with the final size and duration of the pandemic phase. Meanwhile, reinfection and natural changes in the population would have a great impact on the endemic phase. Furthermore, both pharmacological and non-pharmacological interventions (NPIs) can impact the above phases. Based on these factors, we adapted the indicators of onset, hospital and ICU admission, and deaths to simulate epidemic scenarios and evaluate intervention after reopening from a national perspective (Fig. 11).

Model development

We divided the total population into two groups, non-vaccinated and vaccinated, which were described as subscripts 0 and 1, respectively. All simulations of the transition from pandemic to endemic were performed using a vaccinated-exposed-presymptomatic-symptomatic-asymptomatic-recovered/removed (VEFIAR) model (Extended Data Fig. 4). We have added a new compartment (pre-symptomatic) according to the previous susceptible-exposed-symptomatic-asymptomatic-recovered/removed (SEIAR)

model^{14,27,28} and considered the changes in population and reinfection with the virus. The equation of the VEFIAR model is shown in the Supplementary files. The following assumptions should be added to the model:

1. Susceptibility always exists in newborns, and the birth rate is defined as br . All compartments had immigration, and the immigration rate was m . We also considered emigration and natural death in the population; the emigration and death rates were n and d , respectively.
2. Infectivity would arise before symptoms, and this state was described as pre-symptomatic. Vaccinated people are infected by contact with three kinds of people, including pre-symptomatic, symptomatic, or asymptomatic infections. We assumed that the transmissibility of pre-symptomatic and asymptomatic individuals was k and k' times that of symptomatic individuals.
3. We assumed that symptomatic people would be admitted to the hospital and ICU, as well as experience death caused by illness. The proportions of the above were h , u , and d , respectively.
4. The recovered/removed people would be re-infected by contact with the three kinds of infected individuals. The reinfection rate was l .

Furthermore, according to our previous study, the effects of the vaccine played a role in reducing infectivity and susceptibility.¹⁴ The reduction in susceptibility and infectivity were expressed as $1 - x$ and $1 - y$, respectively.

Parameter estimation

The parameters c and q were defined as the contact degree and infection probability from a single contact, respectively. The vaccine and non-vaccine groups were modelled with the same contact degree but different infection probabilities from a single contact. Considering that the contact degree in the epidemic might be lower than the outbreak, we simulated the contact degree from 7 to 11 in the model. Meanwhile, the parameter q was estimated using an outbreak VEFIAR model without considering population changes. The basic reproduction number (R_0) of COVID-19 has always been estimated to be between 4 and 8, especially when applied to the high transmission of the Delta variant.²⁹⁻³¹ We considered that the contact degree in the outbreak (estimated from 10 to 15) might be higher than that in the epidemic. Then, we adapted the next-generation matrix (NGM) method combined with the Monte Carlo method to estimate parameter q (Extended Data Fig. 5). According to the simulation, we finally set q from 0.08 to 0.09 in the epidemic model. The equation for calculating R_0 by NGM (Supplementary files) is as follows:

$$R_0 = \beta \left(\frac{\kappa' \omega (1 - p)}{\omega'' (\omega - \omega p + \omega' p)} + \frac{\kappa \omega' p}{\gamma' (\omega - \omega p + \omega' p)} + \frac{\omega (1 - p)}{(d + \gamma) (\omega - \omega p + \omega' p)} \right)$$

Parameters of natural history included k , k' , p , w , w' , w'' , g , g' and l , and are defined in Table 2. Moreover, 31% (95% confidence interval [CI]: 26%–37%) of the asymptomatic infection was summarized by a

review.³² In the model, we assumed that the proportion of asymptomatic individuals among the vaccinated population was twice that of the unvaccinated population. The possibility of contact with an infected individual in the asymptomatic population was reported to be 0.35 (95% CI: 0.10–1.27) times that of the symptomatic population. Conversely, the possibility of contact with an infected individual among the pre-symptomatic population was 0.63 (95% CI: 0.18–2.26) times that of the symptomatic population.³² Considering that transmission of the virus was lower in asymptomatic and pre-symptomatic individuals than in symptomatic individuals, we simulated k and K in the model to range from 0.1 to 1.0 and 0.18 to 1.00, respectively.

To analyze the model parameters w , w' , w'' , g , and g' , we considered COVID-19 data Guangzhou City recorded between May 11 and June 17, 2021, and from Hunan Province recorded between July 22 and August 15, 2021. We assumed that w and w' were equal in the model. The mean values of parameters w and w' were calculated to be 3 and 2 days, respectively (Extended Data Fig. 6). We simulated parameters w and w' to range from 2 to 5 by a gamma distribution with a shape of 1.00 and a rate of 0.92 in the model (Extended Data Fig. 7). Parameter w'' ranged from 1 to 8 and was estimated by a gamma distribution with a shape of 2.09 and a rate of 0.43. Furthermore, we adapted the general linear model (GLM) to fit the parameter g in Guangzhou City (Extended Data Fig. 8). Because the infectious period was shortened after the intervention, we set it from 4 to 6 according to the early period of the outbreak. We assumed that symptomatic and asymptomatic individuals experienced the same length of time between exposure and being removed/recovered. Meanwhile, asymptomatic people might have a longer infectious period, even more than 10 days, because they are not easily identified.³³ Therefore, the parameter g' was set from 5 to 11 days.

Public data from the United Kingdom, Israel, and Chile from March 1, 2020 to November 22, 2021, were used to analyze the hospital admission rate, intensive care unit (ICU) admission rate, and fatality rate before and after vaccination.³ We compared data from December 13, 2020 to February 14, 2021, and from September 19, 2021 to November 22, 2021. We observed that the median hospital admission rate, ICU admission rate, and fatality rate values were reduced from 6.08% (range: 3.77%–9.02%) to 2.62% (range: 3.77%–9.02%), from 2.19% (2.02%–2.52%) to 1.61% (1.42%–1.85%), and from 1.54% (0.67%–2.11%) to 0.64% (0.38%–0.89%), respectively (Extended Data Fig. 9). Estimation of hospital admissions, ICU admissions, and fatality rates are shown in the Supplementary files.

A previous study reported a reduction in vaccine efficacy over a period of months.²¹ Therefore, we adapted the logistic model to fit the data to reduce the vaccine efficacy proportion, as seen in the Supplementary files (Extended Data Fig. 10). Several studies have reported a vaccine efficacy of 60%–80% for controlling the transmission of the Delta variant.^{34,35} However, the vaccine is weakly effective in controlling the infection of Omicron.⁵ In the VEFIAR model, we assumed that a vaccine efficacy of 60%–90% was needed for controlling the Delta variant, and of 30%–40% for controlling the Omicron variant. We assumed that 80–90% of people would be vaccinated before the pandemic.

One study indicated that 1.3% of the South African population would experience one reinfection.³⁶ The reinfection rate showed a downward trend as the wave progressed. Therefore, we extended the reinfection rate from 0.9% to 1.5% for model simulation.

The demographic parameters included natural and migration changes. The total population was set to 1.4 billion, and the birth and death rates were sourced from the Statistical Yearbook in 2021. We assumed that the number of people involved in immigration and emigration was 30000 per day. Meanwhile, we assumed that 60% of the immigrated population was vaccinated, and 50% of the immigrated population was infected.

Prediction scenarios

We divided the epidemic into two phases, pandemic and endemic, and assumed that one or two seasonal peaks might exist per year. The parameter β , adjusted for seasonality by a sine function, is shown in the Supplementary files.

Markov Chain Monte Carlo (MCMC) was used to simulate the two scenarios of the Delta and Omicron variants. Furthermore, we simulated two scenarios for the future uncertainty of virus mutations, including enhancing and lessening hospital admission and disease severity.

Intervention simulation

We simulated potential pharmacological interventions and NPIs to successfully transition from a pandemic to an endemic (Table 3). Some studies have reported that medical treatment is effective in reducing 60% (30%–90%) of hospital admissions, cases of severe disease, and fatalities.^{23,37} Meanwhile, we assumed that medicine would reduce parameters h , u , and d and shorten the infectious period by 1.5 (0–3) days. In the model, we simulated the proportion of patients taking medicine from 10% to 100%, and vaccine efficacy from 30% to 90%, respectively.

We simulated the contact degree reduced from 5 to 13 in the model to evaluate the effects of increasing social distance. A study reported that mask wearing was very effective (66%–93%) in controlling infection.²⁷ In the model, we considered that mask use played a role in reducing the infection probability from a single contact (q) and simulated that the proportion of mask use was between 10% to 100%. Because there exists a competitive relationship among death, removal, and isolation, we estimated the isolation proportion (q') as 10% to 100%; the calculated the equation is shown in the Supplementary files.

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Tables

Table 1 Conditions of impact factors from pandemic to endemic in the model.

Purpose	Factors	Detail		Condition
Simulated the scenarios form pandemic to endemic	Virus	Infectivity		Estimated by the infection probability from a single contact which was calculated by the range of the basic reproduction number (R_0).
		New variants		Simulating two scenarios including Delta and Omicron variants based on different values of initial VE.
		Reinfection		Assuming recovery/removed person will be re-infected after contact infections with infectivity.
	Host	Contact degree		Each person can contact numbers of people per day, and they are possible to be infected after contact cases.
		Natural changes of population		All newly born people and a proportion of migrated people are susceptible.
		Migrated population		
		Immune barrier		Assuming initial VE for reducing infection will eventually be formed and decayed by a Logistic model. Considering the vaccine effects for reducing severity and death.
		Natural history		Every infected person will experience the process from exposed to asymptomatic/pre-symptomatic/symptomatic to removed/recovered, and some of recovered people will be re-infected. First-hand data and references are used to estimate relevant parameters.
	Interventions	Non-pharmacological	Mask wearing	Simulated by reducing the infection probability from a single contact.
			Isolation	Simulated by isolated a proportion of new cases without any infectivity.
			Social distance	Simulated by reducing the contact degree.
		Pharmacological	Antivirals	Simulated by reducing the hospital and ICU admission, fatality rate, and shortening infectious period.
			Vaccine	Simulated by increasing initial values of VE.
Others	Seasonality	One peak	Adjusted the transmission rate by a	

		Two peak	sine function and simulated the peak of outbreak by changing the period and phase.
Outcomes	Infection	Asymptomatic number	Predicted the epidemic scenarios and estimated the final size.
		Symptomatic number	
	Severity	Hospital admission number	
		ICU admission number	
		Fatality number	

Table 2 Source and value of parameters in the VEFIAR model.

Parameters	Description	Value		Source	Method
		Non-vaccinated	Vaccinated		
-	R_0	5 (4, 6)	-	Assumption	-
c	Contact degree	8 (7, 11)	8 (7, 11)	Reference	MCMC
q	Infection probability from a single contact	0.085 (0.08, 0.09)	0.085 (0.08, 0.09)	Simulation	MCMC
k	Relative transmission rate from asymptomatic to symptomatic	0.35 (0.1, 1)	0.35 (0.1, 1)	Reference	MCMC
k'	Relative transmission rate from pre-symptomatic to symptomatic	0.63 (0.18, 1)	0.63 (0.18, 1)	Reference	MCMC
p	Asymptomatic proportion	0.31 (0.26, 0.37)	0.62 (0.52, 0.74)	Reference	MCMC
ω	Days from exposed to pre-symptomatic	3 (2, 5)	3 (2, 5)	Data analysis	MCMC
ω'	Days from exposed to asymptomatic	3 (2, 5)	3 (2, 5)	Data analysis	MCMC
ω''	Days from pre-symptomatic to symptomatic	2 (1, 8)	2 (1, 8)	Data analysis	MCMC
γ'	Days from asymptomatic to removed	7 (5, 11)	7 (5, 11)	Assumption	MCMC
γ	Days from symptomatic to removed	5 (4, 6)	5 (4, 6)	Data analysis	MCMC
h	Hospital rate	0.0608 (0.0377, 0.0902)	0.0262 (0.0218, 0.0347)	Data analysis	MCMC
u	ICU rate	0.0219 (0.0202, 0.0252)	0.0161 (0.0142, 0.0185)	Data analysis	MCMC
d	Fatality rate	0.0154 (0.0067, 0.0211)	0.0064 (0.0038, 0.0089)	Data analysis	MCMC
λ	Reinfection relative rate	0.012 (0.009, 0.015)	0.012 (0.009, 0.015)	Reference	MCMC
x	Relative susceptibility	1	$\frac{1}{\text{VE}}$	Reference	-
y	Relative infectivity	1	$\frac{1}{\text{VE}}$	Reference	-

-	Coverage with fully vaccination	0.15 (0.1, 0.2)	0.85 (0.8, 0.9)	Assumption	MCMC
-	VE	-	0.7 (0.6, 0.9)	Assumption	MCMC
<i>br</i>	Birth rate	0.000023	0	Statistical Year Book	-
<i>dr</i>	Death rate	0.000019	0.000019	Statistical Year Book	-
<i>m</i>	Imported rate	0.0000214	0.0000214	Assumption	-
<i>n</i>	Exported rate	0.0000214	0.0000214	Assumption	-
-	Vaccinated proportion in imported population	0.6	0.6	Assumption	Sensitive analysis
-	Infected proportion in imported population	0.5	0.5	Assumption	Sensitive analysis

- means not applicable

Table 3 Simulation the interventions in the model.

Description	Value
Mask effect for reducing infection	0.85 (0.66, 0.93)
Proportion of wearing mask	0.1, 0.2, ... 1
Reduction contact degree	13,12, ...5
Isolation proportion	0.1, 0.2, ... 1
Initial VE	0.3, ...0.9
Medicine for reducing hospital/severity/death	0.6 (0.3, 0.9)
Medicine for reducing infectious period	1.5 (0, 3)
Proportion of taking mask	0.1, 0.2, ... 1

Figures

Figure 1

Scenario of predicting Delta variant after 1,000 days in pandemic phase. Scenarios of Delta is predicted according to initial VE (60%-90%) was reduced by Logistic model per day. Each curve and its shaded area represent Mean and Mean $\pm$ SD simulated by MCMC

Figure 2

Scenario of predicting Omicron variant after 1,000 days in pandemic phase. Scenarios of Omicron is predicted according to initial VE (30%-60%) is reduced by Logistic model per day. Each curve and its shaded area represent Mean and Mean $\pm$ SD simulated by MCMC

Figure 3

Scenario of predicting new variants after 1,000 days in pandemic phase in a condition of low VE. Plot A shows scenarios at low initial VE (30%-60%), virus mutation may double hospital admission rate, ICU admission rate, and fatality rate. Plot B shows scenarios at high initial VE (60%-90%), virus mutation may half hospital admission rate, ICU admission rate, and fatality rate

Figure 4

Scenario of predicting Delta variant after 1,000 days with one peak per year in endemic phase. Plot A and C represent the predicted epidemic curve, and B and D represent the average number of cases per day. Each curve and its shaded area represent Mean and Mean $\pm$ SD simulated by MCMC

Figure 5

Scenario of predicting Omicron variant after 1,000 days with one peak per year in endemic phase. Plot A and C represent the predicted epidemic curve, and B and D represent the average number of cases per day. Each curve and its shaded area represent Mean and Mean $\pm$ SD simulated by MCMC

Figure 6

Effects of simulated pharmaceutical and non-pharmaceutical interventions on cumulative symptomatic cases after 1,000 days. Three plots above simulated NPIs combined with different initial VE values based on reduction function (Logistic model). Three plots below simulated NPIs combined with treatment by a scenario of Delta variant

Figure 7

Effects of simulated pharmaceutical and non-pharmaceutical interventions on cumulative hospital admission cases after 1,000 days. Three plots above simulated NPIs combined with different initial VE values based on reduction function (Logistic model). Three plots below simulated NPIs combined with treatment by a scenario of Delta variant

Figure 8

Effects of simulated pharmaceutical and non-pharmaceutical interventions on cumulative ICU admission cases after 1,000 days. Three plots above simulated NPIs combined with different initial VE values based on reduction function (Logistic model). Three plots below simulated NPIs combined with treatment by a scenario of Delta variant

Figure 9

Effects of simulated pharmaceutical and non-pharmaceutical interventions on cumulative fatality cases after 1,000 days. Three plots above simulated NPIs combined with different initial VE values based on reduction function (Logistic model). Three plots below simulated NPIs combined with treatment by a scenario of Delta variant

Figure 10

Sensitivity analysis of mask and medicine effects. Bar and error bar represent Mean and Mean $\pm$ SD simulated by MCMC, respectively

Figure 11

Study design of simulation from pandemic to endemic. The impact factors of transition from pandemic to endemic were summarized for build scenarios to simulate this transition, and the light yellow, and light blue arrows represent the strength of this effect, respectively. Scenarios of Delta and Omicron variants were simulated in the model, respectively. We further simulated the seasonality of waves and uncertainty of scenarios, and propose an optimal transition strategy by comprehensive interventions. Indicators of onset, hospital and ICU admission, and death were used to quantify the transmission and severity.

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